

## EFFECTS OF CHEMICAL AUTAPSE ON INVERSE CHAOTIC RESONANCE IN MORRIS-LECAR NEURON MODEL

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**ABSTRACT.** Inverse chaotic resonance is a phenomenon, in which the mean firing rate of a neuron exhibits a minimum depending on the chaotic signal intensity, which emerges in the firing dynamics of neurons. In this study, we have investigated the effects of inhibitory and excitatory autapses on the inverse chaotic resonance phenomenon in Morris-Lecar (ML) neurons. We show that, for proper constant stimulus current, the ML neurons exhibits inverse chaotic resonance phenomenon in the firing dynamics as a function of the intensity of the chaotic activity. In addition, we find that, at low and medium chaotic activity levels, the ML neuron shows multiple-inverse chaotic resonance phenomenon depending on autaptic time delay for low and intermediate autaptic conductances. Finally, we show that, both excitatory and inhibitory autapse augment the firing rate of the ML neuron, this increase is more in the case of excitatory autapse.

### 1. INTRODUCTION

Neurons serve as the building blocks of the nervous system and play a fundamental role in information processing and transmission. The electrical activity occurring in neurons forms the basis for the processing and encoding of information [1–4]. Researchers have proposed various biophysical models to explain information processing and electrical activity in neurons [5–8]. In the literature, it is observed in experimental and theoretical studies that the electrical activity and membrane dynamics in neurons are not deterministic, meaning that neurons do not always generate firing in the same magnitude and timing in response to the same stimulus [9–11]. The influence of various environmental factors on the processing of information in the nervous system has been extensively documented in the literature. For instance, the phenomenon of stochastic resonance (SR) allows for the optimization of the detection and transmission of weak signals in neurons under certain conditions [12–18]. Gutkin et al. observed in their studies that at a constant critical current value applied to neurons, the firing rate approaches zero within an optimal noise range and then increases again for increasing noise levels [19]. This situation represents a phenomenon that is the opposite of stochastic resonance. This phenomenon, widely investigated in the literature, is known as "inverse stochastic resonance" (ISR) [20, 21]. In their work, Yu et al. reported the presence of inverse chaotic resonance (ICR), a phenomenon similar to inverse stochastic resonance,

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emerges under the influence of chaotic activity in the average firing rate of neurons. This effect manifests itself as a kind of squelch in the average firing rate at a given chaotic signal intensity [22].

Neurons communicate through specialized connections called synapses. In the nervous system, there are two main types of synapses: electrical synapses and chemical synapses. Electrical synapses are synapses where communication between neurons occurs directly through electrical signals. In this type of synapse, nerve impulses are transmitted electrically along the cell of a neuron. On the other hand, chemical synapses are synapses where communication between neurons occurs through chemical signals. In this type of synapse, an excitatory signal from one neuron is transmitted to the receptors of another neuron through chemical signals called neurotransmitters. However, it has been documented in the literature that some neurons form synaptic connections between their own soma and dendrites, creating a feedback structure. This unusual biological structure was first reported by Van der Loos and Glaser and named autapse [23]. In studies using different experimental techniques, the presence of autapses in brain regions has been observed [24–26].

Recently, in addition to the existence of autapse, the effects of autapse on neuron behavior have been extensively examined in numerical studies [27–29]. By inter spike interval histogram analysis, Li et al. showed that electrical autapse reduces the number of spontaneous firings in stochastic Hodgkin-Huxley (H-H) neurons [30]. Qin et al reported that autapse triggers spiral wave formation in an organized network of Hindmarsh-Rose (HR) neurons [31]. Wang et al. demonstrated that autapse provides a transition between silence (no firing state) and periodic and chaotic behavioral patterns in the electrical activity of the Hodgkin-Huxley (H-H) neuron [32]. Baysal et al. examined the effects of chemical autapse on weak signal transmission in scale-free networks and revealed that autapse blocks the weak signal transmission at appropriate parameter values [29]. Yilmaz et al., assuming that only the pacemaker neuron in the small world network has an autapse, demonstrated that the transmission of the local activity of the pacemaker neuron through the network increases significantly at appropriate autapse parameters [33].

