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Research Article

Autaptic Modulation of Electrical Activity in a Network of Neuron-Coupled Astrocyte

Shengli Guo,[1] Jun Tang,[2] Jun Ma,[1,3] and Chunni Wang[1]

[1]*Department of Physics, Lanzhou University of Technology, Lanzhou 730050, China*
[2]*School of Physics, China University of Mining and Technology, Xuzhou 221116, China*
[3]*NAAM-Research Group, Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia*

Correspondence should be addressed to Jun Ma; hyperchaos@163.com

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Autapse connection is considered on a biological neuron coupled by astrocyte, and the effect of autapse driving-induced response in electrical activities is investigated. In this paper, a simple network is developed on the Hodgkin-Huxley (HH) neuron coupled by astrocyte and the autapse effect is also considered. The modulation of autapse connected to HH neuron can change the membrane potential by applying time-delayed feedback along a close loop. It is found that the self-adaption of autapse driving can make the network of neuron-astrocyte generate different modes of electrical activities, and oscillating behavior of Ca^{2+} and IP_3 setting is controlled. This new network model can give potential understanding about self-adaption of neuron to external forcing when the coupling of astrocyte and autapse is considered.

1. Introduction

It is ever believed that neuron is the most important basic unit of nerve system, and many experimental evidences have confirmed that gliocyte, particularly, astrocyte, can play an important role in changing the fluctuation of membrane potential of neuron by adjusting the concentration of Ca^{2+} via IP_3 (inositol triphosphate) [1–3]. It is also found that astrocyte can format the inputting and activity of synapse [4, 5] and regulate the processing propagation of electrical signal in neurons [6–9]. Autapse [10–15] is often connected to some moderate neurons, and the feedback on membrane potential is realized by adding time-delayed forcing current on the membrane, where autapse is a specific synapse connected to the neuron via close loop. When autapse connection is triggered, the electrical activities and dynamical response will be changed [16–18]. Furthermore, autapse driving in the network can regulate the collective behaviors of network by generating continuous pulse or wave fronts, thus synchronization; pattern selection can be realized [19–22]. Readers can find brief survey for neurodynamics and dynamics in neuronal network in [23] and references therein. The author of this paper ever explained the formation mechanism of autapse connection to neuron; it is argued that formation of autapse can be helpful to enhance signal propagation along an auxiliary loop; thus autapse is developed [24]; then time delay and feedback gain are used to describe the properties of this loop. On the other hand, the electrical activities of neurons can be changed when neurons or neuronal tissue are exposed to electromagnetic radiation; for example, failure in heart induced by electromagnetic radiation [25] is discussed. In fact, complex electromagnetic induction is triggered in neurons during the exchange of ions current across membrane because the distribution of charged ions is changed. Therefore, Lv et al. suggested that magnetic flux [26, 27] can be used to detect the effect of electromagnetic induction and further for the effect of electromagnetic radiation [28]. Furthermore, Xu et al. argued [29] that autaptic driving can be helpful for neuron to suppress the electromagnetic radiation. Therefore, it is important to further discuss the network connection of neurons that the self-adaption of autapse connection can be understood.

In fact, most of the previous works about neurodynamics have discussed the neuron-coupled astrocyte model [30–34] and some results could be helpful to understand the occurrence of seizure-like behavior [35]. Based on the well-known neuron models, networks with different topological connections have been set to investigate the synchronization stability [36, 37], pattern selection, and mode transition in collective behaviors [38–45]. Indeed, reliable and biophysical neuron model is critical and important for further investigation on neurodynamics and potential mechanism of some neuronal diseases [46]. Therefore, it is interesting to set a more reliable neuron model that the effect of autapse driving and astrocyte on electrical activities can be explored. In this paper, we propose an improved neuron model coupled by astrocyte and autapse connection is also considered. The modulation of autapse driving on electrical activities in astrocyte-coupled neuron will be discussed, and the exchange of signal between astrocyte and neurons can be detected and understood.

2. Model Setting and Description

For simplicity but biophysical meaning, Hodgkin-Huxley neuron model will be driven by autaptic current, and additive modulation from astrocyte will be considered; it reads as follows:

$$\begin{aligned} C_m \frac{dV}{dt} &= g_k n^4 (V_k - V) + g_{\mathrm{Na}} m^3 h (V_{\mathrm{Na}} - V) \\ &\quad + g_L (V_L - V) + I_{\mathrm{ext}} + I_{\mathrm{astro}} + I_{\mathrm{aut}} \\ \frac{dm}{dt} &= \alpha_m (V)(1 - m) - \beta_m (V) m \\ \frac{dh}{dt} &= \alpha_h (V)(1 - h) - \beta_h (V) h \\ \frac{dn}{dt} &= \alpha_n (V)(1 - n) - \beta_n (V) n, \end{aligned} \tag{1}$$

where the coefficients [7] for (1) are defined by

$$\begin{aligned} \alpha_m &= 0.1 \frac{25 - V}{\exp[(25 - V)/10] - 1}; \\ \beta_m &= 4 \exp\left[\frac{-V}{18}\right]; \\ \alpha_h &= 0.07 \exp\left[\frac{-V}{20}\right]; \\ \beta_h &= \frac{1}{\exp[(30 - V)/10] + 1}; \\ \alpha_n &= 0.01 \frac{10 - V}{\exp[(10 - V)/10] - 1}; \\ \beta_n &= 0.125 \exp\left[\frac{-V}{80}\right], \end{aligned} \tag{2}$$

where V is the membrane potential, m, n, h are the gate variable, and I_{ext} denotes an external forcing current, respectively. I_{aut} represents the autaptic current from autapse connection to the neuron, and in case of electric autapse driving, the autaptic current is calculated as follows:

$$I_{\mathrm{aut}} = g_e (V(t - \tau) - V(t)), \tag{3}$$

where g_e and τ are the feedback gain and time delay, respectively. Positive feedback is triggered to excite and enhance the oscillating behavior by setting negative values for g_e, while positive value for g_e can generate negative feedback to suppress the excitability and bursting behaviors in neuron. I_{astro} defines the additive forcing current generated by astrocyte which changes the concentration of calcium and inositol triphosphate (IP_3) via adjusting the neurotransmitter such as ATP and glutamic acid. The modulation for concentration of IP_3 can be approached by

$$\begin{aligned} \frac{d[\mathrm{IP}_3]}{dt} &= \frac{1}{\tau_{\mathrm{IP}_3}} \left([\mathrm{IP}_3]^* - [\mathrm{IP}_3]\right) \\ &\quad + r_{\mathrm{IP}_3} \Theta (V - 50.0\,\mathrm{mV}), \end{aligned} \tag{4}$$

where $[\mathrm{IP}_3]^*$ is the concentration of IP_3 under equilibrium state and the parameter r_{IP_3} represents the response efficiency of astrocyte to action potential, also called production ratio for IP_3. That is, the larger r_{IP_3}, the larger density of distribution of mGluR on the membrane. $\Theta(*)$ is Heaviside function; as a result, the astrocyte can change the electrical activities of neuron and generate IP_3 when the action potential or membrane potential is beyond 50 mV. The fluctuation of IP_3 makes the receptor of IP_3 trigger release of calcium ion; thus concentration of calcium ion $[Ca^{2+}]$ began to oscillate. For simplicity, Li-Rinzel [47] model is used to describe the oscillating of $[Ca^{2+}]$; it is often calculated by

