The Optimal Size of Stochastic Hodgkin-Huxley Neuronal Systems for Maximal Energy Efficiency in Coding of Pulse Signals

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Abstract

The generation and conduction of action potentials represents a fundamental means of communication in the nervous system, and is a metabolically expensive process. In this paper, we investigate the energy efficiency of neural systems in a process of transfer pulse signals with action potentials. By computer simulation of a stochastic version of Hodgkin-Huxley model with detailed description of ion channel random gating, and analytically solve a bistable neuron model that mimic the action potential generation with a particle crossing the barrier of a double well, we find optimal number of ion channels that maximize energy efficiency for a neuron. We also investigate the energy efficiency of neuron population in which input pulse signals are represented with synchronized spikes and read out with a downstream coincidence detector neuron. We find an optimal combination of the number of neurons in neuron population and the number of ion channels in each neuron that maximize the energy efficiency. The energy efficiency depends on the characters of the input signals, e.g., the pulse strength and the inter-pulse intervals. We argue that trade-off between reliability of signal transmission and energy cost may influence the size of the neural systems if energy use is constrained.

Author Summary

Action potentials are the basic way that information is transmitted in the brain. Those electrical 'spikes' also cost a large fraction of metabolic energy in brains. It is believed the neural systems should be evolved to be energy efficient under the pressure of natural selection. The demand for energy efficiency could be large enough to influence the design of the neural system. Since the neural systems are basically stochastic devices, it is interesting to investigate the effects of noise on the energy efficiency of neural systems. In this paper, using computer simulation and analytical methods, we showed that the energy efficiency exhibits maxima corresponding to optimal number of ion channels in the neuron and optimal number of neurons in a pulse signal detection task. Those results indicate that the size of the neural systems may be optimized to transfer information energy efficiently.

Introduction

Neural processing is metabolically expensive [1]. The human brain accounts for about 20% of an adult’s resting metabolic rate. A large fraction of this energy is used for action potential generations, which rely on the potential energy stored in transmembrane ion gradients [2]. Though action potential itself does not consume energy, maintaining this ionic concentration gradients and restoring them after an
action potential requires energy released during ATP hydrolysis to drive ATPase $Na^+ / K^+$ exchangers. These metabolic demands could be large enough to influence the design, function and evolution of brains. Therefore, it is believed that under the pressure of natural selection, the neurons, neural coding and neuronal circuit will be evolved to be energy efficient if metabolic energy is limited.

In the process of action potential generation, the inward $Na^+$ current depolarizes the membrane and generates the upstroke, whereas the outward $K^+$ current repolarizes the membrane and facilitates the downstroke. The overlap of those two ion fluxes would result in an electrically neutral exchange of positive ions, wasting $Na^+$ and accordingly energy. Thus it is suggested minimizing the overlap of those two ion fluxes will improve the energy efficiency for action potential generation. Recent experimental investigation on the nonmyelinated mossy fibers of the rat hippocampus supported this suggestion.

The energy efficiency of the neural system is also dependent on the size of the neuron. For example, one would expect that neurons with small size will be more efficient because less ion channels are involved, thus less ion exchange through ion pump. However, the ion channels are stochastic devices, less number of ion channels in the neurons will lead to larger fluctuations in the transmembrane ion current. This so called “ion channel noise” has been demonstrated not only give variability in the response of neuron to external stimuli, but also cause spontaneous action potentials, and damage the reliability of signal processing. In this case, trade-offs between information transfer and energy use could strongly influence the number of ion channels used by the neurons.

An elegant theoretical analysis, using a simple model for the generation of graded electrical signals by sodium and potassium channels, showed that there exists an optimum number of ion channels that maximize energy efficiency. The optima depend on several factors: the relative magnitudes of the signaling cost (current flow through channels), the fixed cost of maintaining the system, the reliability of the input, additional sources of noise, and the relative costs of upstream and downstream mechanisms. While this is true, as discussed above, instead of graded electrical signal, it is the action potentials that carry the information in the neural systems, and contribute to major cost of energy. Therefore, it is interesting to study the energy efficiency of neurons which code signals digitally with action potentials when ion channel noise is concerned.

Another interesting question is if this trade-offs between information transfer and energy use could influence the size of the neural network. It is well known that the information process in brain is accomplished with a group of neurons working cooperatively, not with only one neuron. Studies have shown that neurons could be synchronized to prevent from noise perturbation and facilitating reliability of information transmission. However, large number of synchronized spikes generated in the neural systems will give a large energy burden on them. In this case, it is possible that the number of neurons in the neural system is optimized to balance the reliability of information transfer and energy cost.

