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# Modeling of epilepsy based on chaotic artificial neural network

Shirin Panahi[a], Zainab Aram[a], Sajad Jafari[a], Jun Ma[b,*], J.C. Sprott[c]

[a] Biomedical Engineering Department, Amirkabir University of Technology, Tehran 15875-4413, Iran
[b] Department of Physics, Lanzhou University of Technology, Lanzhou 730050, China
[c] Department of Physics, University of Wisconsin - Madison, Madison, WI 53706, USA

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ABSTRACT

Epilepsy is a long-term chronic neurological disorder that is characterized by seizures. One type of epilepsy is simple partial seizures that are localized to one area on one side of the brain, especially in the temporal lobe, but some may spread from there. GABA (gamma-aminobutyric acid) is an inhibitory neurotransmitter that is widely distributed in the neurons of the cortex. Scientists recently discovered the basic role of neurotransmitters in epilepsy. Synaptic reorganizations at GABAergic and glutamatergic synapses not only enable seizure occurrence, they also modify the normal information processing performed by these networks. Based on some physiological facts about epilepsy and chaos, a behavioral model is presented in this paper. This model represents the problem of undesired seizure, and also tries to suggest different valuable predictions about possible causes of epilepsy disorder. The proposed model suggests that there is a possible interaction between the role of excitatory and inhibitory neurotransmitters and epilepsy. The result of these studies might be helpful to discern epilepsy in a different way and give some guidance to predict the occurrence of seizures in patients.



## 1. Introduction

Epilepsy is a relatively widespread disease from which about 1% of people in the world are suffering [1–4]. Roughly 50% of adults with active epilepsy have at least one other medical condition including depression, anxiety, dementia, migraine, heart disease, peptic ulcers,... [5–17]. This disease is characterized by episodes of spontaneous seizures. This abnormal behavior is the result of defective or excessive activity of nerves which are located on cortical or other tissues in the brain. Causes of epilepsy differ depending on the age of the patient [18], and are unknown for about half of epileptic patients [19]. Genetic mutations [20–23], changes in structure of the brain and head injuries [24–27], autism spectrum disorder [28–30], infections [31,32], strokes [33,34] and tumors [35–37], are some of them. The exact cause is yet not certain [19]. Therefore, understanding the mechanism of this disease is of great importance. Computational modeling plays an important role in gaining an insight into this disease.

There is growing evidence that research on brain functions and their modeling benefit by combining classic neuroscience with nonlinear dynamics [38–41]. There are also some strong claims about chaotic behavior in many biological systems, especially in the human brain [42–44]. The dynamics in brain signals called electroencephalograms (EEGs) appear to have random features, but there are some hidden patterns in the signals [44,45]. Moreover, these signals are very sensitive to any changes in the brain's parameters [46]. Such behavior makes these systems similar in some aspects to chaotic systems [43,47]. The brain, like a chaotic system, does not reach equilibrium after a transient time, but it is always going back and forth between different states. In the research of Freeman et al. [48], the information in the odor sensory part of the brain indicates the existence of a pattern that could be discriminated whenever there was a change in the odor environment. Further dissection of the experimental data led to the conclusion that the activity of the olfactory bulb is chaotic and may switch to any desired perceptual state at any time [49]. These states are considered equivalent to attractors in dynamical systems. The authors claimed that some of the activities in mammalian brain dynamics are governed by strange attractors, or in simpler words, show chaotic behavior.

However, sometimes the neural activity in the brain can change from chaotic to periodic. These changes are mostly due to an abnormality or disorder, like some changes in EEG caused by attention deficit disorder [50] or an epileptic seizure [51]. When the brain's behavior starts to change, either because of a disease or other reasons, a bifurcation occurs. Bifurcation is a sudden change in the dynamics of a system when a parameter of the system

* Corresponding author.
*E-mail address:* hyperchaos@163.com (J. Ma).