$$\begin{aligned} \frac{d[\mathrm{Ca}^{2+}]}{dt} &= -J_{\mathrm{Channel}}(q) - J_{\mathrm{Pump}} - J_{\mathrm{Leak}} \\ \frac{dq}{dt} &= \alpha_q (1 - q) - \beta_q q, \end{aligned} \tag{5}$$

where $J_{\mathrm{Channel}}(q)$ denote the calcium ion flux emitted from endoplasmic reticulum to cytoplasm via channels of IP_3 receptor and thus the concentration of calcium ion is increased. J_{Pump} is ATP-independent pump flux that calcium ion is pumped into calcium store. J_{Leak} is leakage current from endoplasmic reticulum to cytoplasm. Order parameter q is

the gate variable that calculates the open probability of ion channels. The calcium flux [34] is described by

$$
\begin{aligned}
J_{\text{Channel}}(q) &= c_1 v_1 {m_\infty}^3 {n_\infty}^3 q^3 \left(\left[\text{Ca}^{2+}\right] - \left[\text{Ca}^{2+}\right]_{\text{ER}}\right);\\
J_{\text{Pump}} &= \frac{v_3 \left[\text{Ca}^{2+}\right]^2}{{k_3}^2 + \left[\text{Ca}^{2+}\right]^2};\\
J_{\text{Leak}} &= c_1 v_2 \left(\left[\text{Ca}^{2+}\right] - \left[\text{Ca}^{2+}\right]_{\text{ER}}\right);\\
m_\infty &= \frac{[\text{IP}_3]}{[\text{IP}_3] + d_1};\\
n_\infty &= \frac{\left[\text{Ca}^{2+}\right]}{\left[\text{Ca}^{2+}\right] + d_5};\\
\alpha_q &= a_2 d_2 \frac{[\text{IP}_3] + d_1}{[\text{IP}_3] + d_3};\\
\beta_q &= a_2 \left[\text{Ca}^{2+}\right].
\end{aligned}
\tag{6}
$$

And the forcing current from astrocyte is often approached by [30]

$$
\begin{aligned}
I_{\text{astro}} &= 2.11\Theta(\ln y) \ln y;\\
y &= \left[\text{Ca}^{2+}\right]/\text{nM} - 196.69.
\end{aligned}
\tag{7}
$$

As reported in [48–50], many chemical neurotransmitters are released to gaps of cells when the concentration of calcium ions is increased; for example, it is argued that the release of glutamic acid can trigger the release of calcium ions. However, blocking the transmission of glutamic acid between astrocytes seldom prevents the release of glutamic acid induced by increase of calcium ion concentration; it could account that glutamic acid comes from the interior of cells. It is believed that concentration increase in calcium ions is necessary setting to trigger the release of glutamic acid. When glutamic acid is released to gaps of cells, it is used as neurotransmitter to act on the ionophilic receptors (NMDA, AMPA), and depolarization of neuron occurs to trigger an action potential; as a result, signal propagation from synapse is regulated. It is found in [50] that slow introverted currents (SICs) via NMDA receptor can connect to thalamus neurons when pulse induced by Ca^{2+} oscillating in concentration was released and propagated to gaps between cells. For simplicity, the forcing current associated with astrocyte dependence on calcium concentration is approached in (7) described as above. The physical unit in astrocyte for calcium ions is μmol/L, pA is used for current, and the cell or neuron is described as a sphere with a radius about 25 μm, and the density of current of I_{astro} is μmol/L·cm^2 to be consistent with the physical units in Hodgkin-Huxley neuron model. For detailed description, Table 1 gives the parameter setting and physical units.

Table 1: Parameter values setting.

Parameter	Value and meaning
C_m	1 μF/cm^2
g_K	36.0 ms/cm^2
g_{Na}	120.0 ms/cm^2
g_L	0.3 ms/cm^2
V_K	−12.0 mV
V_{Na}	115.0 mV
V_L	10.6 mV
$[\text{IP}_3]^*$	160.0 nmol/L
$1/\tau_{\text{IP}_3}$	0.00014 (m/s)
c_0	2.0 μmol/L
c_1	0.185
v_1	6 s^{-1}
v_2	0.11 s^{-1}
v_3	0.9 μmol/L·s
k_3	0.1 μmol/L
d_1	0.13 μmol/L
d_2	1.049 μmol/L
d_3	0.9434 μmol/L
d_5	0.08234 μmol/L
a_2	0.2 μmol/L·s
r_{IP_3}	Response efficiency of astrocyte to action potential
g_e	Feedback gain in autapse
τ	Time delay in autapse

3. Numerical Results and Discussion

The fourth-order Runge-Kutta algorithm is presented to find numerical solution of membrane potential with time step 0.001. The parameter r_{IP_3} is set to change different values, and the electric autapse driving is considered. Then the dynamical response in action potential is investigated to explore the possible biological function of autapse connection in the astrocyte-coupled neuron network. At first, the autapse connection is switched off, the external forcing is imposed on neuron as $I_{\text{ext}} = 10.0$ μmol/L·cm^2 at $t < 40$ s, the calcium concentration of astrocyte and IP_3 is calculated at $r_{\text{IP}_3} = 0.2$, and the results are plotted in Figure 1.

It is found that the membrane potential is decreased to quiescent state when the external forcing current is removed and the oscillating in Ca^{2+} is also stabilized, the mechanism is that astrocyte and neuron are coupled with weak intensity, insufficient IP_3 is not effective to trigger continuous oscillation in calcium concentration, and the exchange of transmembrane current is suppressed. Now, the effect of autapse connection and driving is considered by activating the autapse connection; for example, time delay in electric autapse is set $\tau = 2$, and positive feedback is investigated in Figure 2 by setting different feedback gains in the autapse.

It is found that the membrane potentials of neuron begin to fluctuate when the feedback gain in the electric autapse is increased beyond the threshold ($g_e = -0.48$); furthermore, the IP_3 and Ca^{2+} follow its oscillating behavior to modulate the membrane potential greatly. The potential

