Enhancement of the Neuronal Dynamic Range by Proper Intensities of Channel Noise [*]

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The capability of a biological neuron to discriminate the intensity of external stimulus is measured in its dynamic range. In previous studies, a few factors have been reported to be able to enhance the dynamic range, e.g., electrical coupling and active dendrites. Here we numerically show that intrinsic channel noise within neurons has a subtle effect in neuronal dynamic range modulation. Our simulation results indicate that for relatively weak noise intensity, the dynamic range of the neuron is enhanced significantly. However, as the noise intensity becomes stronger, the dynamic range of the neuron is weakened. Further investigation suggests that sodium channel noise and potassium channel noise play opposite roles in modulating the dynamic range. Consequently, the model results suggest a new function of channel noise, that is, a proper value of noise intensity could optimize the dynamic range of neurons.

The dynamic range characterizes the capacity of a system to discriminate the intensity of an external stimulus. Such ability is important for living beings, in which it has close relations with the avoidance of danger. Thus, larger dynamic range signifies greater probability of survival.[1] In neuronal systems, a number of factors have been reported to play vital roles in modulating the dynamic range of neurons. Using a computational network model of mammalian retina, Publio *et al.*[2] have found that gap junctions between rod-rod, together with proper values of rod I_h conductance, have crucial impacts on the enhancement of the dynamic range of the retina. Gollo *et al.*[3] have conducted a theoretical investigation of a model neuron with complex morphology on which the enhancement of the dynamic range is the primary performance of active dendritic conductance. They further predicted that neurons with larger dendritic trees would exhibit higher levels of dynamic range, while the abolishment of these active dendritic conductances would lead to a reduction in neuronal dynamic range. By means of cortex slice cultures grown on planar microelectrode arrays, some researchers have demonstrated that cortical networks that generate neuronal avalanches correspond to a maximized dynamic range.[4]

The electrical signals in neuronal membranes are largely determined by their intrinsic voltage-gated ion channels. Because the opening and closing of these channels have long been considered to be stochastic in nature, the biophysical mechanisms underlying the neuronal excitability are thus noisy.[5] Previous research has shown that channel noise has many functional roles in modulating neuronal activities, such as inducing spontaneous spiking activity,[6] spike timing variability,[7−9] irregular firings,[10,11] peri-threshold oscillations,[12] neuronal synchronization,[13,14] stochastic resonance and coherence resonance,[15,16] and spatiotemporal activity patterns of networks.[17]

In this Letter, we investigate the issue of whether channel noise has some impact in modulating the dynamic range of spiking neurons. With the aid of computer simulation and the stochastic Hodgkin–Huxley (HH) model, we demonstrate that the dynamic range of the model neuron changes with the variation of noise intensity. Numerical results indicate that a maximal dynamic range is achieved when the noise intensity is relatively weak, while for stronger noise intensities, the neuronal dynamic range is lower compared with the case under weak noises.

For generality, the stochastic HH model is employed to investigate the basic firing properties of neurons. During the last two decades, the conventional HH model neuron as well as its extensions has been recognized to be good enough for studying the dynamical firing behavior of neurons.[6,7,18−20] Neuronal membrane dynamics are described by the equations[21]

$$C_m \frac{dV_m}{dt} = -g_{Na}m^3h(V_m - V_{Na}) - g_K n^4(V_m - V_K)$$
$$- g_L(V_m - V_L) + I, \tag{1}$$

$$\frac{dx}{dt} = \alpha_x(1-x) - \beta_x x + \sigma\xi_x(t), \quad (x = m, n, h) \tag{2}$$

where V_m is the membrane potential, $C_m = 1\,\mu\text{F}/\text{cm}^2$ is the membrane capacitance, and I is the external stimulus; $g_{Na} = 120\,\text{mS}/\text{cm}^2$, $g_K = 36\,\text{mS}/\text{cm}^2$ and $g_L = 0.3\,\text{mS}/\text{cm}^2$ denote the maximal conductance of sodium, potassium and leakage, respectively. $V_{Na} = 50\,\text{mV}$, $V_K = -77\,\text{mV}$ and $V_L = -54.4\,\text{mV}$ are the re-

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versal potentials, respectively; m and h represent the activation and inactivation gating variables for sodium channel, and n represents the activation gating variable for potassium channel. Other expressions are as follows: $\alpha_\mathrm{m} = 0.1(V_\mathrm{m}+40)/[1-\exp(-(V_\mathrm{m}+40)/10)]$, $\beta_\mathrm{m} = 4\exp[-(V_\mathrm{m}+65)/18]$, $\alpha_\mathrm{n} = 0.01(V_\mathrm{m}+55)/[1-\exp(-(V_\mathrm{m}+55)/10)]$, $\beta_\mathrm{n} = 0.125\exp[-(V_\mathrm{m}+65)/80]$, $\alpha_\mathrm{h} = 0.07\exp[-(V_\mathrm{m}+65)/20]$, $\beta_\mathrm{h} = 1/[1+\exp(-(V_\mathrm{m}+35)/10)]$.