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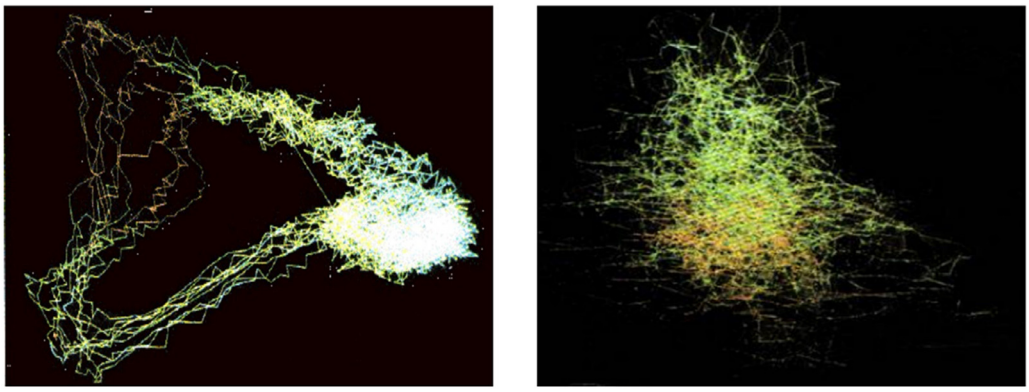


**Fig. 1.** (**a**). Phase space view of the EEG taken from a rat during seizure. (**b**). Phase space view of the EEG taken from a healthy and awake, but resting motionless rat [49].

changes [52]. When a brain working in a normal state (chaotic mode) suddenly undergoes seizure (periodic mode), a bifurcation occurs [53,54]. A trace of an EEG signal of a rat is shown in Fig. 1, which is a comparison with the EEG signal of a healthy and awake rat (Fig. 1(b)) with the EEG of epileptic rat during the seizure (Fig. 1(a)). Fig. 1a illustrates a rather periodic behavior and provides an example of the claim in Ref. [48].

Sometimes when a dynamical system is in its chaotic mode, it bifurcates to a periodic behavior by changing the control parameter. A further change in the parameter restores the chaos. This is called a periodic window in the midst of chaos. In a similar way, the healthy brain has a chaotic activity but epileptic seizure associated with excessive harmonic synchronization of large neuronal populations leads to a hypersynchronous state causing the brain to undergo a bifurcation that switches it from chaotic (normal) to periodic (abnormal).

In previous studies, different epileptic models were proposed in which various scientific views of epilepsy were presented. For instance, Takeshito et al. [55] modified Wilson's neuron model [56] to model the epileptic seizure dynamics by transition between multistable states. They claim that changes in field potential amplitude and frequency during the course of a seizure may be explained by noise-induced transitions among multistable states. Larter et al. [57], developed a lattice model with a type of coupled ordinary differential equations by modifying the Morris–Lecar neuron model [58]. Larter's model describes mechanisms for lack of inhibition and an alteration in conduction time, both of which seem necessary for the development of a realistic seizure model. On the other hand, some researchers argued that models could be developed from Poincare maps. They used the electroencephalographic (EEG) recordings to find the time interval between spikes as a characteristic variable and plotted the time delay interpeak interval (IPI) to study seizure. After that, a one-dimensional map was developed by fitting a polynomial function to the return map obtained by the data [59,60].

In this study, we base our main model on an artificial network since it is similar to the real brain structure. On the other hand, the dynamical and chaotic features of brain behavior are of great importance [61,62]. Therefore, the novelty of this model lies in the fact that it is not only a simple artificial neural network, but it also depicts the chaotic features of the disease.

The rest of the paper is as follows: Section 2 contains a brief review of the biological and physiological mechanisms associated with epilepsy and seizure. Section 3 introduces the proposed model for different behaviors of the brain in a natural versus seizure state. After that, Section 4 illustrates the results and discusses the model. Finally, Section 5 gives conclusions.

