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Effects of the Number of Ion Channels on Information Transmission in a Population of Hodgkin-Huxley Neuron Models with Random Ion Channel Gating: Intrinsic Supra-threshold Stochastic Resonance

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Abstract. This paper presents an influence of the number of ion channels on information transmission when a filtered Poisson process of supra-threshold stimuli is presented to a population of stochastic Hodgkin-Huxley neuron models. It was shown through computer simulations that as the number of ion channels (patch size) of model neurons was decreased, a variation of spike firing times in response to the filtered Poisson process was increased, and eventually, spontaneous spike firings were observed in a smaller number of ion channels. It was found that the mutual information of population spike firing rates increased, reached a maximum, and then decreased as the number of ion channels in model neurons decreased, i.e., a stochastic resonance phenomenon.The typical curve of stochastic resonance was better observed as the number of model neurons was increased. It is suggested that stochastic ion channel gating plays an important role in information transmission in a population of neurons with ``an intrinsic supra-threshold stochastic resonance''.

Keywords: Ion Channel Current Fluctuations, Stochastic Hodgkin-Huxley Model, Supra-threshold Stochastic Resonance, Information Rates, Filtered Poisson Process, Neural Encoding

1. Introduction

Stochastic resonance (SR) is a phenomenon that involves coupling between deterministic and random dynamics in non-linear systems [Gammaitoni et al., 1998]. This phenomenon can be interpreted as an improved detection of sub-threshold stimuli when the noise level in the nonlinear system increases. Supra-threshold stochastic resonance (SSR) refers to a phenomenon what an optimally added noise can enhance information transmission when a supra-threshold stimulus is driven into an array of non-linear systems possessing threshold values [Stocks, 2000]. The fluctuation or noise in neurons has been considered to come up from not only randomness of synaptic vesicle secretions (extrinsic fluctuations) but also stochasticity of ion channel gating (intrinsic fluctuations). Some review articles are found in the literature [Destexhe et al., 2003; Stein et al., 2005; Faisal et al., 2008; McDonnell and Ward, 2011].

However, it has been unclear if and how the SSR could be observed due to randomness of ion channel gating itself (intrinsic fluctuations) in a population of stochastic Hodgkin-Huxley models. In the present paper an intrinsic SSR due to random ion channel gating is investigated through computer simulations when a filtered Poisson process of supra-threshold stimuli is applied to a population of stochastic Hodgkin-Huxley models. Of particular interests are to see if random ion channel gating can enhance information transmission with SSR, and to see how the number of ion channels (patch size) can maximize information transmission.

In this paper, SSR is evaluated using the mutual information of population spike firing rates as the patch size of neuron models varies from 100 to 700 μm^2 in which the stochastic Hodgkin-Huxley neuron model consists of stochastic sodium channels with 60 channels/μm^2 as well as stochastic potassium channels with 18 channels/μm^2. The mutual information is estimated in which the number of neuron models is varied ranging from 1 to 50, and when the intensity of filtered Poisson processes is set at 10 Hz.

2. Material and Methods

2.1. Preliminaries

In this paper, the Hodgkin-Huxley model [Hodgkin and Huxley, 1952] with stochastic ion channel models is used in order to investigate the influence of the number of ion channels on the mutual information. Stochastic ion channels can be modeled well as continuous-time discrete-state Markov processes (Markov Jump Processes) [Neher, 1977; Colquhoun, 1977].

The transmembrane potential $V_m^{[k]}(t)$ of the k-th neuron ($k=1, 2, ..., N; N$, the number of neurons) is described as a function of time by:

$$C\frac{dV_m^{[k]}(t)}{dt} + g_{Na}\frac{N_{Na}^{[k]}(t)}{N_{Na}^{\max}}(V_m^{[k]}(t) - E_{Na}) + g_K\frac{N_K^{[k]}(t)}{N_K^{\max}}(V_m^{[k]}(t) - E_K) + g_L(V_m^{[k]}(t) - E_L) = I_{stim}(t) \quad (1)$$

where C=1 μF/cm^2, g_{Na}=120 mS/cm^2, N_{Na}^{max}=60 channels/μm^2 × patch size, E_{Na}=50 mV, g_K=36 mS/cm^2, N_K^{max}=18 channels/μ m^2 × patch size, E_K=-77 mV, g_L=0.3 mS/cm^2, E_L=-54.4 mV, the resting potential was set at -65 mV. The transition rates were set at those described in Appendix. Other parameters were adopted from [Hodgkin and Huxley, 1952]. $N_{Na}^{[k]}(t)$ and $N_K^{[k]}(t)$ stand for the number of sodium and potassium channels activated at time t in the k-th neuron under consideration, and they were calculated by the channel number tracking algorithm [Mino et al., 2002]. $I_{stim}(t)$ denotes the stimulus current representing the filtered Poisson process. In this algorithms, the number of sodium channels activated, $N_{Na}^{[k]}(t)$, and the number of potassium channels activated, $N_K^{[k]}(t)$, play a key role in introducing its stochasticity into the transmembrane potentials.