In the literature, although the inverse chaotic resonance phenomenon has been studied in single neurons and in neuronal network, the effects of autapse on this phenomenon are not investigated neither in single neurons nor in complex neuronal networks. To address this gap in the related research topic, in the current paper, we have analyzed the effects of chemical autapse on the inverse chaotic resonance phenomenon in Morris-Lecar (ML) neurons via numerical simulations. Obtained results show that for proper autaptic parameter values, the chemical autapse regardless of it is excitatory or inhibitory induces M-ICR phenomenon at low and medium chaotic activity cases.

## 2. MATERIALS AND METHODS

The membrane potential dynamics of the Morris-Lecar neuron, which has an autapse and is exposed to a chaotic signal, is given by the following equations [34, 35]:

$$C \frac{dV}{dt} = -g_{Ca} m_{\infty}(V)(V - E_{Ca}) - g_K w(V - E_K) - g_{Leak}(V - E_L) + I_{app} + I_{chaos} + I_{aut} \quad (1)$$

$$\frac{dw}{dt} = \phi \frac{w_{\infty}(V) - w}{\tau_w(V)} \quad (2)$$

$$m_{\infty}(V) = 0.5[1 + \tanh((V - \beta_m)/\beta_w)] \quad (3)$$

$$w_{\infty}(V) = 0.5[1 + \tanh((V - \gamma_m)/\gamma_w)] \quad (4)$$

$$\tau_w(V) = 0.5[\cosh(\frac{V - \gamma_m}{2\gamma_w})]^{-1} \quad (5)$$

The meanings of the symbols used in these equations are given in Table 1:

TABLE 1. **Model parameters**

Parameter	Value
$C$ : Membrane capacitance of the neuron	$20\mu F/cm^2$
$V$ : Membrane potential	variable
$w$ : Slow recovery variable	variable
$g_{Ca}$ : Conductance of fast $Ca^{++}$ current	$4.4\mu S/cm^2$
$g_K$ : Conductance of slow $K^+$ current	$8\mu S/cm^2$
$g_{leak}$ : Conductance of leak current	$2\mu S/cm^2$
$E_K$ : Potassium equilibrium potential	$-84mV$
$E_L$ : Leak current equilibrium potential	$-60mV$
$E_{Ca}$ : Sodium equilibrium potential	$120mV$
$\beta_m$ : the activation midpoint potentials at which the corresponding currents are half activated	$-1.2mV$
$\beta_w$ : slope factors of the activation	$18mV$
$\gamma_m$ : the activation midpoint potentials at which the corresponding currents are half activated	$2mV$
$\gamma_w$ : slope factors of the activation	$30mV$
$\phi$ : maximum rate constant for $K^+$ channel opening	$0.04$
$m_{\infty}$ : the fraction of open calcium channels at steady state	variable
$w_{\infty}$ : the fraction of open potassium channels at steady state	variable
$\tau_w$ : time constant for the activation of potassium channels	variable

The  $I_{app}$  current given in Equation 1 represents the constant stimulation current injected externally.  $I_{aut}$  represents the autapse current arising from the chemical autapse of the ML neuron and is expressed by the equation given below.

$$I_{aut} = -\kappa(V(t) - V_{syn})S(t - \tau) \quad (6)$$

$$S(t - \tau) = 1/1 + \exp(-k(V(t - \tau) - \theta))$$

where  $V(t)$  represents membrane potential of The ML neuron and  $\kappa$  is autaptic conductance,  $V_{syn}$  is reverse synaptic potential and  $\tau$  is autaptic delay. When the reverse synaptic potential is  $V_{syn}=10mV$ , the autapse shows excitatory behavior, while when  $V_{syn}=-65mV$ , the autapse shows inhibitory behavior. The

other parameters's values are set  $k= 8$  and  $\theta= 0.25$  [36]. The chaotic current  $I_{chaos}$  whose source is assumed to be the chaotic activity of peripheral neurons, is calculated as  $I_{chaos} = \epsilon.x$ , here  $\epsilon$  represents the chaotic current intensity and  $x$  is the chaotic signal source. In this study, the Lorenz system was used as the chaotic signal source. The equations representing this system are given below [37].