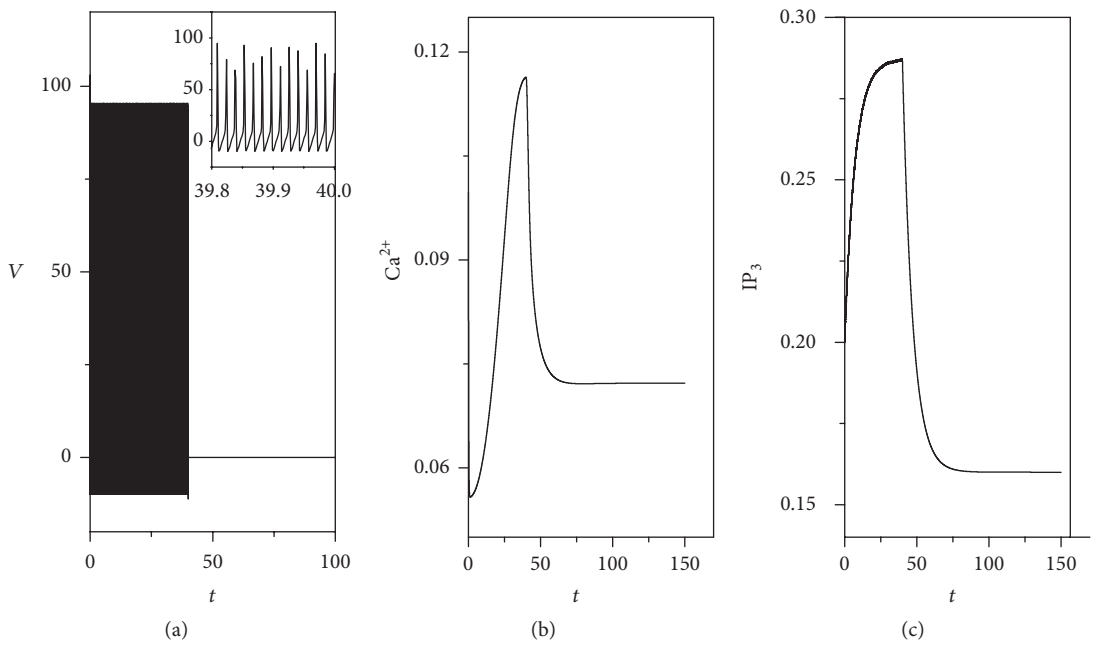

FIGURE 1: Sampled time series for membrane potential (a), calcium concentration in astrocyte (b), and IP_3 in astrocyte (c), $r_{IP_3} = 0.2$, and the external forcing current regulates the neuronal activities by setting $I_{ext} = 10.0\,\mu$mol/L·cm^2 at $t < 40$ s; the autaptic current is set as zero.

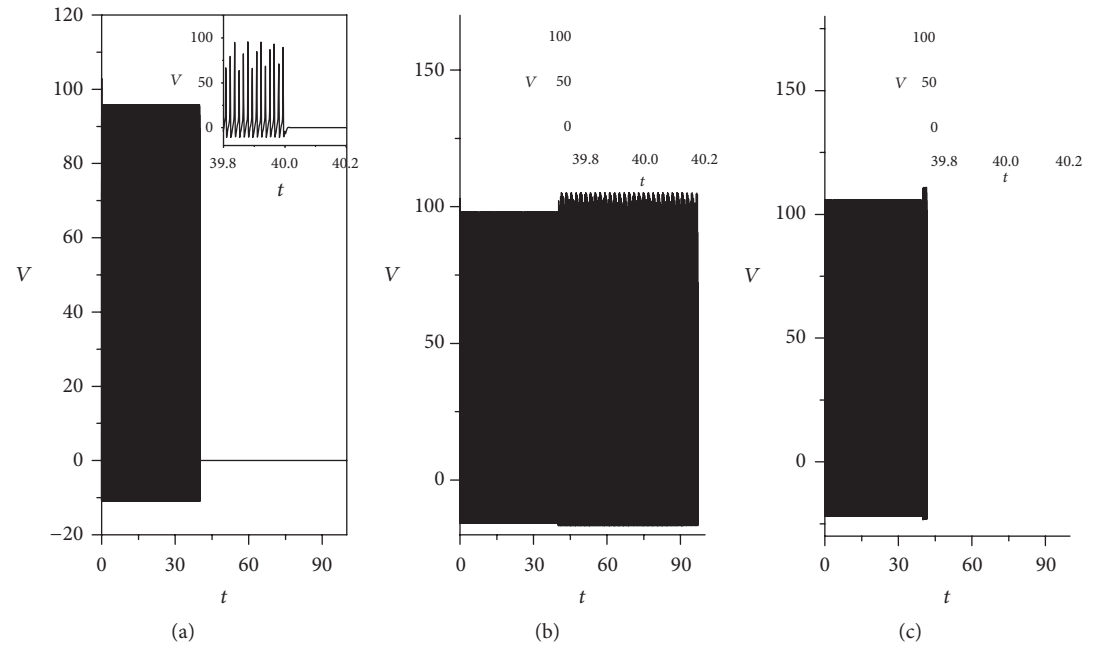

FIGURE 2: Sampled time series for membrane potential of neuron coupled by astrocypte when autapse driving is considered at $\tau = 2$, for (a) $g_e = -0.1$, (b) $g_e = -0.5$, and (c) $g_e = -1.0$. The parameter is set as $r_{IP_3} = 0.2$, and inserted figures are enlarged ones. And the external forcing current regulates the neuron by $I_{ext} = 10.0\,\mu$mol/L·cm^2 at $t < 40$ s.

mechanism is that positive feedback in autapse connection to neuron remembers the previous stimuli and continuous stimuli imposed on neuron can be effective to enhance the excitability of neuron, and then the neuron is excited. Furthermore, the oscillation of Ca^{2+} and changes of IP_3 are calculated in Figure 3.

The results in Figure 3 confirmed that enough high concentration in IP_3 is critical to trigger and enhance continuous oscillation of Ca^{2+} when electric autapse is set with strong feedback gain being applied. When the external forcing current is removed, the concentration of IP_3 is decreased quickly because continuous release of neurotransmitter occurs in

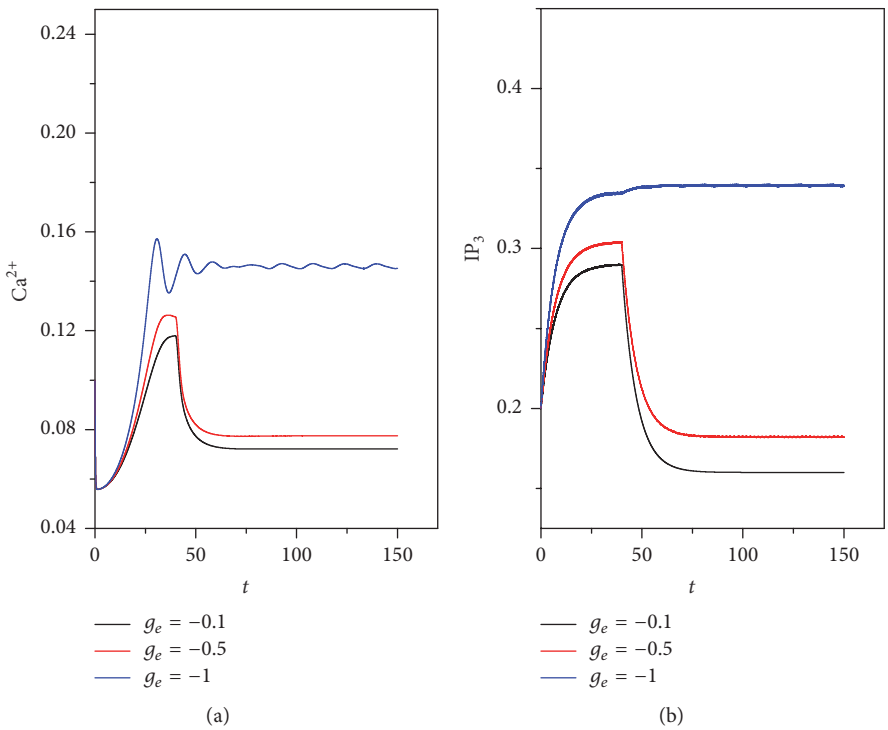

FIGURE 3: Fluctuation in Ca^{2+} concentration and IP_3 concentration is calculated by applying different feedback gains g_e in electric autapse with time delay $\tau = 2$. The parameter is set as $r_{IP_3} = 0.2$. And the external forcing current regulates the neuron by setting $I_{ext} = 10.0\ \mu$mol/L·cm^2 at $t < 40$ s.

presence of external stimuli beyond threshold. The interaction between neurotransmitter and metabolic receptor of astrocyte (mGluRs) can produce more IP_3; as a result, IP_3-independent Ca^{2+} can induce rapid release of Ca^{2+} from endoplasmic reticulum. On the other hand, positive feedback in electric autapse can also increase the IP_3 concentration; thus the concentration of Ca^{2+} can be enhanced; for example, $g_e = -1.0$. Furthermore, the case of negative feedback is considered by setting positive feedback gain in the electric autapse; the results are plotted in Figure 4.

