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## Research Article

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# Energy level transition and mode transition in a neuron

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**Abstract:** During continuous diffusion and propagation of intracellular ions, energy transition between electric and magnetic field is proceeded to present appropriate firing patterns. For theoretical neuron models, an equivalent Hamilton energy is derived by Helmholtz theorem. For neural circuits, the Hamilton energy can also be obtained by applying scale transformation on the field energy function. External stimuli injects energy into the neuron, and the energy level transition is induced accompanying with mode transition in the neuronal activity. On the flip side, large external stimuli can induce shape deformation of the cell and possible parameter shift occurs to keep neuron on appropriate energy level in the deterministic neuron models. In this letter, energy function for Hindmarsh-Rose neuron is estimated and a criterion for transition between energy levels and firing modes is defined and explained. It provides possible clues for understanding the dependencies of pattern selection in discharge mode on energy level and adaptive controllability in neurons, and thus the neural activities in neurons and nervous system can be controlled by regulating energy flow.

**Key words:** Hamilton energy; neuron; bifurcation; multiple firing mode; energy level

## 1 Introduction

The activation of neural activities in nervous system depends on complete cooperation of biological neurons, and the collective behaviors are controlled by biophysical properties, local dynamics and external stimuli synchronously [1-4]. The biophysical features of coupled paths and synaptic junctions are crucial for controllability and self-adaption in neurons [5-8]. The electric synapse behaves its function in transient period for fast information processing and energy exchange between neurons [9-12]. Chemical synapse [13-16] regulates the electrical activities in neurons continuously and energy flow is propagated via field coupling [17-20]. The activation and regulation of chemical synapse rely on the neurotransmitter released from presynaptic membranes and then Calcium flow is guided to regulate the action potentials in a neuron and neural network, and electromagnetic field is induced for fast propagation of field energy and keeping stable signal propagation. In particular, the regulation of chemical synapse on neural activities can be approached by creating suitable memristive synapse [21-24].

For most of the generic neuron models [25-28], external stimuli are mapped into equivalent transmembrane current and thus the membrane potential is controlled effectively. That is, external realistic signals can be filtered and encoded before converting these physical, chemical and mechanical signals into electric signals [29-32]. In presence of complex electromagnetic environment, uniform and nonuniform radiation can induce polarization and magnetization of the media, and energy injection enables energy shunting and regulation on inner electric/magnetic field energy, which has

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distinct impact on mode selection in neural activities under electromagnetic radiation [33-36]. Under noisy disturbance, nonlinear resonance including stochastic resonance, coherence resonance [37-40] and logic resonance [41-44] can be induced in many neuron models. In fact, the majority of the neuron models are stimulated to exhibit distinct behaviors but sole firing mode in the neural activities by constant or periodic stimulus [45], which the neuron will show spiking, bursting, chaotic or quiescent state under certain forcing current. Indeed, multi-channel inputs and noisy driving can induce multiple modes of neuronal membrane potential, and the neuron will present a mixed-mode oscillation [46-50]. From physical viewpoint, energy flow plays important role in regulating the firing patterns and thus appropriate energy level can be selected. For neuron equivalent circuits, the internal field energy is converted to an equivalent dimensionless energy function under scale transformation, and this Hamilton energy [51-54] can be obtained by using Helmholtz theorem [55].

For two or more biological neurons, energy balance accounts for the creation and adaptive growth of the synaptic connection [56-60]. That is, energy injection introduces energy diversity and synaptic connections are created for fast energy propagation until reaching energy balance. In this work, external stimulus is applied and energy is injected and accommodated with time, and then parameter shift is induced to guide the neuron step to appropriate energy level accompanying with suitable firing mode in the neural activities. As a result, mode transition occurs and the electrical activities will show multiple firing modes. That is, a criterion for parameter shift dependence on external stimulus is explained in a simple deterministic neuron model. That is, jumping between different energy levels accounts for the occurrence of mixed mode in the electrical activities.