$$dx/dt = \sigma(y - x) \quad (7)$$

$$dy/dt = px - y - xz \quad (8)$$

$$dz/dt = xz - \lambda z \quad (9)$$

where chaotic system parameters are set as  $\beta = 8/3$ ,  $\sigma = 10$ ,  $p = 28$ . The initial values for the  $(x, y, z)$  variables are determined randomly. On the other hand, initial values of membrane potential variable  $V$  and slow recovery variable  $W$  were randomly determined uniformly between related intervals. After distracting 1 second transition time, the firing frequency is calculated during  $\delta = 5s$  simulation time. 20mV is assumed as a firing threshold in the membrane potential of neuron in deciding whether a spike is present or not. It is accepted that, at each passing of membrane potential with positive slope from this threshold, a spike occurs. This procedure is repeated  $N = 1000$  times and the average is taken to obtain the mean firing rate (MFR). Calculation of mean firing rate (MFR) is given below:

$$MFR = \frac{1}{N\delta} \left( \sum_{k=1}^N N_k^{spikes} \right) \quad (10)$$

where  $N_k^{spikes}$  is the total number of spikes produced by the neuron in  $kth$  realization.

### 3. RESULTS

**3.1. Inverse Chaotic Resonance in Morris Lecar neuron model.** In this section, we investigate the effect of chaotic activity on the firing rhythms of single ML neuron. To do this, firstly, the time-dependent change of membrane potentials of ML neuron at different chaotic activity levels are given in Figure 3.1.

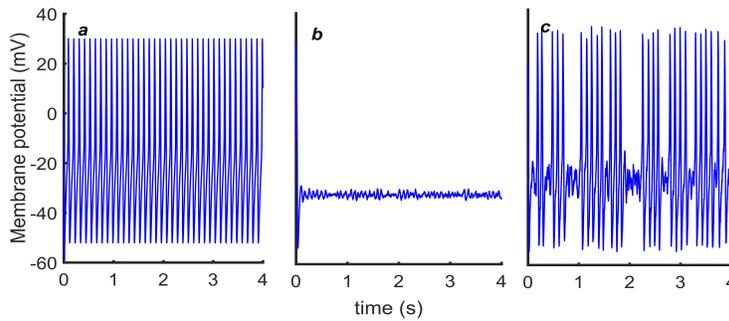


FIGURE 1. Time dependence of membrane potential of ML neuron for different chaotic signal intensities, a)  $\epsilon = 0.01$ ; b)  $\epsilon = 0.5$ ; c)  $\epsilon = 2$  ( $I_{app} = 89\mu A/cm^2$ ).

It is seen in Figure that, at a low chaotic current intensity ( $\varepsilon = 0.001$ ), the neuron fires continuously under the effect of constant stimulus current  $I_{app}$  and has a constant firing rate (Figure 3.1a). For the chaotic current intensities of moderate level, for example  $\varepsilon = 0.5$  (Fig.1b), although the neuron initially emits one spike due to the initial conditions effect, then it emits no spike and remains silent due to the effects of the increasing chaotic activity. At further increase in the chaotic current intensity, as the neuron in Fig.1c in which  $\varepsilon = 2$ , the neuron stays silent first, and then, it emits spikes in some instants, or vice versa, first emits spikes, and then stays silent, and this pattern of activity, known as burst type firing, emerges continuously in the electrical activity of the ML neuron. Eventually, the neuron has a constant, non-zero firing rate. From these results presented in Figure 3.1, it can be deduced that the chaotic signals can induce inverse chaotic resonance phenomenon (ICR) in ML neurons.

To investigate whether the chaotic activity induces the ICR phenomenon, the average firing frequency of the ML neuron for different constant stimulation currents ( $I_{app}$ ) is given as a function of the chaotic current intensity in Figure 2.