In this paper, we employ analytical and computational methods to calculate the metabolic energy efficiency of single neuron and neuron population performing a pulse-signal detection task in the environment of ion channel noise. A simplified model of a one-dimensional bistable Langevin equation, which mimics the action potential generations with a particle crossing the barrier of a double well, are solved analytically for the pulse signal detection rate and spontaneous firing rate. Based on those results, the energy efficiency of single neuron are investigated. Results show that for the single neuron, there is an optimal number of ion channels corresponding to maximal energy efficiency in detection of pulse signals. The optima depend on the signal properties, e.g., pulse strength, inter-pulse interval. To investigate the energy efficiency of neuron population, the pulse inputs are applied to a group of neurons, the outputs of those neurons are received and read out by a downstream coincidence detector (CD) neuron. In this case, the reliability of detection is enhanced, and there is an optimal combination of the number of neurons and the number of ion channels, with which the energy efficiency is maximized. The optimal number of neurons depends on the threshold of downstream coincidence detector neuron. Those results are confirmed with computer simulation of a stochastic Hodgkin-Huxley (HH) model in which the detailed description of ion channel random gating are considered.
Results

Threshold fluctuation and spontaneous firings

The classic HH neuron model is a deterministic device. Action potentials are caused only when it receives superthreshold stimulus. In reality, ion channel noise could bring substantial effect on the action potential initiation process. It makes the neuron fires in response to subthreshold stimuli, or fail to fire in response to supra-threshold stimuli [19]. To investigate the effect of this so call threshold fluctuation on the signal detection ability of neurons, we applied short (duration 1 ms) current pulse inputs in the stochastic HH model, in which the membrane area $S$ controls the number of ion channels, thus the intensity of ion channel noise. If an action potential is generated immediately (less than 8 ms after current injection), then we say the pulse input is detected by the neuron, as demonstrated in Fig. 1. The pulse detection rate of the neuron is measured as the number of pulse signal being detected over the total number of pulses signal applied. In the absence of ion channel noise, i.e., the membrane area is extremely large, the stochastic HH model is equivalent to the deterministic HH model, which has a rigid threshold. However, if the membrane area is limited, the stochastic HH model shows “softed” threshold in response to signals, as shown in Fig. 2(A). Because the ion channel noise could facilitate threshold crossing of subthreshold signals, thus enable the neuron to detect the subthreshold signals [20,21]. The detection rate is increased as the membrane area is decreased for subthreshold pulses. Meanwhile, ion channel noise sabotages the neuron’s detection ability for superthreshold signals. Therefore, for superthreshold pulses, the detection rate drops as the membrane area is decreased. Whereas for the threshold signals, whose strength is just strong enough to make the neurons fire in the absence of noise, its detection rate is 50%, no matter how large the noise intensity. So for threshold pulses, the detection rate is independent on the membrane area of the neuron.

Beside threshold fluctuation, ion channel noise can also trigger action potentials even in the absence of external input. Fig 2(B) demonstrated the firing rate of spontaneous APs for neurons with different membrane area. It is seen that spontaneous firing rate of action potentials decreases rapidly as the membrane area increases, and when membrane area is larger that 200 $\mu m^2$, the spontaneous firings become very rare.

Mimic the threshold fluctuation and spontaneous firings with bistable model

A comprehensive theoretical and numerical analysis of the HH equations with the inclusion of stochastic channel dynamics was done Chow and White [13]. It is shown that the system can be approximated by a one-dimensional bistable Langevin equation, which describes the dynamics of a particle in a double well potential. Due to this fact, we use the following bistable model to mimic the threshold fluctuation and spontaneous firing of a neuron:

$$\dot{x} = ax - x^3 + n^{-1/2}\Gamma(t),$$

where

$$<\Gamma(t)> = 0; \quad <\Gamma(t)\Gamma(t^{'})> = 2\delta(t-t^{'})$$

$x$ is the position of the particle and analogous to the membrane potential. The model has two minimal at $x_1 = -\sqrt{a}$ and $x_2 = \sqrt{a}$, and a saddle point $x_B = 0$. $n$ is taken here as the number of ion channels of the neuron, and control the intensity of ion channel noise [22]. We take the left minimal of the double well as the resting state of the neuron, and the saddle point as the threshold. The firing of the neuron is then analogous to a particle surmounting the barrier and crossing to the other minimum. We will take advantage of simplicity of this bistable neuron model to have analytical description of its firing probability for pulse signal under ion channel noise perturbation, and spontaneous firing rate.
For the double well model at hand, suppose we have a transient pulse signal $\Delta x$ that push the particle to a position $x$ near the saddle point $x_B$, i.e., $\Delta x = x - x_B$. Following Lecar and Nossal’s approach of linearizing around the threshold \[23\], we can obtain the probability of finding the particle in the right well after an enough long time (see see Models and Methods for details), i.e., the probability that a pulse input signal is detected by the neuron, which is

$$p_c = \frac{1}{2}[1 + erf(\sqrt{an/2}\Delta x)],$$

(3)

where $erf$ is so called error function. It is seen from Fig.2(B) that Eq.3 well described the threshold fluctuation due to ion channel noise observed from SHH model.