## 2. The physiological background

Epilepsy emerges from the improper dynamics of neural networks [63]. A neural network is formed by several types of cells in the nerve systems that are interact with each other through different mechanisms such as synapses [64]. Its activities are greatly dependent on the extra cellular environment, while any modification in its structure can induce epilepsy [65]. There are many known types of epilepsy, but partial onset epileptic seizures (also called focal or local seizures) is the most common form of epilepsy [66–71]. It can be distinguished from the others by some unique seizure features (e.g. seizure initiation is from a particular portion of brain tissue (seizure focus or foci) [72,73] and propagates to the other parts but is limited to a specific part of the brain especially the temporal lobe, which is most likely to be resistant to seizure treatment drugs [74–79]). The temporal lobe is the fourth major lobe of the cerebral cortex in the mammalian brain. This complex part of the brain deals with many 'higher function', behaviors and abilities, including hearing, speech, memory, emotions, learning. All these higher functions will be affected if the temporal lobe does not function well [80,81]. The temporal lobe also plays an essential role in the excitation/inhibition balance of information processing [82]. In patients with epilepsy, temporal lobe dysfunction decreases the inhibitory power of the brain or increases the excitatory function of brain [83–87]. It has been reported that some neurotransmitters called GABA (gamma-aminobutyric acid) and glutamate have a significant influence on cortex function [88]. GABA is an inhibitory and glutamate is an excitatory neurotransmitter that is widely distributed in the neurons of the cortex [89]. Synaptic reorganizations at GABAergic and glutamatergic synapses not only enable seizure occurrences, they also modify the normal information processing performed by these networks [90–92]. In the following section, we propose a novel model of temporal lobe epilepsy by using different neurotransmitters as the main bifurcation parameters.

## 3. The proposed model

In this section, we introduce a novel nonlinear neural network [93–96] to model the switching behavior of the brain in epileptic patients (Fig. 3). This model is a network representing different parts in the brain that are interconnected in order to depict the interaction that occurs during seizures. A multilayer perceptron (MLP) artificial neural network (ANN) is used in this model. The main network consists of several sub-networks which were developed by Baghdadi et al. in Ref. [50]. This sub-network or the basic function of the main network is a single layer nonlinear network

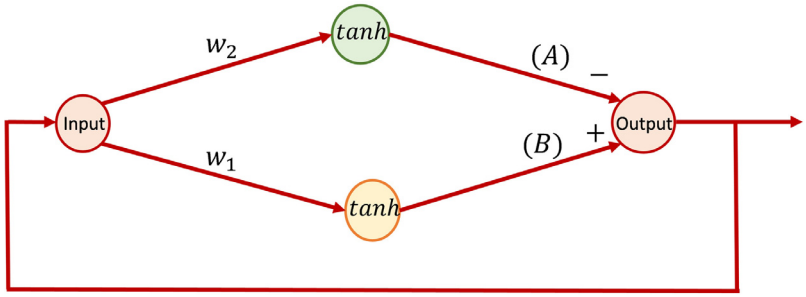


**Fig. 2.** Basic sub-network model (*BJ*), upper part is an inhibition segment because of the negative sign of (*A*), and the lower part is an excitatory section.