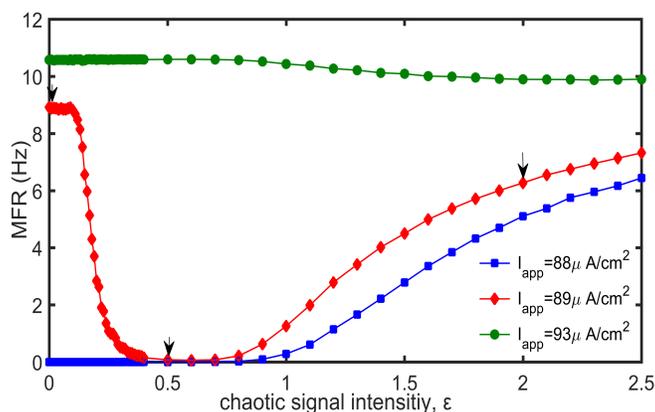


FIGURE 2. The dependence of average firing rate of ML neuron on the chaotic signal intensity for different  $I_{app}$  values

When the constant excitation current  $I_{app} = 88 \mu A/cm^2$ , neither the chaotic signal level nor the applied constant current  $I_{app}$  is enough to induce spiking activity in ML neuron, and consequently the neuron is in silent mode. In addition with the increase in chaotic signal intensity beyond  $\varepsilon > 1$ , the neuron starts to fire and has an increasing firing rate. On the other hand, for  $I_{app} = 93 \mu A/cm^2$ , the neuron produces spikes at an almost constant firing rate and is unaffected by the chaotic signal levels. But, when we choose  $I_{app} = 89 \mu A/cm^2$ , some different firing patterns emerge. It is observed that the neuron is not affected by chaotic signals at a certain level ( $\varepsilon < 0.1$ ) and maintains its firing rate at a constant value of 9 Hz. However, as the chaotic signal intensity increases, the firing frequency of ML neuron decreases swiftly and within a certain range of chaotic signal intensity the neuron becomes completely silent. Then, as the chaotic signal intensity further increases, the neuron starts to fire again and reaches a certain firing rate. These results obtained for  $I_{app} = 89 \mu A/cm^2$  showed that the inverse chaotic resonance effect can

occur in the ML neuron for the appropriate  $I_{app}$  value. That is, under a certain stimulus current value, the neuron is observed to exhibit the inverse chaotic resonance phenomenon depending on chaotic signal level. Finally, the ICR effect was not observed at smaller and larger  $I_{app}$  values, indicating that this effect largely depends on the excitability level of the ML neuron.

The mechanism of the occurrence of this phenomenon can be explained by the bifurcation diagram of the deterministic Morris Lecar neuron depending on the  $I_{app}$  current [35]. For  $I_{app}$  excitation current values of  $88.29\mu A/cm^2 < I_{app} < 93.86\mu A/cm^2$ , the ML neuron has a bistable attractor. One of them is the fixed point, which represents the resting state, and the other is the limit cycle attractor, which represents the spike formation in the neuron. The membrane potential shows chaotic fluctuations, creating loops around these attractors in certain orbits, and in appropriate cases, it remains under the influence of one of these attractors. Fluctuations caused by the chaotic signal in the range of the externally applied  $I_{app}$  current can change the membrane potential from firing to silence, or vice versa, from silence to firing. This triggers to emerge the ICR effect in the ML neuron.

**3.2. Effects of excitatory autapse on inverse chaotic resonance.** In this part of the study, by assuming that the ML neuron has a excitatory chemical autapse, we have analyzed the effects of autapse on the ICR effect in ML neurons. In order to show autapse's effect, first, we keep constant the excitation current as  $I_{app} = 89\mu A/cm^2$ , as the ICR phenomenon is present, and then depending on autaptic time delay  $\tau$ , we calculate the MFR for three different chaotic signal intensities, representing low, intermediate and strong chaotic activity levels, which are marked black arrows in Figure 2. The results obtained for weak chaotic signal activity ( $\varepsilon = 0.001$ ) and four different autaptic conductance values  $\kappa$  are given in Figure 3.