This spontaneous firing of action potential can be treated as a classic barrier escape problem with additive thermal noise described by Eq.1. According to Kramers’s formula for escape rate \[24\], the spontaneous action potential firing rate for this double well model is (see Appendix II for detail)

$$p_r = \frac{\sqrt{2a}}{2\pi} e^{-a^2n/4}.$$  

(4)

It is seen from Fig.2(D) that the spontaneous firing rate of APs increases exponentially as the number of ion channels decreasing.

**The Energy Efficiency of Single Neuron**

Let us investigate the energy efficiency of a bistable neuron in a task of detecting transient pulse train that compose $n_{all}$ pulses, with strength $\Delta x$, separated averagely by $\Delta t$. For the bistable neuron at hand, let us suppose the energy cost for neuron with only one ion channel to generate an AP is 1. Then the neuron would generate $n_{all}p_c$ APs for correctly detecting of $n_{all}p_c$ pulses, with the energy cost $nn_{all}p_c$. The neuron also generates $\approx n_{all}\Delta tp_r$ spontaneous APs due to noise perturbation, with energy cost $nn_{all}\Delta tp_r$. Then the efficiency of energy use for the neuron, can be written as

$$Q = \frac{p_c}{n(p_c + \Delta tp_r)}.$$  

(5)

or we can define the energy cost of correctly detecting one pulse signal as

$$T = n(1 + \Delta t\frac{p_r}{p_c}).$$

(6)

Take $a$, $\Delta x$, and $\Delta t$ as parameters and $n$ as a continuous variables, the condition for $T$ as a function of $n$ has a local minimum, i.e., $Q$ has a local maximum is

$$\frac{dT(n)}{dn} = 0, \frac{d^2T(n)}{dn^2} > 0.$$  

(7)

The above problem can be solved easily with numerical method, the results shows that in certain parameter region of $(a, \Delta x\Delta t)$, there is a root $n^*$ for $\frac{dT(n)}{dn} = 0$, at which $\frac{d^2T(n)}{dn^2} |_{n=n^*} > 0$. To shows the results explicitly, we directly calculate energy efficiency $Q$ as a function of $n$ for parameters $a$, $\Delta x$ and $\Delta t$.

As shown in Fig.3(A), as $n$ increases, the energy efficiency increases to reach a maximum and then drops. This resonance of energy efficiency with the number of ion channels, i.e., noise intensity, implies there is an optimal number of ion channels for the neuron that could take the pulse signal detection task most efficiently in the energy consumption.

For the stochastic HH model, a pulse train that compose $n_{all} = 2000$ pulses, with strength $I$ and duration $1 ms$, separated averagely by $\Delta t = 100 ms$, is applied for detectoin. The energy efficiency to
detect this pulse train is defined as the total number of pulse detected by the neuron over the total energy costed in this detection task (see Models and Methods for details). The results confirms that the energy efficiency do have a maximum with proper input pulse interval $\Delta t$, as is seen from Fig. 3(B). It is seen that the energy efficiency exhibits local maximum with membrane area around $180 \mu m^2$. Above this optimal membrane area, the energy efficiency drops as the membrane area increases. Below this optimal membrane area, the energy efficiency drops to a minimum then increase as the membrane area decreases. We argue this resonance of energy efficiency is actually a balance between energy cost and pulse detection capacity. Because large membrane area implies more ion channels are involved, thus more ions need to be restored by the ATP pump after generation of action potentials, to improve energy efficiency, neurons prefer small membrane area. On the other hand, neurons with small membrane area will generate more spontaneous APs in a certain period, which contribute nothing to information transfer but cost energy. Therefore, a minimum in energy cost, thus a maximin in energy efficiency for a optimal membrane area is expected.

The maximal of energy efficiency depends on properties of pulse input

The optimal number of ion channels for maximal energy efficiency is dependent on the properties of the pulse train the neuron is detecting. As is seen from Fig. 3, neurons are tends to detect strong pulse more reliably. Therefore, increasing the pulse input strength, the energy efficiency increases, meanwhile the optimal $n$ will decrease.