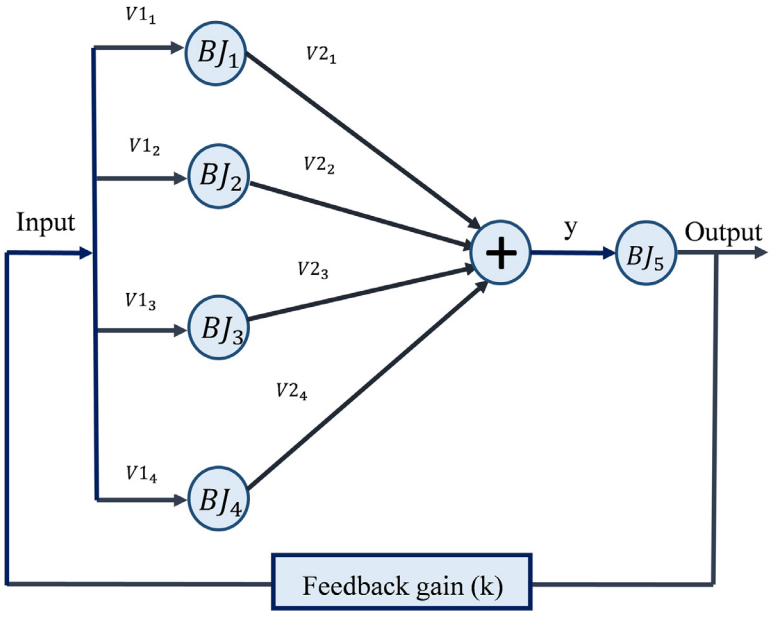


**Fig. 3.** Multilayer perceptron (MLP) artificial network.

illustrated in Fig. 2. This sub-network will be called the BJ network (Baghdadi–Jafari), and its corresponding mathematical formula is in Eq. (1). It should be noted that all the BJ's parameters are set according to Ref. [50].

$$BJ: out(n+1) = B \times \tanh(w_1 \times out(n)) - A \times \tanh(w_2 \times out(n)) \quad (1)$$

In this model, a hyperbolic tangent is the activation function of two neurons whose outputs are respectively multiplied by B and A [50]. However, the output of the upper part enters the output neuron with a negative sign that models the inhibition, and the output of the lower part enters the output neuron with a positive sign that models the excitation [50]. All coefficients (*A*, *B*, $w_1$ and $w_2$) are associated with the brain synapses' weights that are regulated by the release of different neurotransmitters [50]. Hence, the values of A can be correlated with the amount of inhibitory or GABA neurotransmitter and the values of B can be associated with the amount of excitatory or Glutamate neurotransmitter.

The proposed model for seizure contains four interacting *BJ* parts in the first layer. (Four is a number chosen for simplicity. One can use more neurons, but there will be no significant difference in the results). $V1_i$ (i = 1, 2, 3, 4)are the input weights. They multiply to the input and go to the each *BJ*s as an input. Each part is connected to the next layer with a certain weight that indicates the excitatory or inhibitory behavior of synaptic neurotransmitters ($V2_i$).The values of the parameters determine whether the part is functioning normally or is stuck in a periodic state. The graphical illustration is in Fig. 3, and its corresponding mathematical formula is shown in Eq. (2).

$$\begin{cases} y = \sum_{i=1}^{N=4} V2_i \times [B_i \times \tanh(w_{1i} \times V1_i \times (k * out(n))) \\ \quad -A_i \times \tanh(w_{1i} \times V1_i \times (k * out(n)))] \\ out(n+1) = B_5 \times \tanh(w_{15} \times y) - A_5 \times \tanh(w_{25} \times y) \end{cases} \quad (2)$$

## 4. Results and discussion

As it was mentioned before, the cause is unknown for about half of the patients with epilepsy and depends on many different factors. We suggest in this study, that the issues in the foci of seizure (or the place the seizure begins [72,73]) can be caused by one of these three malfunctions: a problem in receiving the input information, a problem in processing the information, or problems in delivering the output information to the target. All of the above reasons can cause a periodic behavior in the foci which can spread to other parts of the network.

Abnormal epileptic behavior as explained before could result from increasing the excitatory or reducing in inhibitory portion [83–87]. Also, we discussed the importance of excitatory and inhibitory neurotransmitters in the processing of the propagating information. Therefore, this malfunction can be modeled by an increased excitation or decreased inhibition. This analysis is done first by assuming a part of our model is a foci and considering its inhibitory coefficient as the bifurcation parameter ($A_4$) while the other parameters are fixed (because they are healthy). In other