## 2 Model and scheme

For a generic an autonomous dynamical systems

$$\begin{aligned} \frac{dX}{dt} &= F(X) = F_c(X) + F_d(X) \\ &= [J(X) + R(X)] \tilde{\nabla} H(X), X \in R^n \quad (1) \end{aligned}$$

That is, the dynamical system can be replaced by an equivalent vector field, which is considered as a sum of divergence-free vector field  $F_c(X)$  and gradient vector field  $F_d(X)$ .  $H$  represents the dimensionless Hamilton energy, and  $\tilde{\nabla} H$  describes the gradient distribution of generalized force in the phase space.  $J(X)$  meets the symmetric matrix condition for approaching position properties in the physical field.  $R(X)$  requires symmetric principal diagonal matrix satisfying the properties for gradient field. According to Helmholtz theorem [55], the energy function  $H$  is controlled by

$$\begin{cases} \tilde{\nabla} H^T F_d(X) = \frac{dH}{dt}; \\ \tilde{\nabla} H^T F_c(X) = 0; \end{cases} \quad (2)$$

For a generic neural circuit or nonlinear circuit composed of capacitors and inductors, the field energy and its equivalent Hamilton energy are approached by

$$\begin{cases} W = \pm \frac{1}{2} C_1 V_1^2 \pm \frac{1}{2} C_2 V_2^2 + L \pm \frac{1}{2} L_1 i_{L1}^2 \pm \frac{1}{2} L_2 i_{L2}^2 + L; \\ H = \frac{W}{CV_0^2} = \frac{W}{C_1 V_0^2} = \pm a_1 x_1^2 \pm a_2 x_2^2 + L \pm \frac{1}{2b_1} y_1^2 \pm \frac{1}{2b_2} y_2^2 + L; \end{cases} \quad (3)$$

where  $V_1, V_2, \square, i_{L1}, i_{L2}$  represent the output voltages from capacitors and induction currents from the inductor of the nonlinear circuits. The dimensionless variables  $x_1, x_2, \square, y_1, y_2, \square$ , are mapped from the physical variables for voltage and current,  $CV_0^2$  is considered as energy unit for obtaining dimensionless Hamilton energy and  $V_0$  is the intrinsic parameter for the nonlinear resistor in the circuit. For the known HR (Hindmarsh-Rose) neuron model presented by

$$\begin{cases} \dot{x} = y - ax^3 + bx^2 - z + I; \\ \dot{y} = c - dx^2 - y; \\ \dot{z} = r[x(x-1) - z]; \end{cases} \quad (4)$$

where the variables  $(x, y, z)$  represent the membrane potential, recovery variable for slow current and adaptive calcium current, respectively. The parameter  $\lambda$  estimates the resting potential of calcium channel and external stimulus  $I$  can regulate the development of different discharge patterns including bursting, spiking and chaotic states in the electric activities. According to Eq.(1), the HR model is considered in physical field as follows

$$\begin{aligned} \begin{cases} \ddot{x} = \ddot{y} - ax^3 + bx^2 - z + I \\ \ddot{y} = c - dx^2 - y \\ \ddot{z} = r[x(x-1) - z] \end{cases} &= F_c(x, y, z) + F_d(x, y, z) = \begin{cases} \ddot{x} - z \\ \ddot{y} - c - y \\ \ddot{z} - rsx \end{cases} + \begin{cases} \ddot{x} + bx^2 + I \\ \ddot{y} - dx^2 \\ \ddot{z} - rz \end{cases} \\ \begin{cases} 0 \\ \frac{1}{2} \\ \frac{1}{2} \\ 0 \end{cases} \begin{cases} \ddot{x} \\ \ddot{y} \\ \ddot{z} \\ \ddot{x} \end{cases} &= \begin{cases} \frac{1}{2} \\ 0 \\ -\frac{rsx}{2z-2y} \\ 0 \end{cases} \begin{cases} \ddot{x} \\ \ddot{y} \\ \ddot{z} \\ \ddot{x} \end{cases} + \begin{cases} \frac{ax^3 + bx^2 + I}{2dx^2 + 2rsx} \\ 0 \\ \frac{c-y}{2y-2z} \\ 0 \end{cases} \begin{cases} \ddot{x} \\ \ddot{y} \\ \ddot{z} \\ \ddot{x} \end{cases} + \begin{cases} 0 \\ 0 \\ -\frac{rs}{2z-2y} \\ 0 \end{cases} \begin{cases} \ddot{x} \\ \ddot{y} \\ \ddot{z} \\ \ddot{x} \end{cases} \end{aligned} \quad (5)$$

Following the criterion defined in Eq.(2), it requires

$$0 = \tilde{N}^T H^T F_c(X) = (y-z) \frac{\partial H}{\partial x} + (-dx^2) \frac{\partial H}{\partial y} + (rsx) \frac{\partial H}{\partial z}; \quad (6)$$