The maximal energy efficiency is also dependent on the inter-pulse interval $\Delta t$ (Fig. 4). Because in a large inter-pulse interval, the neuron tends to fire more spontaneous APs, which contributing nothing to signal detection but cost energy. Thus decreasing $\Delta t$ decreases increases the energy efficiency, meanwhile the optimal $n$ decreases. However, if $\Delta t$ is too small, the local maximum would disappear and energy efficiency declines monotonously with the number of ion channels.

The Energy Efficiency of Neuronal Population

The neural system often transmit signals with synchronous spikes, which has been shown that could prevent signals being damaged by noise. The signal information can be reliably read out with the coincidence-detector neuron. Here we use a simple scenario to describe this process and investigate its energy efficiency. As is shown in Fig. 5, a population of neurons receiving the same pulse train input and send their output to a CD neuron. The CD neuron takes outputs from neuron population as the input, and fires only when multiple inputs arrive simultaneously in a short time window $T_w$.

Suppose the CD neuron is excited by $\theta$ or more than $\theta$ inputs from $N$ neurons whose firing probability in response to pulse stimulation is $p_c$, then the detection ability of this neuron population, i.e., the firing probability of CD neuron, is written as

$$P^\theta(\theta, N, p_c) = \sum_{\alpha=\theta}^{N} \binom{N}{\alpha} p_c^\alpha (1-p_c)^{N-\alpha} = 1 - F(\theta, N, p_c)$$

where $p_c^\alpha (1-p_c)^{N-\alpha}$ is the probability that only $\alpha$ neurons fire at the same time, and $\binom{N}{\alpha} = \frac{N!}{\alpha!(N-\alpha)!}$ is the number of ways of picking $\alpha$ neurons from population $N$. So $\sum_{\alpha=\theta}^{N} \binom{N}{\alpha} p_c^\alpha (1-p_c)^{N-\alpha}$ is the total number of ways of selecting $\theta$ or more than $\theta$ neuron out of population $N$. $F(x, p, n) = \sum_{i=0}^{x} \binom{n}{i} p^i (1-p)^{n-i}$ is the binomial cumulative probability function.

We must note that in the the analysis of detection rate of single neuron, we assumed the response time of single neuron to pulse input could be infinitely large. However, in fact the most response happens immediately after pulse input applied. Therefore, we could expect a peak in the post-stimulus time histogram (PSTH) immediately after stimulus, riding on the baseline of spontaneous firing (for an example,
Detection ability enhanced with neuron population

Can detection ability be improved with neuron population? Combining Eq. 3 and Eq. 8 we calculated the detection rate of CD neuron \( P^\theta \) for different size configuration \((n, N)\) of the upstream neuron population, i.e., the number of ion channels in each neuron and the number of neurons in the population. It is seen from Fig. 6 that for different input pulse strength, there is a critical line in \((n,N)\) plane. The reliable detection \( (P^\theta \approx 1) \) is realized in the area on the right of critical lines. As the input pulse strength increases, this critical line moves to the left in the \((n,N)\) plane, which implies the reliable detection could be realized with less neurons in the population. For subthreshold or superthreshold pulse inputs, this critical lines depend on both the number of neurons and the number of ion channels in neurons. For subthreshold pulse input, the more ion channels in neurons, the lower the detection rate of single neuron, thus the more neurons are needed to transmit the input information to CD neurons to make correct detection(Fig. 6(A)). For superthreshold input, the more ion channels in neurons, the higher the detection rate of single neuron, thus the less neurons are needed to reach reliable detection(Fig. 6(E)). However, for threshold pulse input, the critical line is independent of \(n\)(Fig. 6(C)). Because as discussed above, the detection rate of each single neuron is 0.5 for threshold pulse input, independent of the number of ion channels in neurons.

The enhancement of detection rate of CD neuron in the circuit is a consequence of higher firing probability of neurons in response to pulse inputs in a time window \( T_w \) than the spontaneous firings [18]. The CD neuron is more sensible to the nested high rate outputs of upstream neurons in response to pulse stimuli than the randomly outputs of upstream neurons’ spontaneous firing. For upstream neurons with detection rate \( p_c \), if the number of neurons is large enough, the nested firings due to pulse inputs are able to make CD neuron cross its threshold \( \theta \) and read out the information. Meanwhile, the random spontaneous firings from upstream neurons are filtered by CD threshold.