It is found that the fluctuation of membrane potential can be suppressed, and the neuronal activities are changed to become quiescent state when autapse driving imposed negative feedback on the neuron. Furthermore, the Ca^{2+} and IP_3 concentration are calculated in Figure 5.

That is, negative feedback in electric autapse can suppress the fluctuation of membrane potential and then the ion current of Ca^{2+}; as a result, the concentration of IP_3 is also decreased completely. Indeed, neuron can be induced to trigger hyperexcitability when neuron is coupled by astrocyte with stronger intensity (e.g., larger value setting for r_{IP_3}). In case of smaller r_{IP_3}, the positive feedback in electric autapse becomes dominant and very important to enhance the excitability of neuron and also the oscillation in Ca^{2+} concentration. Furthermore, larger r_{IP_3} (=0.8) is used to investigate the same problem by applying external forcing current $I_{ext} = 10.0\ \mu$mol/L·cm^2 with a transient period $t = 40$ s from beginning, and the results are plotted in Figure 6.

It is confirmed that oscillating behavior of Ca^{2+} concentration and increase in IP_3 concentration can also be detected by setting larger coupling intensity between neuron and astrocyte (larger r_{IP_3}) when autapse connection is removed or the autaptic current is set as zero. In case of large value setting for r_{IP_3}, Ca^{2+} and IP_3 show slight oscillation in concentration when external forcing current is removed. It is interesting to detect the inhibition effect on Ca^{2+} and IP_3 oscillation in concentration by applying negative feedback in electric autapse, and the results are calculated in Figures 7 and 8.

It is found in Figure 7 that the spiking behavior of neuron can be suppressed by electric autapse with negative feedback; even the coupling between neuron and astrocyte is enhanced by setting larger r_{IP_3}. Furthermore, the changes of Ca^{2+} and IP_3 are calculated in Figure 8.

It is consistent with the previous prediction that Ca^{2+} keeps oscillating and IP_3 holds large concentration when autaptic modulation on membrane potential under negative feedback is weak because the astrocyte contributes more in regulating the membrane potential than electric autapse in this case. By further increasing in the negative feedback in electric autapse, the oscillating behavior in Ca^{2+} and IP_3 will be suppressed completely due to the modulation of electric autapse. It is important to detect and discuss whether positive feedback in autapse can enhance the oscillating behaviors of Ca^{2+} and IP_3 in case of larger value setting for r_{IP_3}, and the results are shown in Figures 9 and 10.

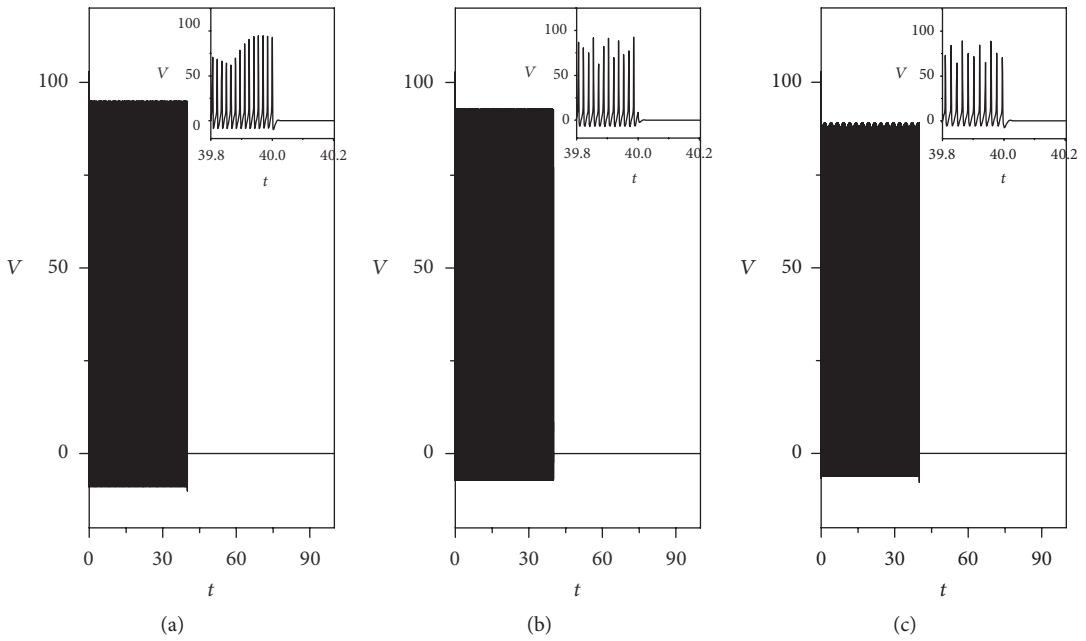

FIGURE 4: Sampled time series for membrane potential of neuron are calculated when neuron is coupled by astrocypte and autapse driving with negative feedback is considered at $\tau = 2$, for (a) $g_e = 0.1$, (b) $g_e = 0.5$, and (c) $g_e = 1.0$. The parameter is set as $r_{IP_3} = 0.2$, and inserted figures are enlarged ones. And the external forcing current regulates the neuron by $I_{ext} = 10.0\,\mu$mol/L·cm^2 at $t < 40$ s. The inserted figures are enlarged to show the sampled time series for membrane potential from $t = 39.8$ to 40.2 ms.