Indeed, a suitable solution for Eq.(6) can be approached by

$$H = \frac{2}{3} dx^3 + rsx^2 + (y-z)^2; \quad (7)$$

As a result, any changes in the normalized parameters  $(d, r, s)$  and membrane potential

and current variable in the neuron model can induce energy release, and then the firing modes can be controlled. Furthermore, the injection or release of external energy may induce certain parameter shift, and the neural activities are regulated synchronously. Furthermore, the energy changes can be estimated by

$$\begin{aligned} \dot{H} &= \tilde{N} H^T F_d(x, y, z) \\ &= 2[(bd - rsa)x^4 + dx^2 - y^2 - adx^5 + (c + rsl)y - (c + rsl)z \\ &\quad + (1+r)yz + rsbx^3 + rslx - rz^2] ; \end{aligned} \quad (8)$$

The external excitation  $I$  is usually considered as constant, periodic function and even filtered signals from chaotic source, after that the excitability is adjusted to develop different firing patterns. The evolution of energy (transient power) in isolated neuron is dependent on the selection of these intrinsic parameters ( $a, b, c, d, r, s, \lambda$ ). It is known that neuron can select multiple neural activities such as quiescent, spiking, bursting and chaotic modes, and the energy changes will keep four levels by taming one parameter in adaptive criterion as follows

$$p = \begin{cases} \rho_1, & \bar{P} \in P_1 \sim \frac{1}{4} \langle \frac{dH}{dt} \rangle, \\ \rho_2, & P_1 < \bar{P} \in P_2 \sim \frac{2}{4} \langle \frac{dH}{dt} \rangle, \\ \rho_3, & P_2 < \bar{P} \in P_3 \sim \frac{3}{4} \langle \frac{dH}{dt} \rangle, \\ \rho_4, & P_3 < \bar{P} \sim \frac{4}{4} \langle \frac{dH}{dt} \rangle \end{cases} \quad (9a)$$

$$\bar{P} = \frac{1}{T} \int_0^T I^2(t) dt = \frac{1}{T} \int_0^T (A \cos \omega t)^2 dt = \frac{A^2}{2}; \quad (9b)$$

where the symbol  $\langle * \rangle$  represents a average of variable or function over time,  $p$  is one sensitive parameter in the normalized parameters ( $a, b, c, d, r, s, \lambda$ ). For external excitation with periodic type as  $A \cos(\omega t)$  or  $A \sin(\omega t)$ , its average power is approached by  $A^2/2$  within a transient period. The energy changes in the HR model are classified with four levels for selecting four different firing modes. Therefore, the average power for the external stimulus will control the parameter jump for reaching different energy levels. From Eq.(9), it is suggested that the four energy levels are spaced evenly, therefore, one of the parameter is jumped to another value when the power of injection energy is approached to 1/4, 2/4, 3/4, 4/4 average power of the neuron. That is, enough energy injection and absorption can break the energy balance and induce transition of energy level, and firing mode is also changed synchronously. In fact, biological neurons may require adaptive parameter shift under energy injection when mixed signals are applied to excite neurons as follows

$$\begin{aligned}
& \begin{array}{l}
\rho_1, \quad \bar{P} \in k_1 \left\langle \frac{dH}{dt} \right\rangle, \\
\rho_2, \quad k_1 \left\langle \frac{dH}{dt} \right\rangle < \bar{P} \in k_2 \left\langle \frac{dH}{dt} \right\rangle, \\
\rho_3, \quad k_2 \left\langle \frac{dH}{dt} \right\rangle < \bar{P} \in k_3 \left\langle \frac{dH}{dt} \right\rangle, \\
\rho_4, \quad k_3 \left\langle \frac{dH}{dt} \right\rangle < \bar{P}
\end{array} \quad (10a) \\
& \bar{P} = \frac{1}{T} \int_0^T I^2(t) dt; \quad (10b)
\end{aligned}$$