For the simulation of stochastic HH model population, the same pulse train composed by 2000 pulses (duration 1\( ms \)) and separated averagely by 100\( ms \) is applied to each neuron in the population. The output APs of those neurons are converted to a point process in time, and scanned by a sliding window of width \( T_w = 8\( ms \). If \( \theta \) or more than \( \theta \) events are found in the sliding window, the CD neuron is marked with a “firing” at the time the last event in the window happens. Then the window starts to slide again after the last event. The pulses are detected if there are “firing”s in CD neuron that happen less than 8\( ms \) after pulses applied. The detection rate of the CD neuron is calculated as the number of pulses being detected by the CD neuron over total number of pulses applied. Simulation results in Fig. 7 shows same behavior of pulse detection rate depending on the size of the SHH neuron population and the size of each SHH neuron.

Optimal size of the neuron population for energy efficiency

Next, we investigated the energy efficiency when input information is transmitted with a population of neurons and read out by CD neuron. To detect the same pulse train described above, this neuron population will response with \( Nn_{all}p_c \) APs in the population and \( n_{all}P^\theta \) APs of CD neuron. Meanwhile, there will be about \( Nn_{all}p_c\Delta t \) spontaneous APs in the population. Thus the neuron population detect \( n_{all}P^\theta \) pulses with energy cost of \( n(Nn_{all}p_c + Nn_{all}p_c\Delta t) \). Then the energy efficiency of this neuron...
population is
\[ Q = \frac{P(\theta, N, p_c)}{Nn(p_r + p_r \Delta t)}. \] (9)

Combining Eq. 3, Eq. 8, and Eq. 9, we calculated the energy efficiency for the neuron population with different size configuration \((n, N)\). We found that the energy efficiency of the neuron population could be maximized by the number of neurons. Therefore, there is an optimal combination of the number of neurons and the number of ion channels in neurons, with which the energy efficiency of the neuron population is at its maximum (Fig. 6 (B), (D), (F)). It implies the energy efficiency could be optimized not only by the number of the ion channels, but also the number of the neurons. We argue that the optimal number of neurons \(N^*\) is a compromise between reliability of signal detection and the energy cost. As discussed before, with the increasing of the number of neurons, the detection rate of CD neuron increase, which gives an increasing in energy efficiency. However, more neurons will generate more APs due to pulse inputs, or spontaneous firings. As the number of neurons increases, the energy cost increases too, which will decrease the energy efficiency. When \(N\) is large enough to cross the critical lines for reliable detection, the detection rate becomes 1 and no longer depends on \(N\), but the energy cost continue to increase because redundancy of spikes induced by input pulses, and the spontaneous firing spikes.

In the pulse detection process, the energy cost of the neuron population is calculated as the total number of APs generated in the SHH neuron population, multiplied with the membrane area of each neuron, assuming each AP generated in unit membrane area cost one unit energy. Then the energy efficiency is calculated as the detection rate of CD neuron over the energy cost of neuron population. The simulation results shows that the energy efficiency of the stochastic HH neuron population is maximized with optimal combination of the number of ion channels and the number of neurons, as demonstrated in Fig. 6.

Maximal energy efficiency depends on pulse strength and CD threshold

The optimal configuration of \((n, N)\) is dependent on the inter-pulse interval (results not show), input pulse strength, and the coincidence-detector threshold, as is seen from Fig. 9. It is seen that the maximal energy efficiency increases, as the input pulse strength increases, meanwhile the optimal \((n, N)\) configuration moves towards the direction both \(N\) and \(n\) decreases.

We can also find in Fig. 9 that for the same input pulse strength, as the coincidence detector threshold increases, the optimal \((n, N)\) configuration moves towards the direction \(N\) increases, independent of \(n\). Indeed, CD threshold has no effects on the detection rate of upstream neurons, but large CD threshold requires more synchronous spikes induced by the input pulses to make correct detection. We must note that the role of CD neuron in our study is to enhance the detection rate for pulse signals, but it has another role as suppressing the transduction of spontaneous firings. Because spontaneous firings happens randomly in time and has little chance to be synchronized, it will be filtered by the CD neuron [24]. Therefore, although our results point out that the lower CD threshold gives higher energy efficiency, for the purpose of suppressing the spontaneous firings, the CD threshold should be larger than 1.

Discussion

Neural systems employ action potentials to carries input information. The generation and propagation of action potentials are supported by metabolic energy, which is a large burden for animals and is believed to shape the neural system through evolution pressure. Here we investigated the energy efficiency of neural system performing a pulse signal detection task under the perturbation of ion channel noise. We found the energy efficiency exhibits peak values, corresponding to an optimal sizes of the neural system, i.e., number of the ion channels in the neuron, number of neurons in the network.
The optimal size of the neurons for maximal energy efficiency is actually a balance between reliability of signal processing and energy cost, as previously pointed out by Schreiber et al. with linear input-output neurons composed by sodium and potassium channels [15]. In our study, we showed this principle holds if neurons use action potentials to transfer information. Furthermore, we also showed that this principle also holds for neuron population, and the number of neurons is optimized for maximal energy efficiency.