2.2. Simulation procedures

The filtered Poisson process of supra-threshold stimuli, $I_{stim}(t)$, was applied into an array of 50 stochastic Hodgkin-Huxley (HH) neuron models:

$$I_{stim}(t) = \int_{-\infty}^{t} h(\tau)dN_s(t-\tau) \quad (2)$$

in which the intensity, λ, of the counting process $N_s(t)$ was adopted as 10 Hz. The impulse response function of $h(t)$ was expressed as:

$$h(t) = \begin{cases} a_s & (0 \le t < \tau_\omega) \\ 0 & \text{(otherwise)} \end{cases} \quad (3)$$

where the pulse width τ_w was set at 1 ms, and the amplitude a_s was set at 10 nA / μm^2 so that $I_{stim}(t)$'s can be a supra-threshold pulsatile stimulus. The transmembrane potentials $V_m^{[k]}(t)$ were generated in 1 s time length by numerically solving Eq. 1 with the Euler method at a sampling step of 5 μs. The spike firing times in a population of neuron models were determined by finding the peak amplitude of the action potentials in transmembrane potentials to generate the output spike trains $s^{[k]}(t)$. Each output spike train taking a value of zero or one was gathered like post-stimulus time histograms and moving-averaged with a triangle window of the 5 points widths for calculating the population spike firing rate, $r(t)$:

$$r(t) = \frac{1}{w_{bin}}\frac{1}{N}\sum_{k=1}^{N} s^{[k]}(t) \quad (4)$$

where in practical situations $r(t)$'s were discretized with a bin width of 10 ms, w_{bin}.

Ten kinds of input realizations were applied repeatedly ten times to a population of neuron models in order to estimate the total and noise entropies of the spike firing rate for calculating mutual information, $I_m(I_{stim},r)$:

$$I_m(I_{stim}(t),r) = H_{total}(r) - H_{noise}(r|I_{stim}(t))$$

(5)

where

$$H_{total}(r) = -\sum_{i=0}^{\infty} p(r_i)\log_2 p(r_i)$$

(6)

and

$$H_{noise}(r|\ I_{stim}(t)) = -E[\sum_{i=0}^{\infty} p(r_i|I_{stim}(t))\log_2 p(r_i|I_{stim}(t))]$$

(7)

where $p(r_i)$, $p(r_i|I_{stim}(t))$ denote the probability and the conditional probability of the spike firing rate discretized with a bin width of 5 Hz, $r_i(t)$. E[ ] stands for the expectation operation. In practical situations, E[ ] was performed by taking an ensemble average of ten sample realizations.

The patch size was set at 100, 200, ..., or 700 μm^2 in order to investigate a dependency of the patch size on mutual information.

Computer simulations were performed on an IBM compatible PC with an Intel Core 2 Quad Q9650 CPU. The computer codes were written in JAVA, while the graphics were depicted with MATLAB.

3. Results

It was shown [Chow and White, 1996; Schmid and Haggi, 2007] that the stochastic Hodgkin-Huxley model can create a large variation of spike firing times (i.e., jitter), and then generate spontaneous spike firings as the patch size decreases (i.e., a smaller number of ion channels), while it may approach asymptotically to the deterministic regular Hodgkin-Huxley model as the patch size gets close to infinity.