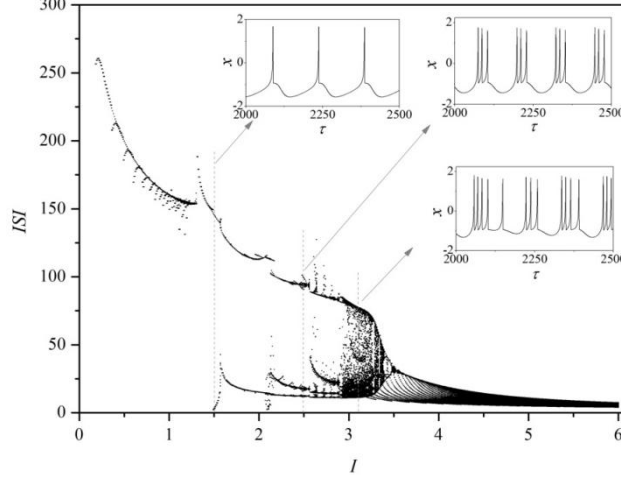
That is, realistic stimuli can be a filtered wave from chaotic source and more periodic signals are combined. Therefore, parameter shift can be induced when the injection energy is beyond certain energy levels and gains ( $k_1, k_2, k_3$ ) can be dependent on the intrinsic property of the media. That is, the energy level spacing becomes uneven. From physical viewpoint, the average power will become close to certain constant when a neuron is kept with certain firing mode. External can inject energy into the neuron, but the redundant energy supply is not effective to induce neuron to jump next higher energy level and shape deformation becomes available, therefore, parameter shift is induced to present suitable firing modes corresponding to the appropriate energy level. In this way, the intrinsic parameter  $p$  has relation to the external stimulus  $I$  as follow

$$p = p(I); \text{ or } I = I(p); \quad (11)$$

where  $p = p(I)$  indicates that one intrinsic parameter depends on the external excitation, and energy injection from external forcing can induce parameter shift due to energy accommodation in the neuron. On the other hand,  $I = I(p)$  can be explained that the effect of external stimulus can be mapped into equivalent transmembrane current, and it is dependent on one intrinsic parameter  $p$  for the neuron. To be point out, parameter shift occurs within finite range so that the average power of the neuron should match with (keep pace with) the average power from external stimulus, and the shape deformation accompanying with parameter shift is controlled by the supply of redundant energy of external energy injection.

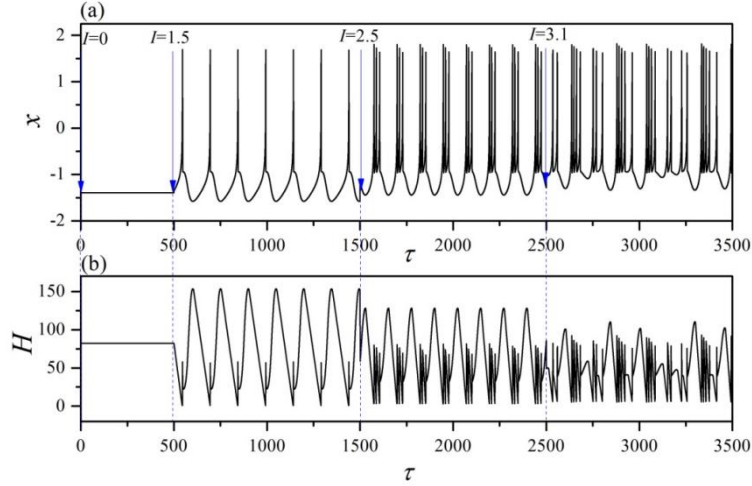
### 3 Numerical results and discussion

In this section, the fourth Runge-Kutta algorithm is applied to approach exact numerical solutions for the neuron model by setting time step  $h=0.001$ . Firstly, external excitation is changed to discern the firing modes in the neural activities, and the dependence of firing patterns on external stimulus is plotted in Fig.1.