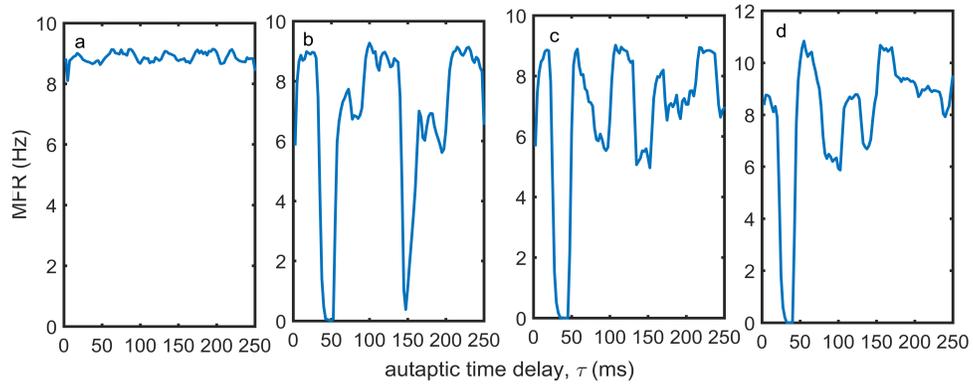


FIGURE 3. Variation of the mean firing frequency (MFR) of the ML neuron with chemical excitatory autapse according to the autaptic time delay ( $\tau$ ) at different autapse conductance values: (a)  $\kappa = 0.01$ , (b)  $\kappa = 0.1$ , (c)  $\kappa = 0.5$ , (d)  $\kappa = 0.9$  ( $\varepsilon = 0.001$ ,  $I_{app} = 89\mu A/cm^2$ ).

When we examine Figure 3, for low autaptic conductance level  $\kappa = 0.01$  (Figure 3a), the neuron is not affected by  $\tau$  and has approximately  $9Hz$  firing frequency. At a low-intermediate value of  $\kappa = 0.1$ , it exhibits some minimums almost with zero firing rate and maximums with around  $9Hz$  depending on  $\tau$ , implying the occurrence of multi-ICR (M-ICR) phenomenon in the firing activity of ML neuron. The ML neuron exhibits complete silent state in firing dynamics at around  $\tau = 50, 150ms$  which are closely related to the integer multiple of the half of the intrinsic firing period ( $T_{int} \cong 110ms$ ) of ML neuron. In addition, at higher autaptic conductance values (Figure 3c, Figure 3d), it is seen that the M-ICR phenomenon gradually loses its effect depending on increasing autaptic time delay, and the minima reflecting the silent mode in the firing dynamics of the ML neuron disappear to some extent except for the first minima.

The effects of excitatory autapse at an intermediate chaotic activity level are given in Fig.4. As can be seen in Figure 4a, for an intermediate chaotic activity intensity  $\varepsilon = 0.5$ , the MFR of ML neuron is consistent with the result obtained in Figure 2 (at  $\varepsilon = 0.5$  in red curve) at low  $\kappa$ , except for some small peaks. But, when the autaptic conductance is increased to  $\kappa = 0.1$ , the neuron starting from silent mode shows patterns such as silence-firing-silence-firing, which is a clear indication for M-ICR phenomenon, depending on the autaptic time delay. But, for relatively strong autaptic conductance values (Figure 4c, 4d), The M-ICR phenomenon weakens due to strong autaptic effects.