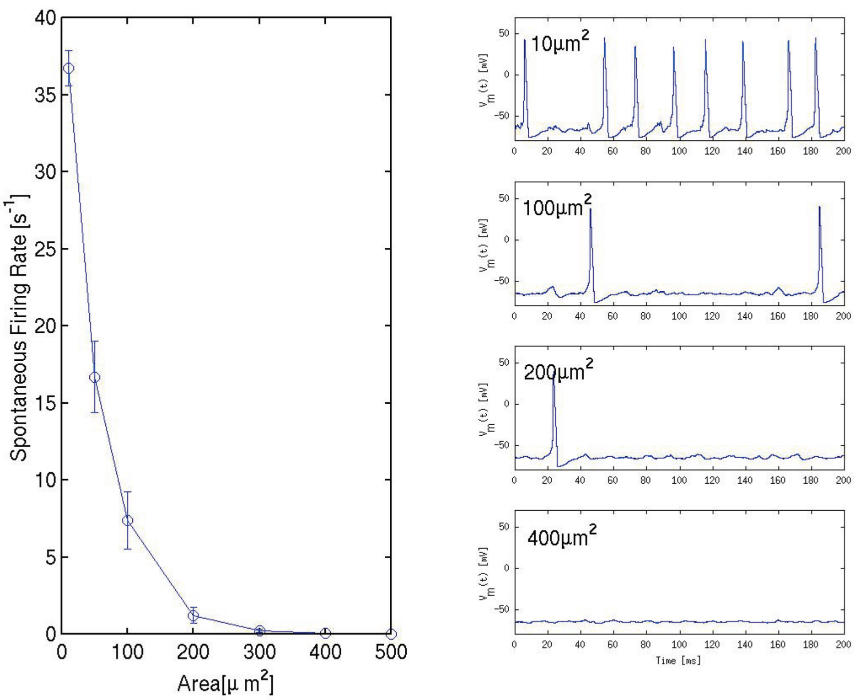

***Figure 1** Spontaneous spike firing rate as a function of patch size. Spontaneous firing rate with mean (circle) and standard deviation (bar) calculated from ten samples decreases as the patch size increases (left column). The transmembrane potentials $V_m(t)$ as a function of time are plotted as an illustrative example for various patch areas of 10 (right top), 100 (right 2nd row), 200 (right 3rd row), and 400 μm^2 (right bottom). Note that fluctuations of $V_m(t)$ between spikes are observed due to stochastic gating of the sodium channels: the*

fluctuations tended to decrease as the patch size increases, since increasing the number of sodium channels makes it more deterministic.

Figure 1 shows spontaneous spike firing rate as a function of patch size. Spontaneous firing rate with mean (circle) and standard deviation (bar) calculated from ten samples decreases as the patch size increases (left column). Spontaneous firing rate tended to disappear when the patch size was greater than 500 μm^2. The transmembrane potentials $V_m(t)$ as a function of time are plotted as an illustrative example for various patch areas of 10 (right top), 100 (right 2nd row), 200 (right 3rd row), and 400 μm^2 (right bottom). Note that fluctuations of the transmembrane potentials between spikes are observed due to stochastic gating of the sodium channels: the fluctuations tended to decrease as the patch size increases, since increasing the number of sodium channels makes it more deterministic.

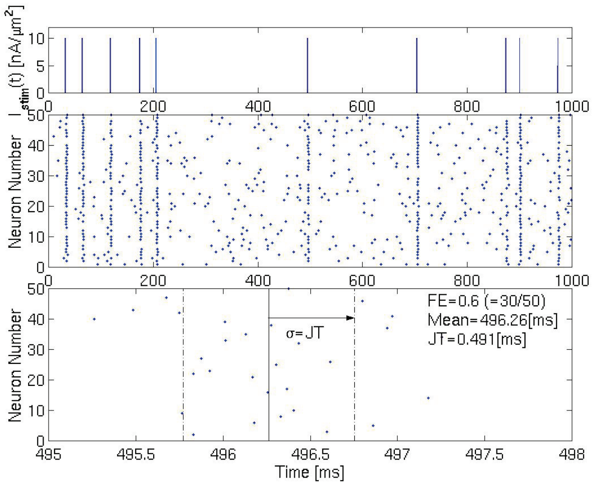

Figure 2 *Raster plots of spikes for 50 neurons (middle) in response to the pulsatile stimulating current $I_{stim}(t)$ with a duration of 1 ms and an amplitude of 10 [nA/μm^2] (top) at a patch area of 100 [μm^2]. Expanded raster plots (495-498 [ms]) are drawn (bottom) where the mean and jitter (σ=JT) of spike firing times and the firing efficiency (FE) are calculated to be 496.26 [ms], 0.491 [ms], and 0.6.*