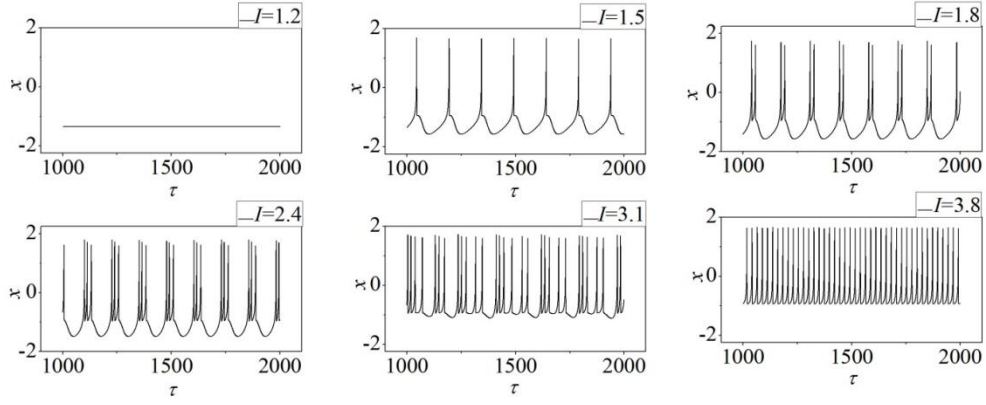
**Fig.1** Bifurcation of ISI (interspike interval) is calculated by applying different external stimuli  $I$ . The parameters are fixed at  $a=1$ ,  $b=3$ ,  $c=1$ ,  $d=5$ ,  $r=0.006$ ,  $s=4$ ,  $\lambda=-1.6$ . The small image in the upper right corners represent the evolution of membrane potentials presenting different discharge states.

From Fig.1, it is demonstrated that the firing patterns in membrane potentials can be regulated by the external stimulus effectively because of continuous energy injection. Therefore, it is important to confirm the regulation of Hamilton energy in Eq.(7) by setting external stimulus as four different constants, which are effective to develop four different kinds of firing patterns.



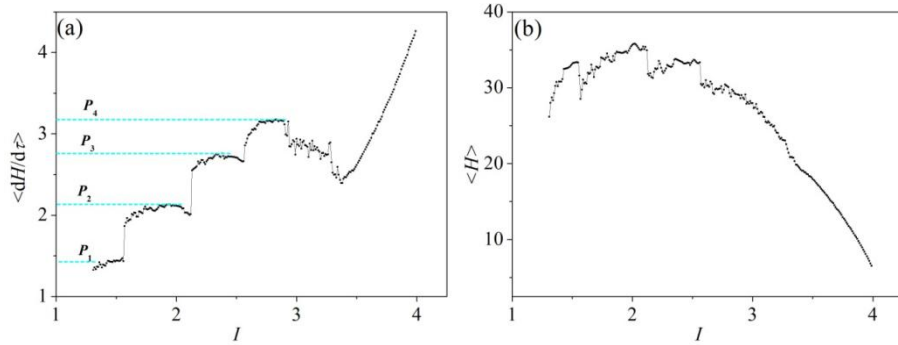
**Fig.2** Sampled time series for membrane potentials and transition of energy level by switching the external stimulus to four different values.

Any changes in the external stimulus can modify the excitability of the neuron, the firing patterns are adjusted accompanying distinct transition in the Hamilton energy. Under quiescent state, the Hamilton energy is kept as a lower constant. During mode transition from spiking to bursting and chaotic patterns, the amplitude of Hamilton energy is decreased because of continuous dense firings. Indeed, the deterministic neuron model keeps distinct firing mode in neural activities when external stimulus and parameters are fixed, and then external stimulus is selected with some constants to detect the changes in the membrane potential in Fig.3.



**Fig.3** Sampled time series for membrane potential in an isolated neuron under constant forcing. The parameters are fixed at  $a=1$ ,  $b=3$ ,  $c=1$ ,  $d=5$ ,  $r=0.006$ ,  $s=4$ ,  $\lambda=-1.6$ .

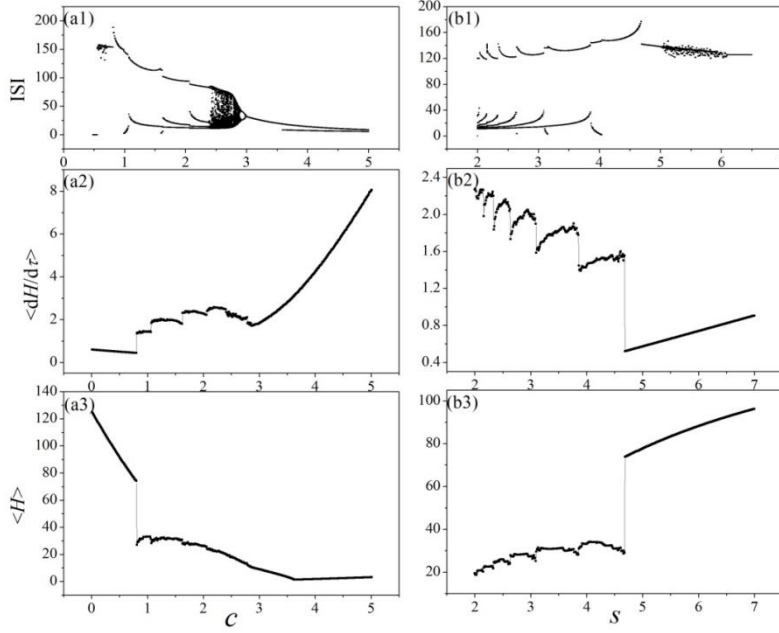
That is, firing modes show distinct transition by applying an external excitation of various strengths, and thus periodic stimulus is effective to raise various firing modes. It is important to discern the energy consumption within each time unit by calculating the average power when external stimulus is fixed at different values.  $dH/d\tau$  is estimated within certain transient period and the firing patterns are also plotted in Fig.4 by applying suitable forcing currents.