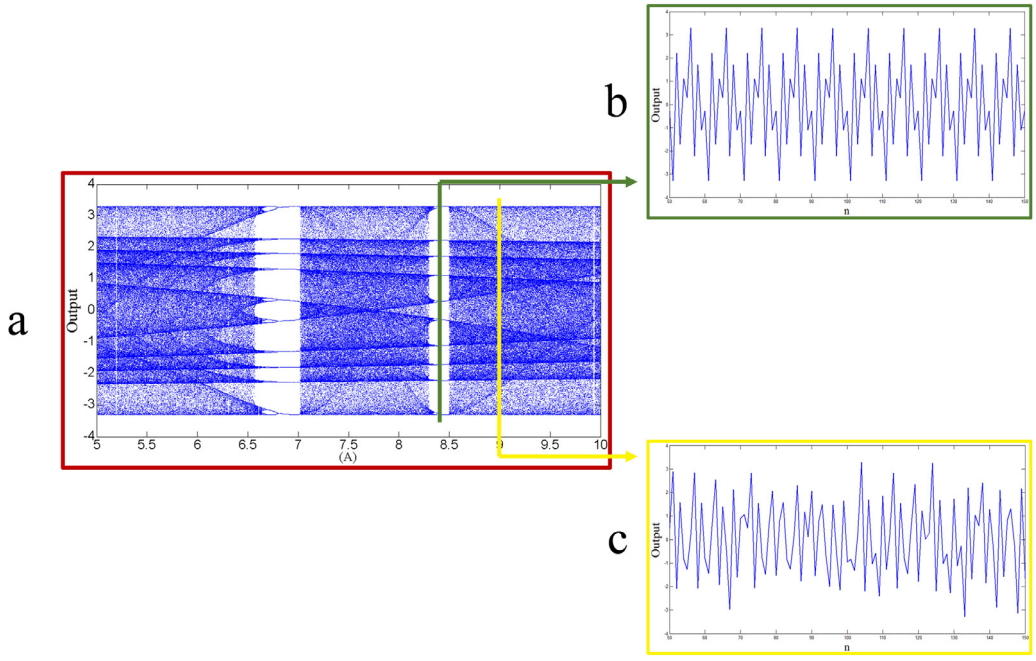


**Fig. 4.** (**a**). Bifurcation diagram of the proposed neural network for different values of $A_4$ (inhibitory parameter of $BJ_4$, while other parameters are set at their normal values. (**b**). Neural network output at $A_4 = 8.5$ (periodic) c. Neural network output at $A_4 = 9$ (chaotic).