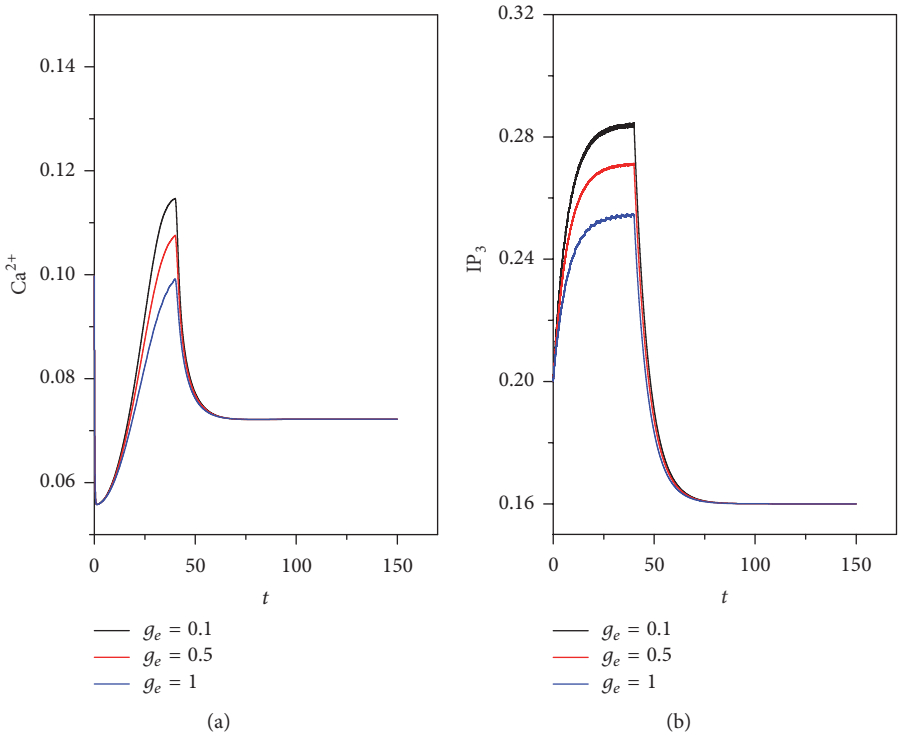

FIGURE 5: Fluctuation in Ca^{2+} concentration and IP_3 concentration is calculated by applying different feedback gains g_e in autapse with time delay $\tau = 2$. The parameter is set as $r_{IP_3} = 0.2$. And the external forcing current regulates the neuron by setting $I_{ext} = 10.0\,\mu$mol/L·cm^2 at $t < 40$ s.

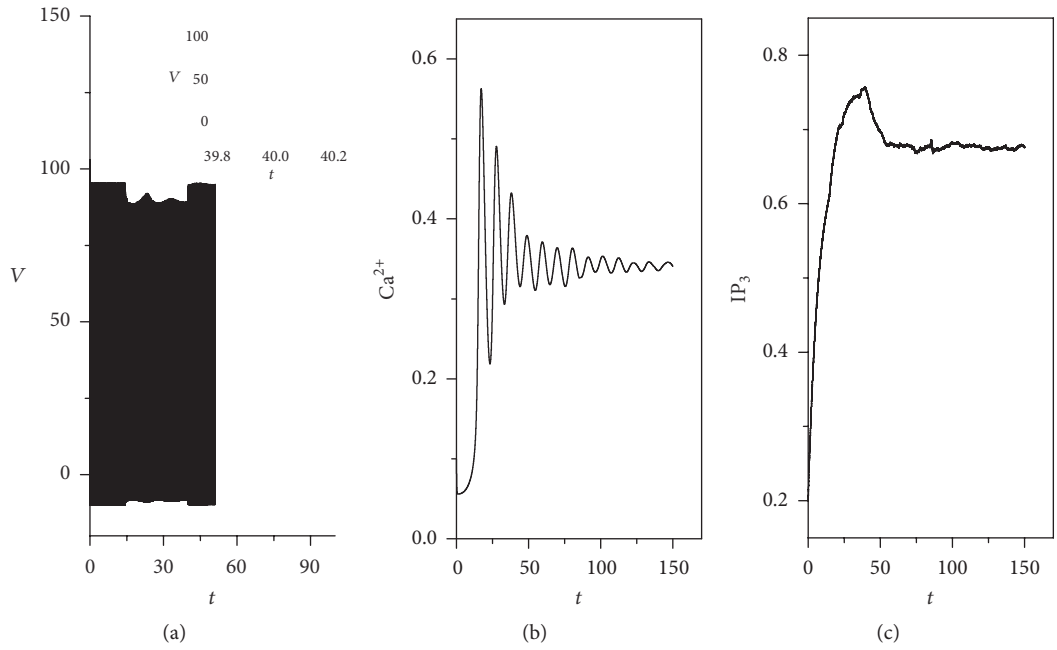

FIGURE 6: Sampled time series for membrane potential (a), calcium concentration in astrocyte (b), and IP_3 in astrocyte (c), $r_{IP_3} = 0.8$, and the external forcing current regulates the neuron by $I_{ext} = 10.0\ \mu mol/L{\cdot}cm^2$ at $t < 40$ s. The autaptic current is set as zero, and the inserted figure is enlarged to show the sampled time series for membrane potential from $t = 39.8$ to 40.2 ms.

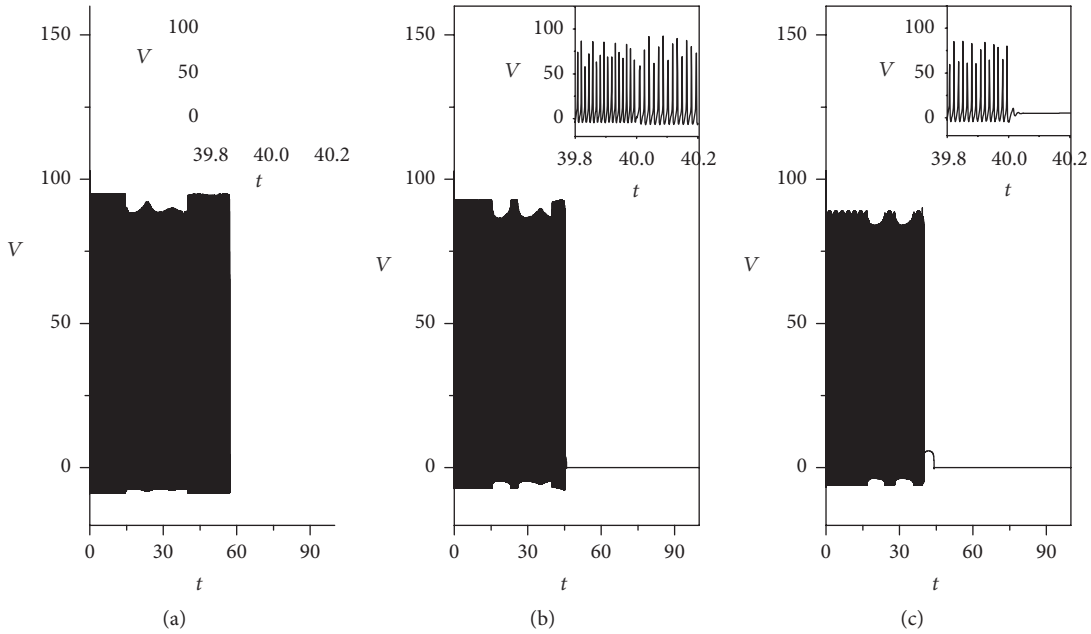

FIGURE 7: Sampled time series for membrane potential of neuron coupled by astrocypte when autapse driving is considered at $\tau = 2$, for (a) $g_e = 0.1$, (b) $g_e = 0.5$, and (c) $g_e = 1.0$. The parameter is set as $r_{IP_3} = 0.8$, and inserted figures are enlarged ones. And the external forcing current regulates the neuron by $I_{ext} = 10.0\ \mu mol/L{\cdot}cm^2$ at $t < 40$ s. The inserted figure is enlarged to show the sampled time series for membrane potential from $t = 39.8$ to 40.2 ms.