The intrinsic ion channel noise, which is inversely proportional to the number of ion channels, play a double-edged sword role in the signal process of neurons, as well studied in the context of stochastic resonance [26, 27]. In this paper we show that it is also important in the energy efficiency of neurons in signal processing. Ion channel noise helps neurons to detect subthreshold signals, thus improves the energy efficiency. Meanwhile, it damages the reliability of neurons for superthreshold signal detection, and generate spontaneous action potentials, thus decreases the energy efficiency. Form the deduction of detection rate and spontaneous firing rate for the bistable neuron model, we see that the resonance of energy efficiency is a kind of stochastic resonance. For example, the maximal energy efficiency exists if we use other kind of noise, e.g., synaptic noise, which is caused by many independent presynaptic current. So we expect, in general, energy efficiency of single neuron could be maximized for certain level of noise, and the number of neurons in the noisy environment could be optimized for maximal energy efficiency.

In this study, we evaluated the energy efficiency in a simple coding scenario of neural systems, in which the input pulse signals are encoded digitally with the action potentials. We concluded that the neural system size could be optimized for maximal energy efficiency. In a general way, the information conveying ability of neural systems could be measured by information theory formulated by Shannon [28]. Then this rule could be rechecked in this general framework by defining the energy efficiency as the ratio between the amount of transmitted information and the metabolic energy required [29]. The analysis in our work provides a starting point on this direction and can guide further experimental and theoretical work.

**Models and Methods**

**The Stochastic Hodgkin-Huxley model**

According to classic HH model, the current flowing across the giant axon membrane is represented by the sum of the capacitative current and the ionic currents through the corresponding conductive components, which are averaged deterministic terms assuming the numbers of ion channels are large [30]. For limited numbers of ion channels, the total ion conductances for Na$^+$ and K$^+$ should be replaced with the single-channel conductances of potassium and sodium channels, resulting in equivalent circuit demonstrated in Fig. 10(A). The membrane dynamics of the HH equations is then given by

$$C_m \frac{dV}{dt} = -(G_K(V - V_{K^{rev}}) + G_{Na}(V - V_{Na^{rev}})) + G_L(V - V_L) + I,$$

where $V$ is the membrane potential and $I$ the input current. $V_{K^{rev}}$, $V_{Na^{rev}}$, and $V_L$ are the reversal potentials of the potassium, sodium and leakage currents, respectively. $G_K$, $G_{Na}$, and $G_L$ are the corresponding specific ion conductances, and $C_m$ is the specific membrane capacitance. The conductances for potassium and sodium channel are given by

$$G_K(V, t) = \gamma_K[n_4]/S, \quad G_{Na}(V, t) = \gamma_{Na}[m_3h_1]/S,$$

where $\gamma_K$ and $\gamma_{Na}$ are the single-channel conductances of potassium and sodium channels. $[n_4]$ refers to the number of open potassium ion channels and $[m_3h_1]$ refers to the number of open sodium ion channels. $S$ is the membrane area of a neuron. The total number of sodium channels and potassium channels are
given by $\rho_{Na}S$ and $\rho_{K}S$, where $\rho_{Na}$ and $\rho_{K}$ are the densities of sodium and potassium channels. In this work, we use $S$ to control the number of ion channels, thus the ion channel noise intensity.

The gating dynamics of each ion channels are modeled with corresponding Markov process, as demonstrated in Fig. 10(B)) and Fig. 10(C). The $K^+$ channels can exist in five different states and switch between these states according to the voltage dependence of the transition rates, and the channels opens only when it is in $n_4$ state. Similarly, the $Na^+$ channel has eight states, with only one open state $m_3 h_1$.

In each time step, the number of open $K^+$ channels and $Na^+$ channels are determined by stochastic simulation of Markov chain model of those channels, and Eq. 10 is integrated by Euler-forward method with time step 0.01ms. The parameters and rate functions used in the simulation of stochastic HH model are listed in Table S1.