**Fig.4** (a) Dependence of average energy consumption per unit time  $\langle dH/d\tau \rangle$  and (b) average Hamilton energy in single neuron by applying constant stimulus.

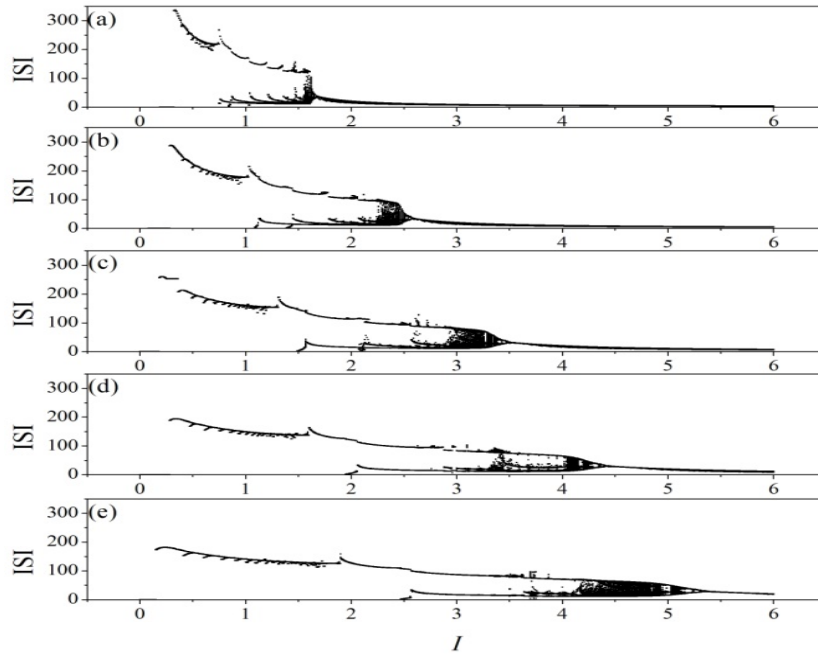
The firing modes in neuronal membrane potential are dependent on the external excitation, and four distinct steps are found in the curve for average power in an isolated neuron. In presence of quiescent state, the average energy consumption is kept lower value, and spiking patterns requires higher energy consumption in the neuron. From bursting to chaotic state and multiple modes, energy consumption is further increased. As shown in Eq.(7), any changes for parameter  $s(=S)$  has distinct impact on the Hamilton energy, and then the bifurcation analysis and evolution of energy and average power are estimated in Fig.5.





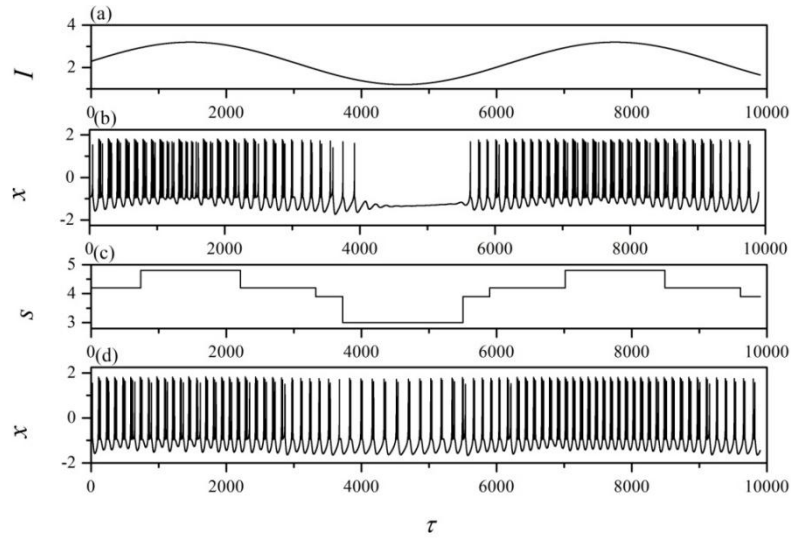
**Fig.5** Bifurcation of ISI (interspike interval) and evolution of average power and Hamilton energy are simulated by changing parameter  $c$  or  $s$ . For (a1, a2, a3)  $s=4$ ; (b1, b2, b3)  $c=1$ , and other parameters are fixed at  $a=1$ ,  $b=3$ ,  $d=5$ ,  $r=0.006$ ,  $\lambda=-1.6$ ,  $I=1.5$ .