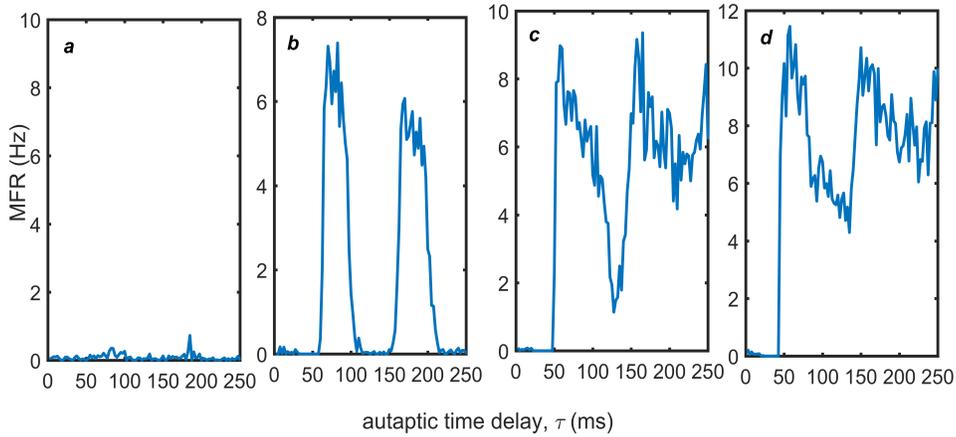


FIGURE 4. Variation of the mean firing frequency (MFR) of the ML neuron with chemical excitatory autapse depending on the autaptic time delay ( $\tau$ ) at different autapse conductance values:(a) $\kappa = 0.01$  , (b) $\kappa = 0.1$ , (c) $\kappa = 0.5$ , (d) $\kappa = 0.9$  ( $\varepsilon = 0.5, I_{app} = 89\mu A/cm^2$ ).

Finally, for excitatory autapse, we investigate its effects at high level of high chaotic activity in Figure 5. It can be seen in Figure 5 that when autaptic conductance is low  $\kappa = 0.01$  the ML neuron fires around the firing rate of the without autapse case. If the  $\kappa$  is increased to higher values (Figure 5b, Figure 5c and Figure 5d) the neuron's firing rate increases up to  $15Hz$  which is two fold increase in firing rate. Also, the MFR curves resemble the curves in the M-ICR phenomenon, but complete quietness in the

firing activity of the ML neuron does not occur. From the above results obtained for excitatory autapse, it can be deduced that, for weak and intermediate chaotic activity levels, the presence of excitatory autapse with moderate autaptic conductance levels can induce the M-ICR phenomenon in the firing activity of the ML neuron. In addition, regardless of the chaotic activity level, although strong autaptic conductance can increase the firing rate of the neuron, it prevents the occurrence of the M-ICR phenomenon.

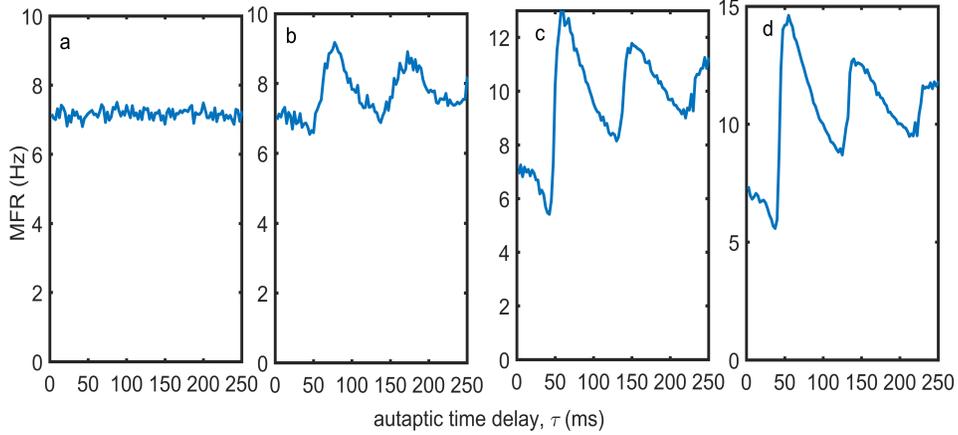


FIGURE 5. Variation of the mean firing frequency (MFR) of the ML neuron with chemical excitatory autapse according to the autaptic time delay ( $\tau$ ) at different autapse conductance values:(a) $\kappa = 0.01$  , (b) $\kappa = 0.1$ , (c) $\kappa = 0.5$ , (d) $\kappa = 0.9$  ( $\varepsilon = 2$ ,  $I_{app} = 89\mu A/cm^2$ ).