It is confirmed that positive feedback in electric autapse can further enhance the oscillating behavior of Ca^{2+} and IP_3 and also the excitability of neuron when the coupling intensity between neuron and astrocyte is set as higher value. As it is known, the autaptic modulation in autapse also depends on the value setting for time delay, which is dependent on the close loop. As a result, different time delays in electric autapse are selected to check the response of electrical activities and the oscillating behaviors of Ca^{2+} and IP_3, and the results are plotted in Figures 11 and 12.

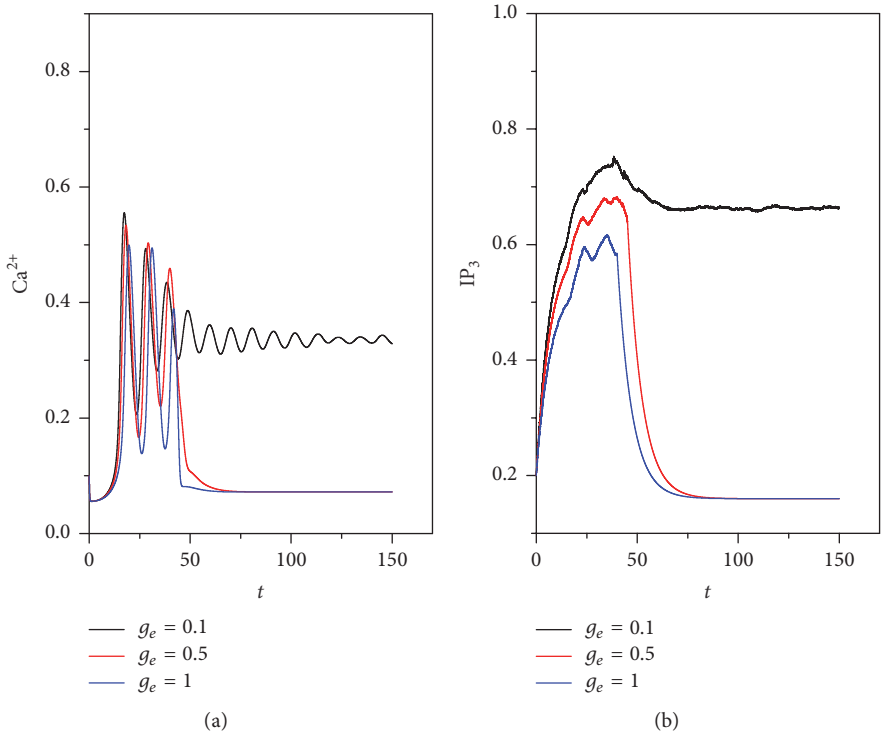

FIGURE 8: Fluctuation in Ca^{2+} concentration and IP_3 concentration is calculated by applying different feedback gains g_e in autapse with time delay $\tau = 2$. The parameter is set as $r_{IP_3} = 0.8$. And the external forcing current regulates the neuron by $I_{ext} = 10.0\ \mu mol/L{\cdot}cm^2$ at $t < 40$ s.

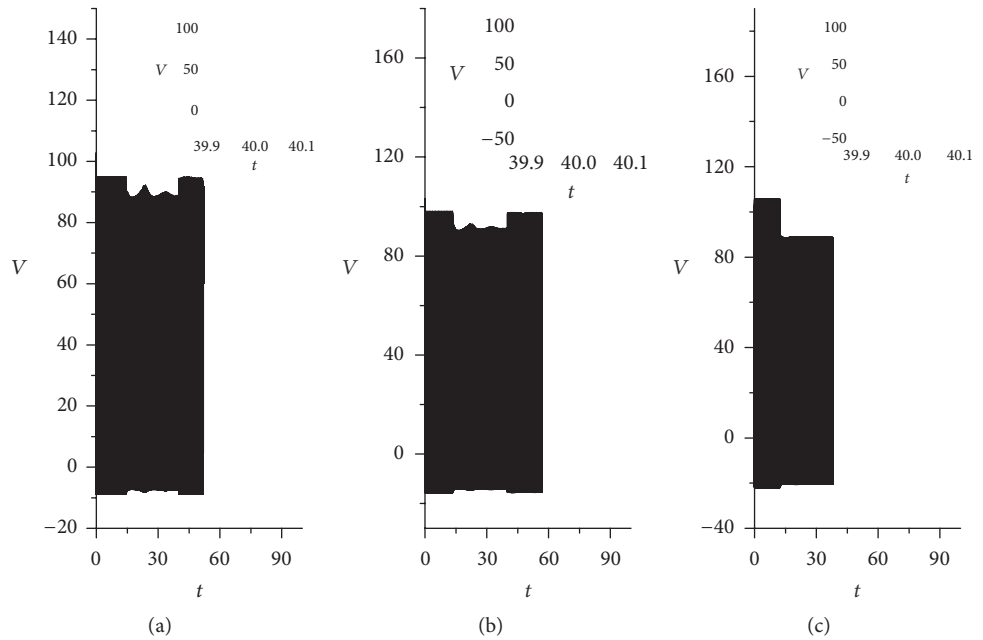

FIGURE 9: Sampled time series for membrane potential of neuron coupled by astrocypte when autapse driving is considered at $\tau = 2$, for (a) $g_e = -0.1$, (b) $g_e = -0.5$, and (c) $g_e = -1.0$. The parameter is set as $r_{IP_3} = 0.8$, and inserted figures are enlarged ones. And the external forcing current regulates the neuron by $I_{ext} = 10.0\ \mu mol/L{\cdot}cm^2$ at $t < 40$ s. The inserted figure is enlarged to show the sampled time series for membrane potential from $t = 39.8$ to 40.2 ms.

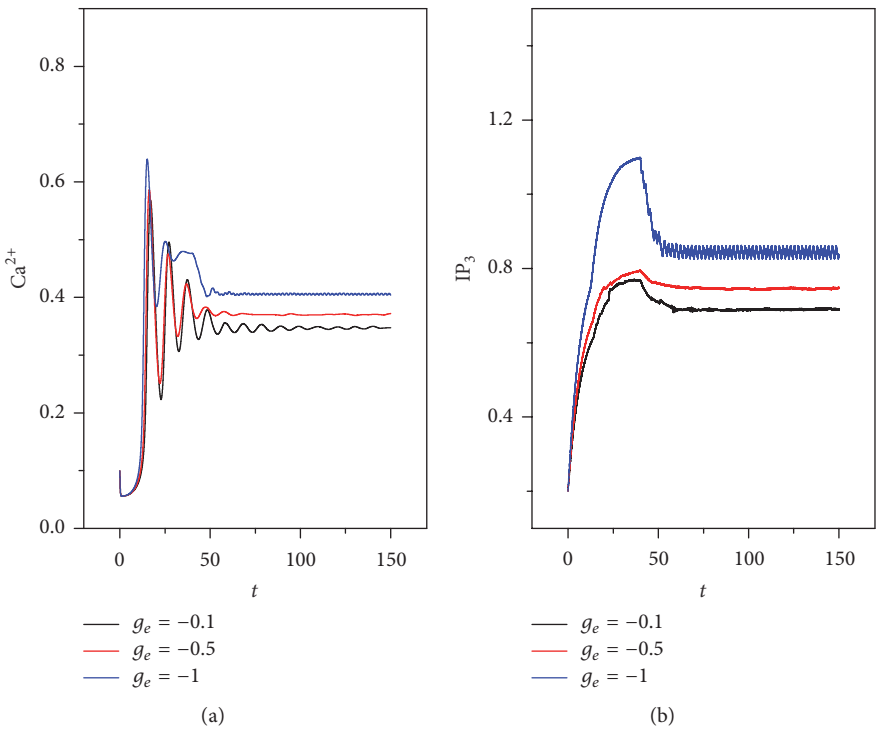

FIGURE 10: Fluctuation in Ca^{2+} concentration and IP_3 concentration is calculated by applying different feedback gains g_e in autapse with time delay $\tau = 2$. The parameter is set as $r_{IP_3} = 0.8$. And the external forcing current regulates the neuron by setting $I_{ext} = 10.0\,\mu$mol/L·cm^2 at $t < 40$ s.