From Fig.5, it is demonstrated that firing modes can be controlled by the intrinsic parameters ( $s$ ,  $c$ ), the average power shows distinct levels, in particular, the Hamilton energy for the neuron also shows distinct level transition by changing the parameter  $s$ . Furthermore, bifurcation is simulated by taking distinct values for parameter  $s$  during the changes of external stimulus  $I$ , and the results are plotted in Fig.6.



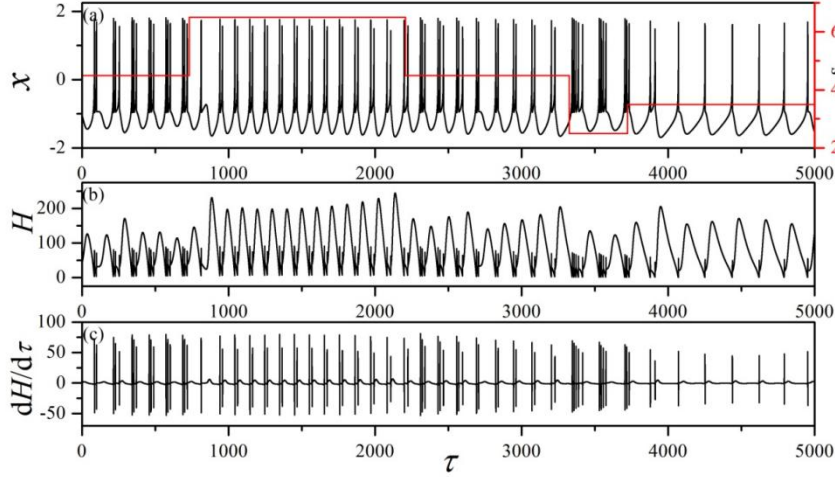
**Fig.6** Bifurcation of ISI is simulated by changing external stimulus  $I$ . For (a)  $s=2$ ; (b)  $s=3$ ; (c)  $s=5$ ; (d)  $s=6$ , and the other parameters are fixed at  $a=1$ ,  $b=3$ ,  $c=1$ ,  $d=5$ ,  $r=0.006$ ,  $\lambda=-1.6$ .

It is confirmed that shift of parameter  $s$  can induce similar discharge pattern in the neural activities. Furthermore, both external stimulus and parameter  $c$  are adjusted to detect the changes in the membrane potentials in Fig.7.



**Fig.7** (a) External stimulus in periodic form  $I$ , (b) sampled time series for membrane potential, (c) parameter shift  $s$  and (d) evolution of membrane potential. (a)  $I=\sin 0.001 \tau+2.2$ ; (b)  $I=\sin 0.001 \tau+2.2$ ,  $s=4.0$ ; (c)(d)  $I=\sin 0.001 \tau+2.2$ ,  $s=3.0$  ( $I \leq 1.57$ );  $s=3.9$  ( $1.57 < I \leq 1.92$ );  $s=4.2$  ( $1.92 < I \leq 2.94$ );  $s=4.8$  ( $I > 2.94$ ).

As presented in Fig.7(a, b), transition in firing modes is controlled by the periodical stimulus without parameter shift. That is, external stimulus is fluctuated within large range and energy injection is adjusted to induce jumping between different energy levels. From Fig.7(c, d), parameter shift is considered when neuron is excited by periodic current, and fast mode transition is suppressed to keep each kind of firing mode within certain period. That is, appropriate parameter shift is helpful to prevent fast pattern transition in neuron membrane potential and the average Hamilton energy and average power will not be fluctuated sharply when external stimulus is changed within large range. It is interesting to discern the energy changes and transition in average power in neuron accompanying parameter shift under periodic stimulus, and the results are plotted in Fig.8.