**3.3. Effect of inhibitory autapse on inverse chaotic resonance.** In the present paper, finally, we have investigated the effects of inhibitory autapse on the ICR phenomenon in ML neurons. For this purpose, we consider that the ML neuron has an inhibitory autapse instead of excitatory one used in previous case. Then, following the way used in the case of excitatory autapse, we calculate the MFR of the ML neuron for weak, intermediate and strong chaotic activity cases. The results obtained are shown in Figure 6.

When analyzed Figure 6, for weak chaotic activity case  $\varepsilon = 0.01$  (top panels of Figure 6), if the autaptic conductance is small (top left panel in Figure 6), there is no autaptic effects on the MFR of ML neuron, and the ML neuron has the firing rate similar to without autapse case. But, when  $\kappa$  is increased to  $\kappa = 0.2$  (top-middle panel in Figure 6), due to the inhibiting effect of autapse the neuron becomes silent at some  $\tau$  values. Besides, the autaptic time delay induced M-ICR phenomenon occurs. With the further increase in  $\kappa$  ( $\kappa = 0.7$ ), the M-ICR effect almost disappears. In the case of intermediate chaotic activity case  $\varepsilon = 0.5$  (middle panels in Figure 6 with red colored curves), the ML neuron is in silent mode at small  $\kappa$  due to too weak autaptic effects. When the  $\kappa$  is increased to  $\kappa = 0.2$ , due to increased autaptic effects some peaks emerge on the MFR of the ML neuron depending on  $\tau$ . This pattern with multiple peaks in the MFR of ML neurons is a concrete evidence of the M-ICR phenomenon in the firing activities of the neuron. For strong autaptic conductance value ( $\kappa = 0.7$ ), the silent mode corresponding to approximately

zero firing rate disappears at high values of autaptic time. This result implies that under strong autaptic effects, the M-ICR phenomenon can not occur in the firing activity of the ML neuron. On the other hand, for high chaotic activity case ( $\varepsilon = 2$ ) at which the neuron without autapse produces spikes approximately at the frequency of  $6.5Hz$ , if the  $\kappa$  is low, that is,  $\kappa = 0.01$ , the neuron continuous to fire without being affected by the autapse. However, for medium and high  $\kappa$  cases, although small amplitude fluctuations occur in the MFR of the neuron, no strong evidence of M-ICR phenomenon is observed. From all the results obtained for inhibitory autapse, we can conclude that, on the one hand an inhibitory autapse, with proper time delay and conductance values, can induce the M-ICR phenomenon at low and medium levels of chaotic activity. On the other hand it increases the firing rate of the ML neuron to some extent.