Measure the energy cost of stochastic HH neuron model

Usually, the energy cost of a neuron can be calculated by integrating the sodium current or potassium current over the time, then convert into the number of sodium or potassium ions pumped in and out of the cell. Then energy cost is obtained if the powers the $Na^+/K^+$ pump is measured from experiment(for example, 50 kJ/mol in heart [31]) [9]. However, this method is not efficient when the energy cost of a neuron is estimated in a long time intervals. In fact, the shape of the action potential is stereotyped, and the currents flow in and out of the membrane are described in unit area in the model. So in an action potential generation process, the energy cost in unit area is a constant, independent of input signals. Therefore, in this study, we counted the number of action potentials generated in the whole pulse detection process, then multiplied with the membrane area of the neuron as the measurement of energy cost for this neuron. With this approach, we ignored the energy cost in the subthreshold fluctuation of membrane potential caused by ion channel noise. Because the amplitude of subthreshold fluctuation is very small comparing to the amplitude of action potentials [12], the energy cost of subthreshold fluctuation is trivial comparing to the energy cost of action potentials.

Bistable neuron model and its response function to pulse input

For a neuron subjects to a pulse signal and noise, its dynamics is analogous to a particle in a double well potential with pulse force and noise perturbation, thus could be described with the following equation:

$$\dot{x} = -U'(x) + \Gamma(t)$$

where

$$<\Gamma(t)> = 0; <\Gamma(t)\Gamma(t')>=2D\delta(t-t').$$

$U = -\frac{a}{2}x^2 + \frac{x^4}{4}$ is a double well potential, which has two minimal at $x_1 = -\sqrt{a}$ and $x_2 = \sqrt{a}$ and a saddle point $x_B = 0$. $D$ is noise intensity. Let’s assume that a short duration force moves the particle parallel to the x-axis into the region of the saddle point. After the force is removed, the particle drifts up to the region of the saddle point. Near the saddle point, the phase trajectories are repelled, causing the particle to accelerate away from the saddle- point region towards one of the minimal. Thus we can calculate the probability that, after a long time, the particle is found in the $x > x_B$ domain.

Next we expand Eq. 12 in the neighborhood of the threshold singular point $x_B$. Letting

$$\epsilon = x - x_B$$

and remember $x_B = 0$, we obtain the equation:

$$\dot{\epsilon} = a\epsilon + \Gamma(t)$$
the solution of Eq. (15) has the form
\[ \epsilon(t) = \epsilon(0)e^{at} + \int_0^t e^{a(t-s)}\Gamma(s)ds \] (16)

This integral can be rewritten as:
\[ X(t) = \epsilon(t) - \epsilon(0)e^{at} = \int_0^t e^{a(t-s)}\Gamma(s)ds \] (17)

Since $\Gamma(t)$ is a gaussian random variable. It follows that the time integral $X(t)$ also obey a gaussian distribution. Then we have
\[ P(X, t) = (2\pi < X^2 >)^{-\frac{1}{2}}exp\left(-\frac{-X^2}{2 < X^2 >}\right) \] (18)

where the angular bracket denote an expectation value. The expectation value of of $X^2$ can be expressed in terms of the joint expectation of the variable $\Gamma$ taken with itself at a different time. From Eq. (17) one finds
\[ < X^2 > = \frac{D}{a} (e^{2at} - 1). \] (19)

The probability of the neuron firing after a pulse input is equal to the probability that $\epsilon(t) > 0$ when $t \rightarrow \infty$, given an initial displacement $\epsilon(0)$. Then
\[ P[\epsilon(t) > 0|\epsilon(0)] = \lim_{t \rightarrow \infty} \int_{-\epsilon(0)e^{at}}^{\infty} P(X, t)dX \] (20)

or
\[ P[\epsilon(t) > 0|\epsilon(0)] = \frac{1}{2}[1 + erf\left(\frac{\epsilon(0)}{\sqrt{2D/a}}\right)] \] (21)

where $erf$ is the so-called error function, defined as
\[ erf(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-t^2} dt. \] (22)

The Spontaneous firing rate of bistable neuron model

The spontaneous firing rate of a bistable neuron is considered as the escaping rate of a particle from one well to the other. According to Kramers’s formula, the escaping rate is
\[ K = \frac{1}{2\pi} \sqrt{U''(x_u)U''(x_s)} \exp\left(-\frac{\Delta U}{D}\right), \] (23)

where $\Delta U = U(x_u) - U(x_s)$. $x_u$ and $x_s$ are the position of stable state and the threshold the particle will cross, respectively. $x_u = 0$ and $x_s = -\sqrt{a}$ in our case. Therefore, the escaping rate of a particle in the double well potential is
\[ K' = \frac{\sqrt{2a}}{2\pi} \exp\left(-\frac{a^2}{4D}\right). \] (24)

Supporting Information

Table S1  Parameters and Rate Functions in the Stochastic Hodgkin-Huxley Model.
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Author contributions

Conceived and designed the experiments: LCY. Performed the experiments: LCY LWL. Analyzed the data: LCY LWL. Wrote the paper: LCY.