It is found in Figure 11 that the spiking behavior is enhanced and began to show bursting behavior with increasing the time delay in electric autapse; even the coupling intensity between neuron and astrocyte is set as small value for $r_{IP_3} = 0.2$. Furthermore, the oscillating behavior of Ca^{2+} and changes of IP_3 concentration are calculated in Figure 12.

It is confirmed in Figure 12 that the concentration of IP_3 is decreased and the oscillating behavior in Ca^{2+} is also suppressed when the time delay in autapse is small. By further increasing the time delay in autapse, the memory effect makes neuron remember the action potential and oscillating behavior for Ca^{2+} though the intrinsic time delay in electric autapse is finite. Finally, the bifurcation analysis is carried out and the dependence of Ca^{2+}, IP_3, and ISI on parameters r_{IP_3} and g_e is discussed in Figure 13, respectively.

It is confirmed that the consistent oscillating behaviors of Ca^{2+} and IP_3 are dependent on the selection of r_{IP_3}, and positive feedback in autapse is effective to enhance the oscillating behaviors and bursting firing in electrical activities. In fact, the Ca^{2+} oscillating in astrocyte is much complex when uncertain perturbation such as noise and time delay is considered [51–53]. Different disturbances on excitable media are often described by applying different types of noise (additive or multiplicative) on the media and possible statistical properties are discussed [54]. Mutual coupling between astrocyte and neuron driven by autapse can trigger complex stimuli for neuron, astrocyte by setting different external forcing currents, and time delay and feedback gain in autapse; as a result, the response of electrical activities becomes more complex. That is, both of autaptic modulation and astrocyte can cooperate and contribute the mode selection of electrical activities in neurons; thus the self-adaption of neurons can be enhanced.

In summary, autapse connection and driving, external forcing, and also the coupling between neuron and astrocyte all contribute the oscillating behavior for Ca^{2+} by increasing the IP_3 concentration beyond the threshold to keep continuous oscillating in Ca^{2+} concentration. As a result, continuous action potential is triggered to propagate the electric signal between neurons. As mentioned in [24], formation and development of autapse can be associated with the self-adaption of neuron to external stimuli; particularly, it could be associated with injury in the neuron loop of circuit because only a few of neurons are found to be connected with autapse. Extensive evidences also confirmed that external setting of electric field can be effect to bridge the injured parts of axon; thus blocked signal can be propagated [55]. In this way, it could give guidance to further understand the formation mechanism of autapse; in the case of astrocyte modulation, the autaptic driving still plays an important role in regulating the signal exchange between neurons and astrocyte; these results could be helpful for further investigation on collective neuronal network composed of a large number of neurons coupled by astrocytes.

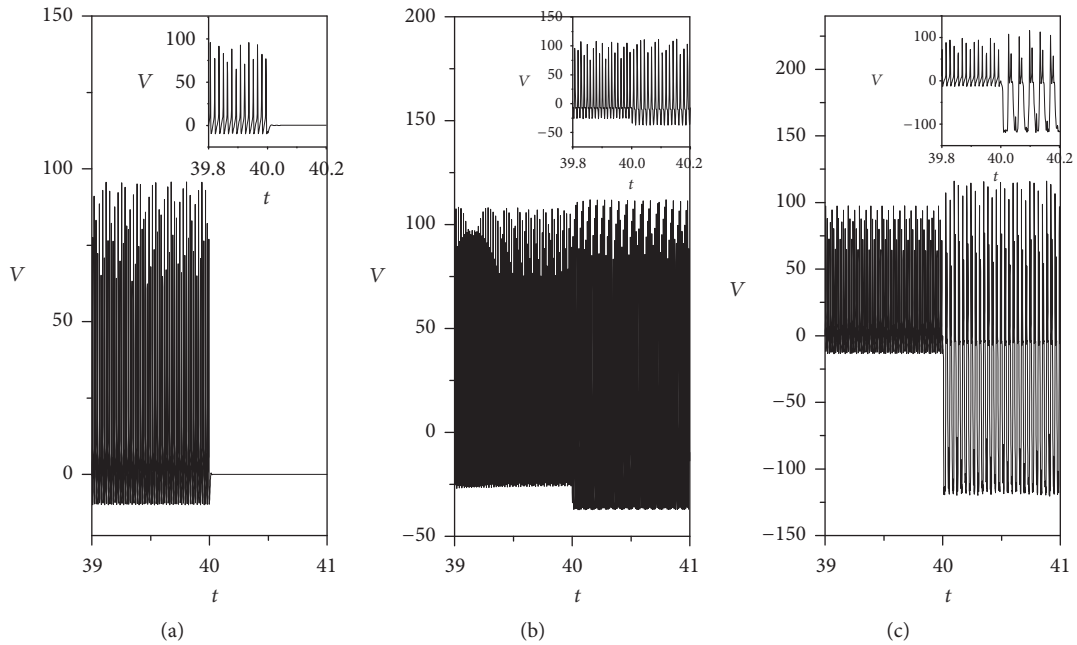

Figure 11: Sampled time series for membrane potential of neuron coupled by astrocypte when autapse driving is considered different time delays at $g_e = -0.5$, for (a) $\tau = 0.1$, (b) $\tau = 6$, and (c) $\tau = 15$. The parameter is set as $r_{IP_3} = 0.2$, and inserted figures are enlarged ones. And the external forcing current regulates the neuron by setting $I_{ext} = 10.0\ \mu$mol/L·cm^2 at $t < 40$ s. The inserted figure is enlarged to show the sampled time series for membrane potential from $t = 39.8$ to 40.2 ms.