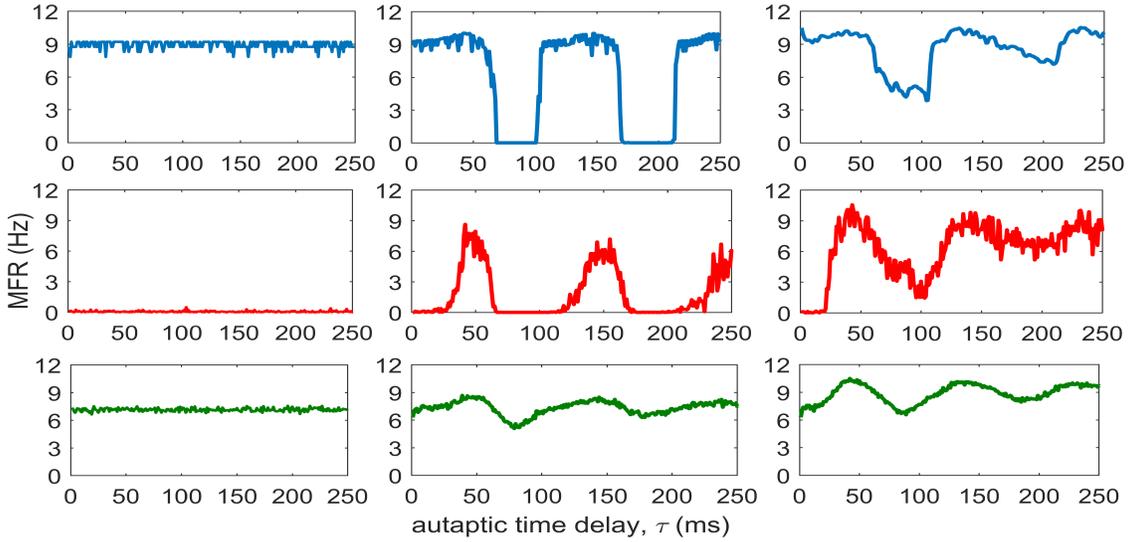


FIGURE 6. The mean firing frequency (MFR) of the ML neuron with chemical inhibitory autapse under different chaotic current intensities: Top panels  $\varepsilon = 0.001$ , middle panels  $\varepsilon = 0.5$ , bottom panels  $\varepsilon = 2$  with the various autaptic conductances: left column  $\kappa = 0.01$ , middle column  $\kappa = 0.2$  and right column  $\kappa = 0.7$  ( $I_{app} = 89\mu A/cm^2$ ).

#### 4. CONCLUSIONS

Autapse is unusual synapse which forms between the dendrite and soma of the same neuron. After the discovery of its presence in different brain regions, its effects on neuronal dynamics have been aroused curiosity in the neuroscience community. Therefore a lot of studies some in numerical other are experimental are dedicated to investigate the effects of autapse on neuron dynamics. In the present paper, we study the effects of chemical autapse, by considering its excitatory and inhibitory types separately, on the ICR phenomenon. In excitatory autapse case, for weak chaotic activity level and at medium autaptic

conductance values, we found that when the autaptic time delay equals to integer multiple of half the intrinsic firing period of ML neuron, the presence of autapse causes the neuron stop firings, and by this way triggers the occurrence of M-ICR effect. In moderate chaotic activity level and at medium autaptic conductances, the presence of excitatory autapse induces firings in silent neuron when the autaptic time delay is proper values, and thus triggers the emergence of M-ICR phenomenon. Also, we obtained that this M-ICR effects gradually disappears as the autaptic conductance is increased regardless of the chaotic activity level. In case of inhibitory autapse, it is revealed that, for high chaotic activity level, the presence of inhibitory autapse does not have prominent effects on the firing dynamics of the ML neuron and not to induce any ICR effect. But, for low and moderate chaotic activity levels, the presence of autapse has distinct effects on the ML neuron dynamics, and causes the appearance of M-ICR phenomenon for medium autaptic conductances. In low chaotic activity level, it leads to the ML neuron, which fires a fixed firing rate, stop firings at some autaptic time delays and thus, induce the emergence of the M-ICR effect. But, in intermediate chaotic activity levels, the presence of inhibitory autapse gives rise to firing in silent neuron at some autaptic time delays and triggers the occurrence of autaptic time delay induced M-ICR phenomenon.

It has prominent importance of understanding the single neuron dynamics in different realistic conditions, since the single neuron is the basic building blocks of complex neuronal networks in brain. On the other hand, it is known that spiking neural networks (SNNs) mimics natural neuronal networks in the brain in a more realistic way than the classic artificial neural networks (ANNs) [38]. In this neuronal networks, the computation unit is a realistic neuron instead of artificial neuron or activation function in classical ANNs. In this context, Zhao et al. have investigated the performance of a deep SNN with autapse on standard data sets such as MNIST, CIFAR10, F-MNIST and N-MNIST, and obtained state-of-the-art performance [39]. Therefore, a clear understanding of the single neuron dynamics is of significant importance in designing more powerful and accurate SNNs model in solving real world problems with the approach of deep learning.

We, here, investigate ICR phenomenon in single ML neuron. However, in the brain, neurons are found in communities with different form of network topologies. Therefore, the investigation of the presented phenomenon in the complex neural networks is worthy. Thus, we want to put our efforts to investigate the ICR phenomenon in complex networks such as scale-free and small-world neural networks, in future studies.

#### DECLARATIONS

- **Conflict of Interest:** The authors declare no competing financial interests.

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