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Figure 1. Demonstration of membrane potential traces for stochastic HH models receiving pulse inputs. The membrane area of the neuron is 120\(\mu m^2\) in (A) and 240\(\mu m^2\) in (B). Wide gray lines correspond to input pulses with strength \(I = 5 \mu A/cm^2\) and red lines \(I = 8 \mu A/cm^2\). The black triangles mark the time the pulse inputs applied. The black stars mark the APs in response to pulse inputs with strength \(I = 5 \mu A/cm^2\) and red stars \(I = 8 \mu A/cm^2\).
Figure 2. The pulse detection rate and spontaneous firing rate of neurons with ion channel noise. (A) and (B) Simulation results from SHH model. Lines are for guiding the eyes. S is the membrane area. (C) and (D) Analytical solutions of Eq.3 and Eq.4 from bistable model.
Figure 3. The Energy efficiency of a single neuron in the pulse inputs detection task for different pulse strength. (A) Energy efficiency $Q$ as a function of number of ion channels $n$ of bistable neuron model for different input pulse strength $\Delta x$. $a = 1$ and $\Delta t = 100$. (B) Energy efficiency as a function of membrane area of stochastic Hodgkin-Huxley neuron model for different input pulse strength $I$. The inter-pulse interval is 100ms.
Figure 4. The Energy efficiency of a single neuron in the pulse inputs detection task for different inter-pulse interval. (A) Energy efficiency $Q$ as a function of number of ion channels $n$ of bistable neuron model for different inter-pulse interval $\Delta t$. $a = 1$ and $\Delta x = 0.1$. (B) Energy efficiency as a function of membrane area of stochastic Hodgkin-Huxley neuron model for different input pulse strength $I$. The input pulse strength $I = 8\mu A/cm^2$. 
Figure 5. Pulse signal detection scenario for neural systems with neuron population. The front layer is composed with stochastic neuron with ion channel noise (SHH), each of which receives the same pulse train input. CD is coincidence detector neuron with threshold $\theta$, it fires an action potential when $\theta$ or more than $\theta$ front layer SHH neurons fire at the same time.
Figure 6. Signal detection rate and energy efficiency for the bistable neuron population for different input pulse strength. Left column corresponds to the signal detection rate and right column corresponds to the energy efficiency. The top row corresponds to the subthreshold pulse input: $\Delta x = -0.1$; The middle row corresponds to threshold pulse input: $\Delta x = 0$; The bottom row corresponds to suprathreshold pulse input: $\Delta x = 0.1$. In all calculation, parameters are $a = 1$, inter-pulse interval $\Delta t = 100$, the CD threshold is $\theta = 3$. 
Figure 7. The pulse detection rate as a function of membrane area in SHH model and the number of SHH neurons in neuron population. The input pulse strength is $8 \mu A/cm^2$ in (A) and $5 \mu A/cm^2$ in (B). The inter-pulse interval is 100ms. The threshold of CD neuron $\theta = 4$ and the time window for coincidence detection is 8ms.
Figure 8. The energy efficiency as a function of membrane area in SHH model and the number of SHH neurons in neuron population. The input pulse strength is $8\mu A/cm^2$ in (A) and $5\mu A/cm^2$ in (B). The inter-pulse interval is 100ms. The threshold of CD neuron $\theta = 4$ and the time window for coincidence detection is 8ms.
Figure 9. Dependence of the maximal energy efficiency and corresponding optimal neuron population size on CD threshold and input pulse strength. (A) Analytical results for neuron population with bistable model. From right to left, each dashed line corresponds to $\Delta x = 0.1, 0, -0.1$. $\circ$: $\theta = 5$; $\square$: $\theta = 4$; $\nabla$: $\theta = 3$; $\diamond$: $\theta = 2$; $\triangle$: $\theta = 1$. Inter-pulse interval $\Delta t = 100$. (B) Simulation results for neuron network with SHH model. The right line corresponds to $I = 8$ and left $I = 5$. $\circ$: $\theta = 10$; $\square$: $\theta = 8$; $\nabla$: $\theta = 6$; $\diamond$: $\theta = 4$; $\triangle$: $\theta = 2$. The inter-pulse interval is 100 ms.
Figure 10. The scheme of stochastic Hodgkin-Huxley model. (A) Electrical equivalent circuit for the Hodgkin-Huxley Model with consideration of each ion channel conductance. (B) The Markov chain model for potassium channels. Channels are opened when they are in $[n_4]$ state and closed in other states. (C) The Markov chain model for sodium channels. Channels are opened when they are in $[m_3h_1]$ state and closed in other states.