The effect of channel noise is introduced by adding a noise term on the variation of gating variables (see ξ_x in Eq. (2)). Here σ characterizes the relative noise intensity, larger value of σ indicates larger effect of channel noise. Similar to the previous studies, in which the noise input applied to neuronal systems was usually adopted the Gaussian white noise,[22−24] ξ_x in Eq. (2) is also generated by Gaussian processes with zero mean and the following convariance function.[6,7,24,25]

$$\langle\xi_x(t_1)\xi_x(t_2)\rangle = \frac{\alpha_x(1-x)+\beta_x x}{N_\mathrm{Na}}\delta(t_1-t_2), \quad (x=m,h) \tag{3}$$

$$\langle\xi_x(t_1)\xi_x(t_2)\rangle = \frac{\alpha_x(1-x)+\beta_x x}{N_\mathrm{K}}\delta(t_1-t_2), \quad (x=n) \tag{4}$$

where δ is the Dirac delta function, N_Na and N_K represent the total number of sodium and potassium channels respectively on a given membrane area. We choose $N_\mathrm{Na} = \rho_\mathrm{Na}S$ and $N_\mathrm{K} = \rho_\mathrm{K}S$, here $\rho_\mathrm{Na} = 60\,\mu\mathrm{m}^{-2}$ and $\rho_\mathrm{K} = 18\,\mu\mathrm{m}^{-2}$ are the channel densities of sodium and potassium, respectively.[18,25] S means the total membrane area, and its value is $10\,\mu\mathrm{m}^2$.

The dynamic range is a quantitative measure in characterizing the ability of a system to discriminate the intensity of external inputs. It is calculated by taking the logarithm of the difference between large (10% below the maximum) and small (10% above the minimum) levels of sensation produced by stimulus as follows.

Before the calculation, we should obtain the stimulus-frequency curve. Usually the curve can be approximately fitted by the classical power law function,[26−28]

$$F = aI^b, \tag{5}$$

where F is the firing frequency (spikes per second), I is the stimulus intensity, a and b $(0 < b < 1)$ are constants.

The dynamic range Δ of the model neuron is calculated by[2,3]

$$\Delta = 10\log\left(\frac{I_{90}}{I_{10}}\right), \tag{6}$$

where I_{10} and I_{90} denote, respectively, the stimulus intensities for which the firing frequency of the model neuron is 10% above the minimum and 10% below the maximum.

Simulations are performed by using the MATLAB software, and the fourth-order Runge–Kutta algorithm is employed to calculate the values of the four first-order equations (1) and (2) with integration step of 0.01 ms.

Firstly, we compare the firing behavior of the model neuron with and without channel noise. The simulation results are demonstrated in Fig. 1. In the absence of noise ($\sigma = 0$), the model neuron fires periodically with a high degree of regularity. However, when the noise is applied ($\sigma = 5$), interspike intervals of the neuron become very irregular. Such a kind of channel-noise-induced irregularity in neuronal spike trains has been previously reported in many studies.[10,25]
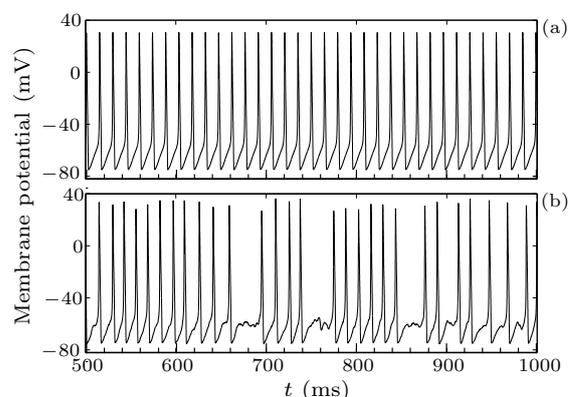