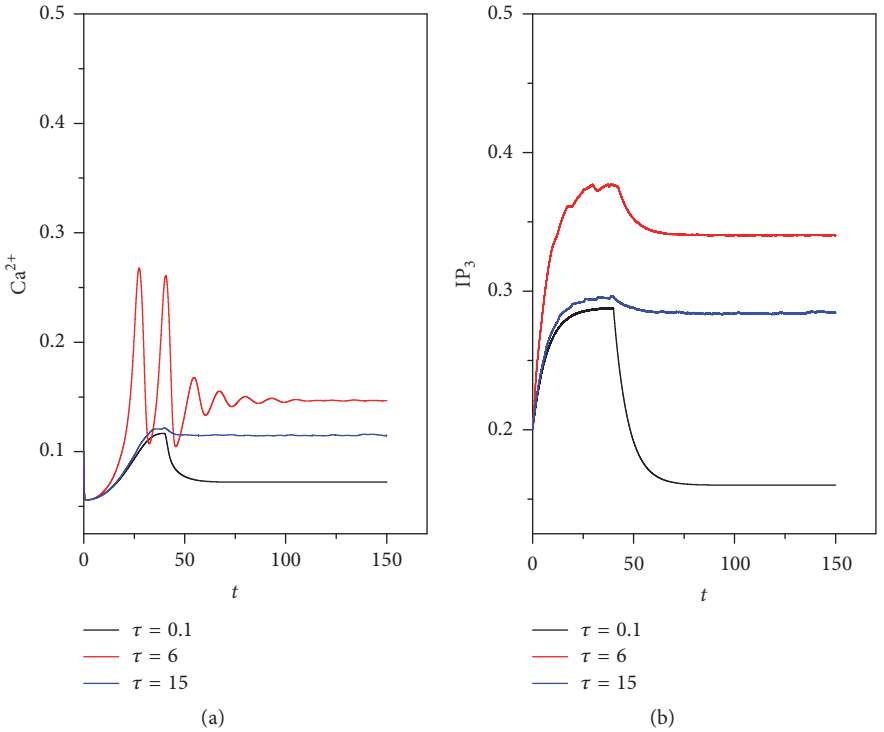

Figure 12: Fluctuation in Ca^{2+} concentration (a) and IP_3 concentration (b) is calculated by applying different time delays in autapse with feedback gain $g_e = -0.5$. The parameter is set as $r_{IP_3} = 0.2$. And the external forcing current regulates the neuron by setting $I_{ext} = 10.0\ \mu$mol/L·cm^2 at $t < 40$ s.

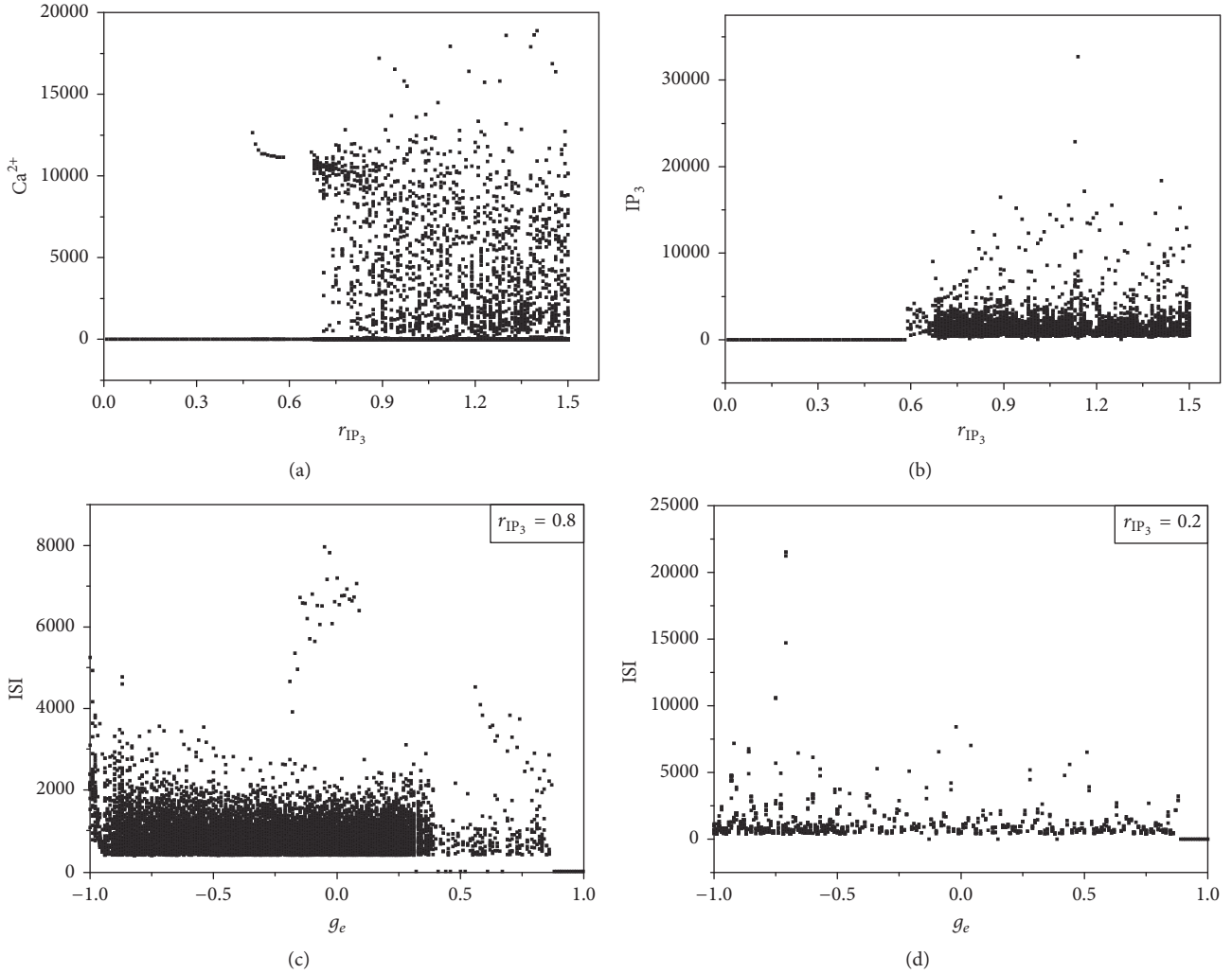

FIGURE 13: Bifurcation diagram for Ca^{2+}, IP_3, and ISI is calculated by setting different r_{IP_3} and g_e, respectively.

4. Conclusions

Based on the Hodgkin-Huxley neuron model, the effects of astrocyte modulation and autapse connection are considered to set an improved neuron-astrocyte-autapse network model so that the biological function of autapse can be discussed. For the isolate neuron models, the dynamical properties in electrical activities have been extensively investigated to be consistent with the experimental series. The biological role of astrocyte is confirmed on the mode transition of electrical activities in neuron coupled by astrocyte, and action potential is controlled by Ca^{2+} oscillation and changes of IP_3 via release of neurotransmitter. Autapse connection to neuron has confirmed that autaptic modulation could be helpful to enhance excitability of neuron under positive feedback while spiking and bursting behaviors can be suppressed by negative feedback in autapse. As a result, it is important to set a complete neuron model so that the biological function of astrocyte and autapse connection can be estimated completely. Based on our proposed new neuron model, it is found that autapse connection can also be helpful to change the oscillating behaviors for Ca^{2+} and also the changes of IP_3; as a result, electric response to external forcing and mode selection in neuron can be self-adaptive.

The main contribution of this submission could be that we proposed a new neuronal network model developed from the biological HH model with the biological effect of astrocyte and autapse connection being considered. It explains the biological function of autapse connection and intrinsic exchange of signal in neuron from molecular level. It could be helpful to investigate the collective behavior of neuronal network composed of large number neurons.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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