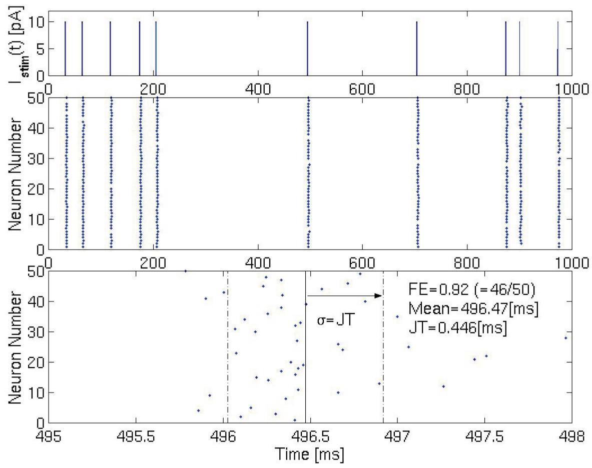

Figure 3 *Raster plots of spikes (middle) in response to $I_{stim}(t)$ (top) at a patch area of 500 [μm^2]. Expanded raster plots (495-498 [ms]) with a mean, jitter, and FE being estimated as 496.47 [ms], 0.446 [ms], and 0.92.*

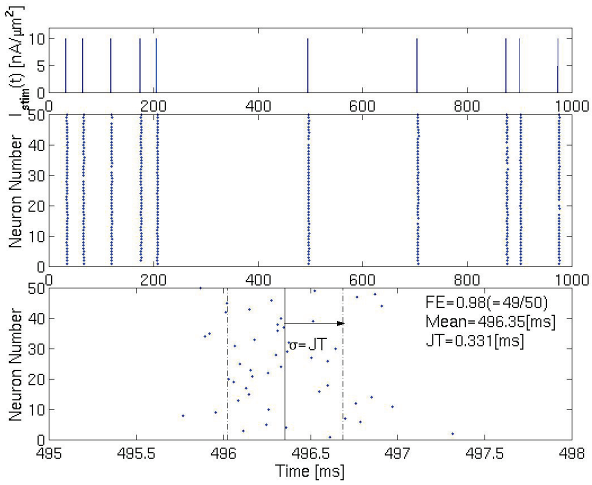

Figure 4 *Raster plots of spikes (middle) in response to $I_{stim}(t)$ (top) at a patch area of 700 [μm²].Expanded raster plots (495-498 [ms]) with a mean, jitter, and FE being estimated as 496.35 [ms], 0.331 [ms], and 0.98.*

The dot raster plots of spike firings for 50 neurons are shown in Figures 2-4. Figure 2 depicts raster plots of spikes for 50 neurons (middle) in response to the pulsatile stimulating current $I_{stim}(t)$ with a duration of 1 ms and an amplitude of 10 nA/μm² (top) at a patch size of 100 μm². The temporally expanded raster plots (495-498 ms) are drawn (bottom) where the mean and standard deviation (jitter) (σ=JT) of spike firing times and the firing efficiency (FE) are calculated to be 496.26 ms, 0.491 ms, and 0.6. The firing efficiency is defined by the number of spike firings, divided by the number of stimuli applied. Figures 3 and 4 show those data at a patch size of 500 μ m² and of 700 μm². The temporally expanded raster plots (495-498 ms) are drawn with a mean, jitter, and FE being estimated as 496.47 ms, 0.446 ms, and 0.92 for 500 μm² (bottom in Fig.3), and as 496.35 ms, 0.331 ms, and 0.98. for 700 μm² (bottom in Fig.4), respectively.

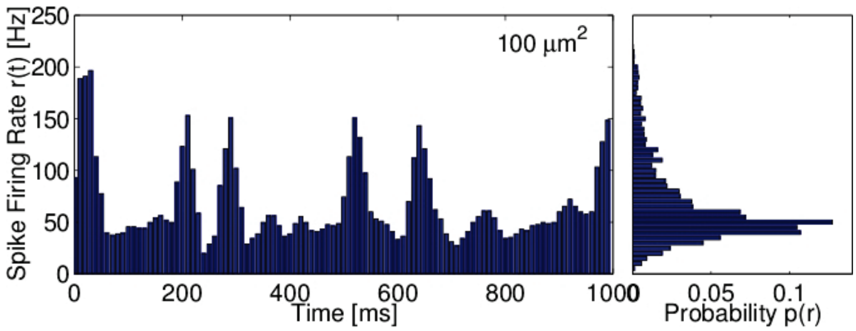

Figure 5 *Spike firing rate [Hz] as a function of time (left) and histogram of spike firing rate (right) at a patch area of 100 [μm²]. These are used for estimating the total and noise entropies to calculate the mutual information.*