Fig. 1. Membrane potential of the model neuron with and without channel noise: (a) $\sigma = 0$, (b) $\sigma = 5$.
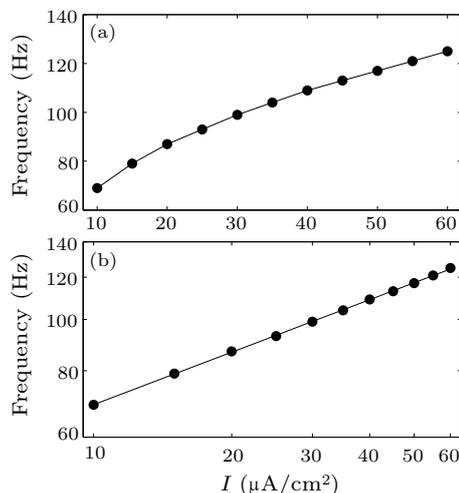

Fig. 2. Firing frequency of the model neuron as a function of external stimulus strength: (a) linear-linear scale, (b) logarithmic-logarithmic scale.

We then investigate the dynamic range of the neuron in the absence of noise. In Fig. 2(a), the relation between stimulus and frequency is illustrated, where data points could be well fitted by the classical power law function. In Fig. 2(b), the logarithmic-logarithmic plot of stimulus-frequency curve is well fitted by a straight line, with $a = 32.36$ and $b = 0.33$, and the corresponding dynamic range is 11.96 dB.

Next, the impact of channel noise on neuronal dynamic range is considered. The intensity of channel noise is changed by varying the value of parameter σ. As shown in Fig. 3, the logarithmic-logarithmic plots of the stimulus-frequency curve could always be fitted by straight lines when noise intensity varies from 1 to 10, while with different slopes and intercepts; and meanwhile, the larger the intensity of noise, the larger the standard deviation. In Fig. 4(a), the values of neu-

ronal dynamic range corresponding to these noise intensities are shown. It is obvious that a maximal value of neuronal dynamic range is obtained when the noise intensity is relatively weak (σ is around 2 in our simulation). However, the values of neuronal dynamic range are decreased under high levels of noise intensity. This result may indicate that channel noise with proper intensities has potential effect in the enhancement of neuronal dynamic range.
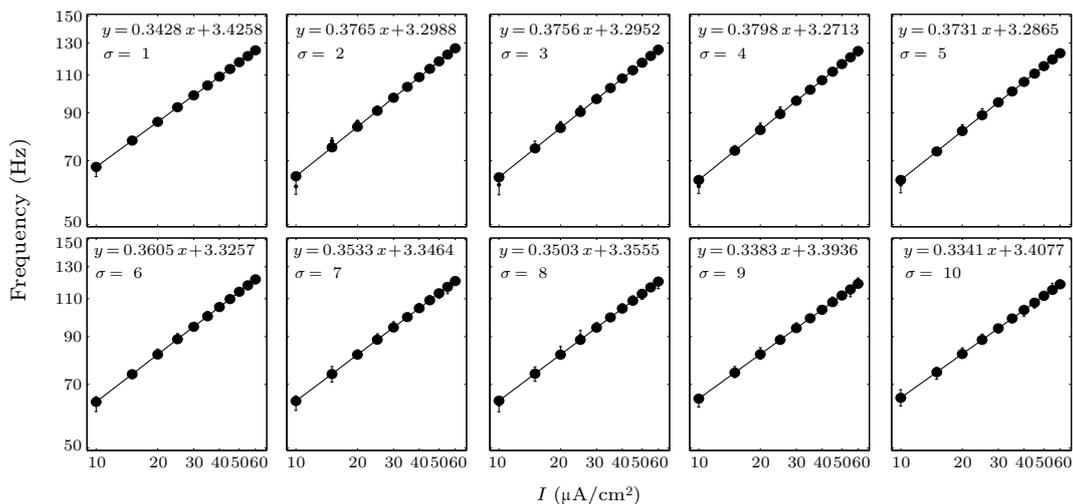

Fig. 3. Logarithmic-logarithmic plots of the relationship between stimulus and frequency under different noise intensities. Points in the figure are the average values for 20 repetitions, and with their corresponding standard deviation.
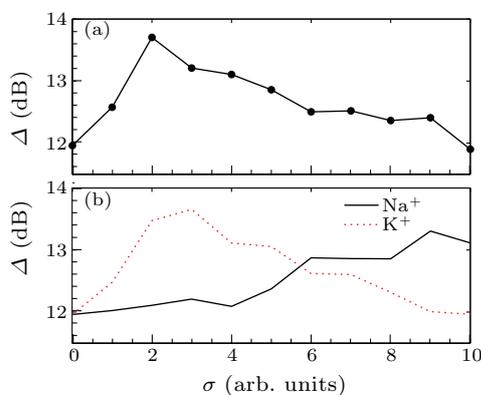

Fig. 4. Variation of neuronal dynamic range induced by channel noise in the cases when sodium and potassium channel noises vary (a) simultaneously and (b) separately.