**Fig.8** (a) Mode transition in the firing patterns for membrane potentials and changes in parameter  $s$ . (b) Evolution of Hamilton energy and power (c) in presence of periodic stimulus and parameter shift.  $I = \sin 0.001\tau + 2.2$ ,  $s = 3.5$  ( $I \leq 1.57$ ),  $s = 2.5$  ( $1.57 < I \leq 1.92$ ),  $s = 4.5$  ( $1.92 < I \leq 2.94$ ),  $s = 6.5$  ( $I > 2.94$ ), and the parameters are fixed  $a=1$ ,  $b=3$ ,  $c=1$ ,  $d=5$ ,  $r=0.006$ ,  $\lambda=-1.6$ .

From Fig.8, changes in external stimulus are continued but the firing modes are kept stable by regulating the parameter  $s$  in appropriate way. Therefore, the Hamilton energy is kept the same oscillatory mode within certain period by taming the parameter synchronously. The firing modes in neuron membrane potential show distinct transition, and firing modes kept stable by adjusting the parameter carefully even the external stimulus is changed continuously.

In a summary, selection of each firing mode is mainly controlled by its intrinsic energy level and external stimulus can break the stability of energy level because of external energy injection. It needs enough energy absorption when neuron is jumped from a lower energy level to a higher energy level, and the surplus energy will induce shape deformation accompanying with appropriate parameter shift. In this way, it prevents frequently jumping between different energy levels and mode transitions in electrical activities. Therefore, each firing mode can keep stable within certain transient period. Therefore, maximal energy absorption from external stimulus is realized and neuron select the most suitable firing mode by taming one or more intrinsic parameters synchronously, it accounts for the self-adaptation property of biological neurons. When the energy level becomes stable, the firing mode also keeps stable. In particular, multiple firing patterns occur in the neural activities, and it is helpful for making decision in the nervous system. In most of the previous studies, the intrinsic parameters are suggested as constant even large external stimulus is applied, and the neuron based on the deterministic models have to sole firing modes, and the occurrence of multiple firing modes emerge only when external stimulus are changed in large range or activating noisy disturbance. Our results clarified the physical mechanism for inducting multiple modes in electrical activities in these deterministic neuron models. It also indicates that jumping between energy levels occurs under specific physical condition by capturing enough energy from external stimulus, and the surplus energy is encoded by trigger possible parameter shift, which explains the dependence of equivalent transmembrane

current on some intrinsic parameters in the neuron. From dynamical approach, readers can define  $I=I(s)$  or  $s=s(I)$  in special form and these deterministic neuron models can be excited to present multiple firing modes. In particular, similar parameter-dependent external stimulus can be defined to explain the bifurcation mechanism in Hindmarsh-Rose and similar neuron models, and the theoretical analysis is consistent with experimental results [61, 62].

#### 4 Conclusions

Based on the deterministic Hindmarsh-Rose neuron mode, Hamilton energy is defined and estimated by using Helmholtz theorem. The dependence of pattern selection and energy level on external excitations is discussed in detail. Continuous change and increase of the external excitations can induce distinct firing modes in neuron membrane potential; in particular, the average energy consumption (power) in per time unit shows four distinct levels. When external stimulus is fixed, bifurcation of ISI confirmed that energy level can be switched by taming one of the bifurcation parameters. We claimed that continuous energy injection from external stimulus/stimuli can induce parameter shift in the neuron model because of energy accommodation as  $p=p(I)$ , which one of the parameter  $p$  is independent on the power from the external stimulus  $I$ . As a result, the neuron will jump to next energy level under parameter shift and appropriate firing mode is triggered. Furthermore, time-varying stimulus with large fluctuation will induce another jump between energy levels and a different firing mode is developed, therefore, the neural activities will show multiple firing modes with time in this deterministic neuron model. Our results confirmed that this firing mode in neuron membrane potential is mainly dependent on the energy level, and enough energy injection from external stimulus will induce jump of energy levels and thus mode transition is induced in the neural activities.

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**Data availability:** The data in this study are available from the corresponding author upon right request.

**Conflict of Interest:** The authors declare no conflict of interest with this publication.

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