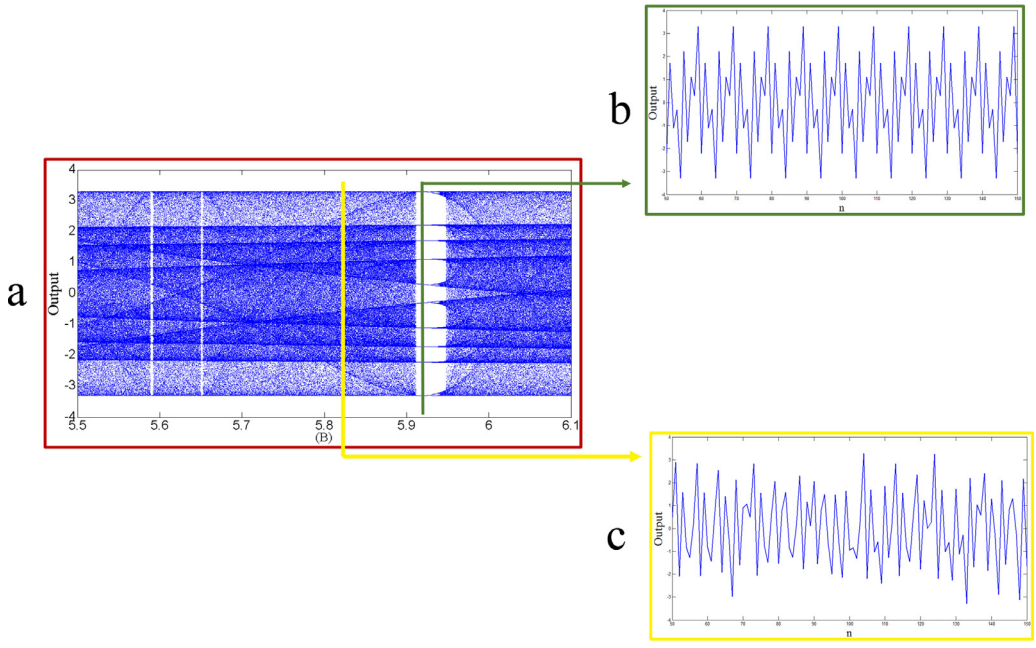


**Fig. 5.** (**a**). Bifurcation diagram of the proposed model for different values of $B_4$ (excitatory parameter of $BJ_4$), while other parameters are set at their normal values. (**b**). Neural network output at $B_4 = 5.92$ (periodic) (**c**). Neural network output at $B_4 = 5.821$ (chaotic).

words, only one of the BJ units is malfunctioning, and therefore it is playing the role of the foci. Thus the bifurcation diagram plotted in Fig. 4 is based on only the parameter related to inhibition of that unit, and the other parameters representing other units are in the normal range. Therefore, hyperactivity will propagate from the foci (malfunctioning unit) to other parts of the network and disturb its overall activity.

Note that the goal of this study is not to model any of the real values of the parameters or output time series in a quantitative biological sense. However, the aim is to show how some small changes in the parameter values can lead to a completely different and undesired behavior of the brain. The normal brain automatically regulates these weights every moment in every condition.

We set the parameter value for normal brain function ($BJ_{1\text{-}3\&5}$) as follows: $A_i = 9$, $B_i = 5.821$, $w_{1i} = 1.487$, $w_{2i} = 0.2223$, $k = 1$, $V1_i = 0.2$, $V2_i = 0.5$. The bifurcation diagram of this neural network for different values of $A_4$ and $B_4$ when the rest of the parameters have normal values is plotted in Fig. 4 and Fig. 5, respectively.

Parameter $A_4$, as explained before is representing the GABA or inhibitory neurotransmitters in $BJ_4$. When the inhibitory neurotransmitter is decreased, the brain is more likely to undergo a seizure. Therefore, we expect to see the brain model stuck in a periodic window if we change the parameter $A_4$from its normal