As in the HH model, there are two main kinds of ion channels: inward sodium channel and outward potassium channel. To investigate how these two ion channels contribute to the modulation of neuronal dynamic range, we separately vary noise intensity in one channel, and keep the other unchanged. Simulation results presented in Fig. 4(b) can definitely show that sodium channel noise and potassium channel noise play opposite roles in modulating the dynamic range of neurons. The main reason for this distinction may be associated with the corresponding action of these two ion channels in the generation of neuronal spikes. Generally speaking, sodium current is responsible for

the uptrend of action potential, while potassium current is responsible for the downtrend of action potential. From Fig. 4(b) we can also observe that the variation trace induced by the potassium channel noise is quite similar to the case when both noise intensities in the sodium channel and potassium channel changed simultaneously (Fig. 4(a)). This may imply that the modulation of neuronal dynamic range by channel noise is probably due to the noise intensity variation of the outward ion channels. However, this speculation still needs to be examined by experiments.
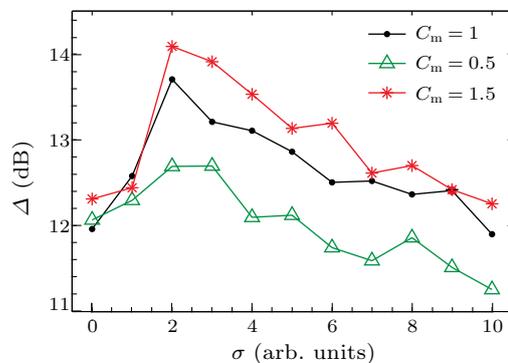

Fig. 5. Variation of neuronal dynamic range induced by channel noise under different membrane capacitances.

Finally, we analyze the influence of membrane capacitance on the variation of neuronal dynamic range,

since a previous report has shown that the fluctuations of membrane capacitance can result in the reduction of channel noise in neurons.[18] We consider two cases, i.e., the $C_{\rm m}$ decreases ($C_{\rm m} = 0.5$) and the $C_{\rm m}$ increases ($C_{\rm m} = 1.5$) while the other parameters are unchanged. The results shown in Fig. 5 illustrate that variation in the amplitude of neuronal dynamic range with respect to noise intensity is weakened when $C_{\rm m}$ is decreased. Although the dynamic range still shows an upward tendency under relatively weak noise intensities, the relative increment is reduced. While the increase of $C_{\rm m}$ exerts little effect on the amplitude of this variation. Thus, we conclude that the decrement of $C_{\rm m}$ may reduce the effect, of which the dynamic range of neurons could be optimized by a proper intensity of channel noise.

A previous report has indicated that the intrinsic channel fluctuation could modulate the signal detection ability of an array of neurons,[16] in particular, proper intensities of channel noise could promote the neurons to encode more information from a given stimulus. However, in our results we suggest that proper intensities of channel noise could also enable a single neuron to encode a larger range of stimulus.

In summary, we have performed a numerical study of the influence of channel noise on the variation of neuronal dynamic range. Using the stochastic HH model neuron as a basis, we show that dynamic range of the neuron varies with the change of channel noise intensity. For channel noise with relatively small intensity, neuronal dynamic range is increased, while for large noise intensity, neuronal dynamic range is weakened. Thus, we conclude that there exists an optimal noise intensity under which the value of neuronal dynamic range can be maximized, and this result also demonstrates a new role of channel noise in modulating the dynamical firing behavior of neurons. Meanwhile, our further study reveals that sodium channel noise and potassium channel noise play opposite roles in modulating the dynamic range. Finally, we show that the variation of membrane capacitance ($C_{\rm m}$) may influence this noise-induced enhancement of neuronal dynamic range. When $C_{\rm m}$ is decreased, the dynamic range induced by channel noise is reduced; while the increment of $C_{\rm m}$ has little impact on the increase of neuronal dynamic range.

It should be noted that we have only investigated the influence of channel noise on the variation of dynamic range in a single model neuron, and ignored the synaptic connections with many other neurons. However, neurons are organized in networks to function, thus future investigations can analyze the variation of neuronal dynamic range in neuronal networks.

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