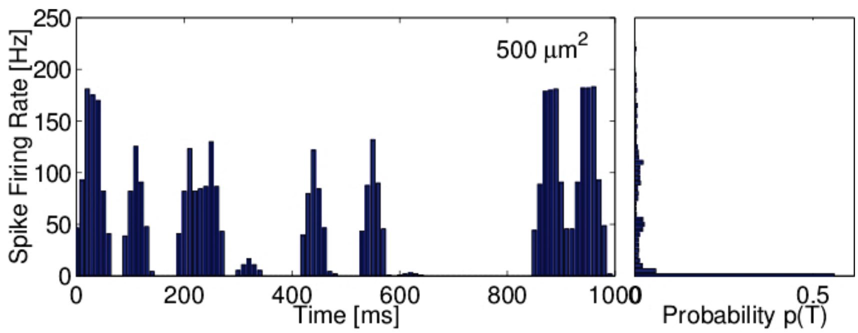

Figure 6 *Spike firing rate as a function of time (left) and histogram of spike firing rate (right) at a patch area of 500 [μ m²]***.**

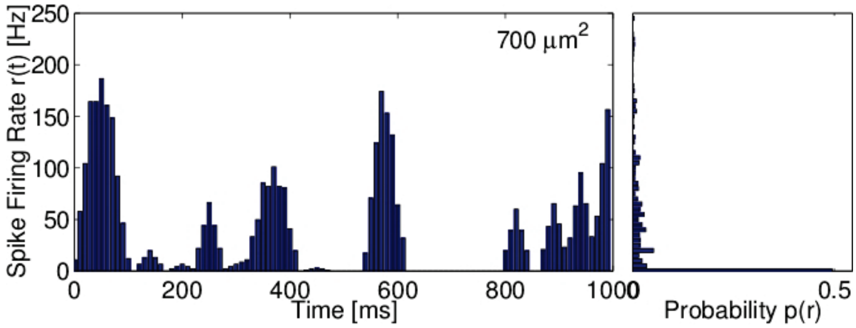

Figure 7 *Spike firing rate as a function of time (left) and histogram of spike firing rate (right) at a patch area of 700 [μm^2].*

The population spike firing rate in Hz as a function of time (left) and histogram of population spike firing rate (right) are depicted at a patch size of 100 μm^2 in Fig.5, of 500 μm^2 in Fig. 6, and of 700 μm^2 in Fig. 7. The spike firing rate with a constant value means an activity of spontaneous spike firings, like that at patch size of 100 μm^2 in Fig. 5. It also follows from those histograms that the mean value of the spike firing rates decreases as the patch size increases, indicating a decrease in spontaneous spike firings. The histograms of the spike firing rates, *p(r)*, were used for estimating the total and noise entropies to calculate the mutual information according to Eq. 5.

The mutual information in bits is depicted as a function of patch size for *N*=50, 20, 5, and 1 in which λ = 10 Hz with error bars calculated from three samples, as shown in Fig. 8.The mutual information increases, reaches a maximum value, and then decreases as the patch size increases. This implies that the mutual information is maximized at an optimal number of ion channels (patch size) with intrinsic supra-threshold stochastic resonance due to random ion channel gating. SSR was observed remarkably for *N* greater than 20, while it was not clearly shown in *N* smaller than 5.