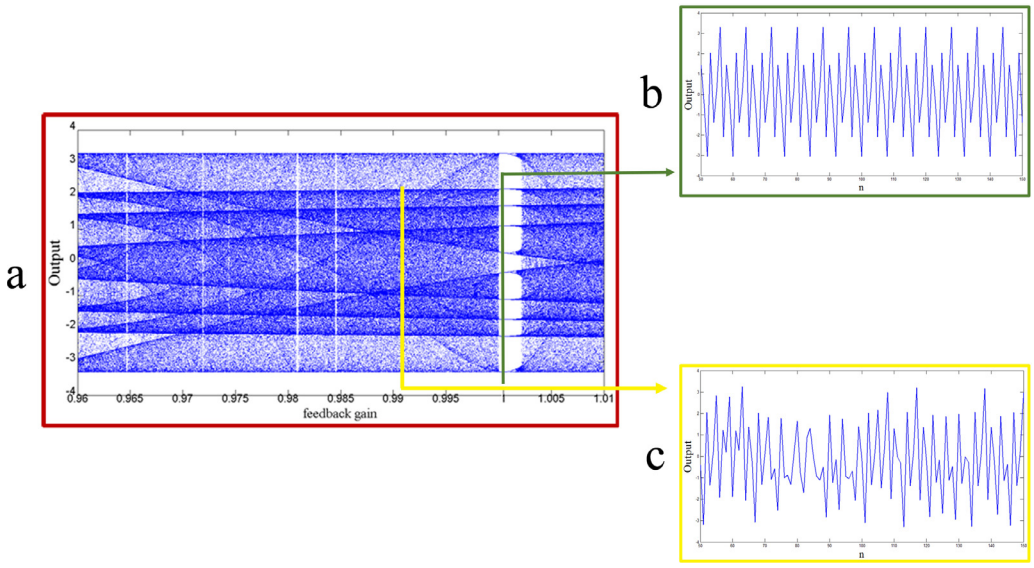


**Fig. 6.** (**a**). Bifurcation diagram of the proposed model for different values of feedback gain, $A_i = 9$(except $A_4 = 8.5$), $B_i = 5.821$, $w_{1i} = 1.487$, $w_{2i} = 0.2223$, $V1_i = 0.2$, $V2_i = 0.5$. (**b**). Neural network output at feedback gain (k) = 1 (periodic) (**c**). Neural network output at feedback gain (k) = 0.99 (chaotic).

value. As we expected, this result can be seen in Fig. 4. When $A_4$ is decreased from 9 (the normal value) to 8.5, the seizure propagates from $BJ_4$ to all the network, and the normal chaotic activity of the whole network (Fig. 4(**c**)) changes to an abnormal periodic behavior (Fig. 4(**b**)).

Changing parameter $B_4$ (which is modeling the effect of excitatory or glutamate neurotransmitter) from its normal value could also cause the network's output to switch from its normal chaotic behavior to periodic (seizure episode). The results in Fig. 5, which are similar to the results in Fig. 4, illustrate the changes in the model's output when $B_4$ is varied. The chaotic (healthy) output of the model at $B_4 = 5.821$ is shown in Fig. 5(c). By increasing the value of $B_4$ (from $B_4 = 5.821$ to $B_4 = 5.92$), the output is in a periodic window (Fig. 5(**b**)).

Modeling the treatment methods of epilepsy can be very important as well. Drugs and electrical stimulation are among the most popular prescriptions for controlling the seizure [97–100].

We observed that a small change in a particular parameter can lead the system to a different behavior. Thus an efficient way to stop the periodic behavior is by changing a parameter in a way that restores the chaotic mode in the system. This can model how a treatment for epilepsy works.

As previously mentioned, a systematic perturbation is required to change the behavior of the system. This can be done by a proper feedback. Some drugs or electrical stimulation may have an effect in the feedback mechanisms of the brain. To investigate such effects in the proposed model, we simply change the feedback gain. First we set the weights in a periodic mode and then plot the bifurcation diagram of the model for different values of feedback gain (Fig. 6).

As shown in Fig. 6, the system is in a periodic mode when the feedback gain is 1. Time series are shown in Fig. 6(**b**) and (**c**). The behavior of the proposed model comes back to its healthy (chaotic) mode when the feedback gain is reduced to 0.99.

In a summary, this behavior model is just proposed to describe what happened when the nervous system is going under seizure. Chaotic network can contain more mixed information than periodical network. In fact, more relevant factors [101–103] should be considered in artificial neural network. For a review about algorithm reliability, readers can find clues in reference [103]. On the other hand, noise and electromagnetic induction [104] should be considered in dealing with signal encoding and processing. Maybe, more nodes, diffusive disturbance and memristor-based memory can be further considered to propose more reliable neural models [105].

## 5. Conclusions

Following some facts about temporal lobe epileptic seizure and the basic role of neurotransmitters in initiating seizures, and using applications of chaos theory in biological modeling, a behavioral model is proposed to model the brain behavior of an epileptic patient. Epileptic seizure is behaviorally similar to periodic windows in the midst of chaos. Our proposed model not only represents the problem of undesired epileptic seizures, but also tries to suggest different possible mechanisms for epilepsy disorder. This model suggests that there is a possible interaction between the role of excitatory and inhibitory neurotransmitters and epilepsy. The results might help us in the future to gain more perspective about epilepsy and develop some prediction methods and cures for seizure occurrence in the patients.

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