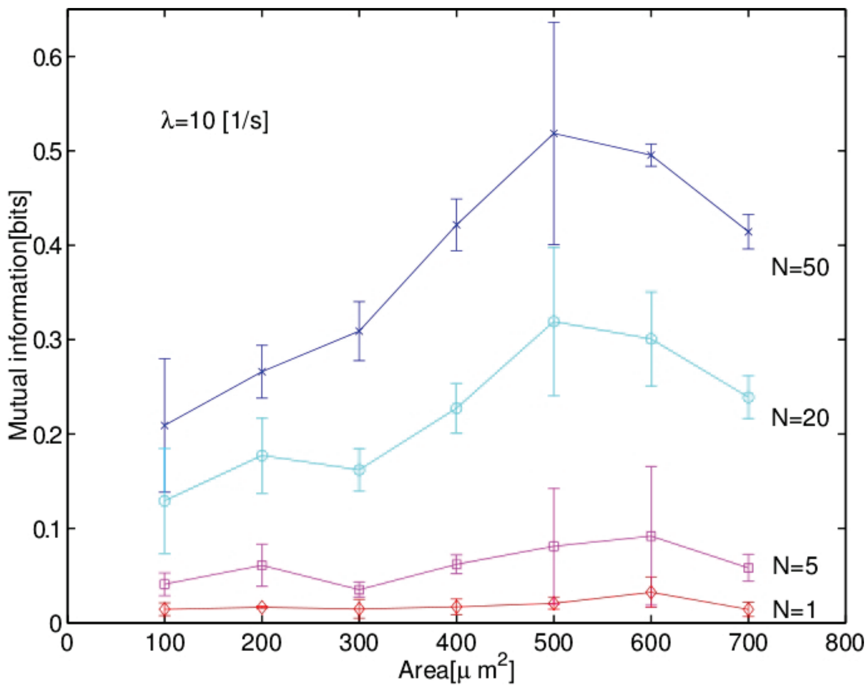

Figure 8 *Mutual information [bits] as a function of patch size for N=50, 20, 5, and 1 in which λ = 10 [Hz] with error bars calculated from three samples.*

4. Discussion

In the present paper, an intrinsic supra-threshold stochastic resonance due to random ion channel gating has been investigated when a filtered Poisson process of supra-threshold stimuli is applied to a population of stochastic Hodgkin-Huxley models. It follows from the results that the mutual information was maximized at an optimal number of ion channels (patch size) in a population of stochastic HH neuron models, and therefore that SSR was observed in the presence of intrinsic fluctuations. It was also shown that the typical curve of stochastic resonance was better observed as the number of model neurons was increased.

As shown in Fig. 1, as the patch size decreased (i.e., the number of ion channels decreased), spontaneous spike firings can be observed as is expected from the literature [Chow and White, 1996; Schmid and Haggi, 2007]. Although the spontaneous spike firings have shown to play a key role in enlarging dynamic range of the sinusoidal signals encoded in the auditory nervous system [Liberman, 1978; Liberman, 1982; Liberman, 1991; Liberman, 1993], in this investigation it may act as a disturbance to encoding the filtered Poisson process of supra-threshold stimuli into individual spike trains in a population of neuron models. The dot raster plots in the middle row of Fig. 2 tells us a noisy encoding due to spontaneous spike firings, so that the information transmission could be expected to be degraded. When the patch size increased (i.e., the number of ion channels increased), randomness of spike firing times got smaller, as shown in the dot raster plots of the middle raw in Fig. 4. These data may verify the fact that stochastic Hodgkin-Huxley neuron models possessing a greater number of random ion channels can asymptotically approach to the deterministic regular Hodgkin-Huxley neuron model. The deterministic model is expected to encode the filtered Poisson process of supra-threshold stimuli into individual spike trains with the same spike firing pattern in a population of neuron models. It is implied, therefore, that there exists an optimal number of ion channels, which enables neuron models not to create spontaneous spike firings and not to generate spike firings without temporal jitter.

In recent years, as many investigators have focused on and paid attention to some different categories of stochastic resonance phenomena [McDonnell and Ward, 2011], an intrinsic supra-threshold stochastic resonance has been reported as one of those publications [Ashida and Kubo, 2010]. However, the situations in that paper [Ashida and Kubo, 2010] were quite different than those adopted in the present paper, since the mutual information presented in this paper was quantified in the case where the stimulus waveform was assumed to be a more biologically realistic filtered Poisson process, rather than a single alpha function stimulus repeatedly presented without temporal dynamics.

5. Conclusions

Taken together, these results shows that an optimum number of ion channels makes it possible to efficiently encode a supra-threshold stimulus being filtered Poisson processes to a population of stochastic Hodgkin-Huxley neuron models with the intrinsic supra-threshold stochastic resonance due to stochastic ion channel gating.

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Appendix

The transition rates of the sodium channels possessing eight discrete states are expressed as:

$$\alpha_m(V_m) = \frac{0.1\,(V_m + 40)}{1 - \mathrm{e}^{-(\mathrm{V_m}+40)/10}}$$

$$\beta_m(V_m) = 4\mathrm{e}^{-(\mathrm{V_m}+65)/18}$$

$$\alpha_h(V_m) = 0.07\mathrm{e}^{-(\mathrm{V_m}+65)/20}$$

$$\beta_h(V_m) = \frac{1}{1 + \mathrm{e}^{-(\mathrm{V_m}+35)/10}}$$

while those of the potassium channels possessing five discrete states are expressed as:

$$\alpha_n(V_m) = \frac{0.01\,(V_m + 55)}{1 - \mathrm{e}^{-(\mathrm{V_m}+55)/10}}$$

$$\beta_n(V_m) = 0.125\mathrm{e}^{-(\mathrm{V_m}+65)/80}$$

in which the transition rates have units of ms^{-1} and the transmembrane potential V_m has units of mV.

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