Chaotic analysis of the human brain cortical model and robust control of epileptic seizures using sliding mode control

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In this paper, chaotic analysis of the human brain cortical model is presented. Based on these analysis, controlling of epileptic seizures, using a robust control method is considered. To this end we have utilized the mathematical model of cortical tissue activity. Chaotic behavior of this model is investigated through variations of pathological parameters. Utilization of two chaotic criteria known as entropy and largest Lyapunov exponents allowed us to monitor the chaotic behavior of the model during the research. Moreover, both conning and ending time of seizures are determined using chaotic analysis. The sliding mode method is used to design a robust controller with the purpose of controlling the seizures. The effectiveness of the proposed method is shown via analysis and simulation results. Previous approaches on controlling seizures did not considered robustness against the uncertainties. This problem is addressed here through designing a controller which is robust against system uncertainties. In addition to the guaranteed finite time control of the seizures, consideration of the practical medical limitations for the control signal is another advantage of the proposed method.

Keywords: epileptic seizures; cortical model; pathological parameters; entropy; largest Lyapunov exponents; sliding mode controller

1. Introduction

Epilepsy is a common disorder that is characterized by recurrent and unprovoked seizure-like activities. These epileptic seizures have destructive effects on everyday life of those who suffer this disease. These devastating effects could be much more important and dangerous when the patient is in special positions of everyday life like driving or climbing. Almost 50 million people all over the world suffer from this disease (Lopour & Szeri, 2010). Medication and other treatments can be very useful for many patients, and about 70% of patients respond to the various treatments so that their seizures could be controlled. Unfortunately, the remaining 30% do not respond to treatment and are inevitably forced to choose other alternatives like surgery (Lopour & Szeri, 2010). The surgical procedure is complex and might involve after effects and disarranges a special part of the patient’s cortex such as speech and memory. As this process does not guarantee the success, the control engineering approaches are being considered by researchers. Totally, the mathematical investigations on seizures can be seen in two categories: (1) researches that focus on investigating the chaotic behavior of the human brain (Dafilis, Bourke, Liley, & Cadusch, 2002; Dafilis, Liley, & Cadusch, 2001; Kramer, Lopour, Kirsch, & Szeri, 2006), (2) researches that focus on control algorithms (Chakravarthy, Sabesan, Tsakalis, & Iasemidis, 2009; Colpan, Li, Dwyer, & Mogul, 2007; Gluckman, Nguyen, Weinstein, & Schiff, 2001; Kramer, Lopour, et al., 2006; Lopour & Szeri, 2010). The first approach investigates the chaotic behavior of the human cortex based on chaotic analysis of the human cortical model (CM). In the second approach, the various control algorithms are presented to control and suppress epileptic seizures. All of these control approaches suffer from a common problem. They are not robust against variations of pathological parameters. Any change in pathological state of the patient results in ineffective control system and thus changing the control systems characteristics is inevitable. For example, the presented method by Kramer, Lopour, et al. (2006) which is highly regarded by researchers uses a supervisory on/off controller. When the patient is in the normal state (seizure free), the feedback controller is turned off and when the patient is in the epileptic state the controller is turned on. In this paper, we have dealt with this issue by applying the robust sliding mode controller which is able to control the patient’s condition without changing the controller parameters in different states. We utilized the mathematical model of human brain cortex and the CM, which has been used by previous researchers (Liley, Cadusch, & Wright, 1999).

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2. Electrical CM of human cortex

To investigate the chaotic behavior of the human brain cortex and propose a suitable control approach, the human cortex activity needs to be expressed using mathematical models. The presented CM which represents the electrical activity of the human cortex in different states includes a set of stochastic partial differential equations (SPDEs) that has been developed and accommodated in recent decades (Bojak & Liley, 2005; Liley, Cadusch, & Dafilis, 2002; Liley et al., 1999). Considering stochastic and nonlinear behavior of this model, which is suitable for investigating the applications based on Electroencephalography (EEG) such as epilepsy (Kramer, Kirsch, & Szeri, 2005; Kramer, Lopour, et al., 2006; Kramer, Szeri, Sleight, & Kirsch, 2006; Lopour & Szeri, 2002; Lopour & Szeri, 2010), sleep (Lopour, Tasoglu, Kirsch, Sleight, & Szeri, 2011; Wilson et al., 2006), and anaesthesia (Bojak & Liley, 2005; Bojak, Liley, Cadusch, & Cheng, 2004; Steyn-Ross, Steyn-Ross, & Sleight, 2004; Steyn-Ross, Steyn-Ross, Sleight, & Whiting, 2003). The CM provided in Liley et al. (1999) and Steyn-Ross et al. (2003) is represented by the following SPDEs:

\[
\tau_e \frac{\partial h_e}{\partial t} = (h^\text{rest}_e - h_e) + \psi_{ee}(h_e) I_{ee} + \psi_{ie}(h_e) I_{ie},
\]

\[
\tau_i \frac{\partial h_i}{\partial t} = (h^\text{rest}_i - h_i) + \psi_{ei}(h_i) I_{ei} + \psi_{ii}(h_i) I_{ii},
\]

\[
(\frac{\partial}{\partial t} + \gamma_e) I_{ee}(h_e) = \left[ N_e^\beta S_e(h_e) + \phi_e + p_{ee} \right] G_e \gamma_e e + \Gamma_1,
\]

\[
(\frac{\partial}{\partial t} + \gamma_e) I_{ie}(h_e) = \left[ N_e^\beta S_e(h_e) + \phi_e + p_{ee} \right] G_e \gamma_e e + \Gamma_2,
\]

\[
(\frac{\partial}{\partial t} + \gamma_i) I_{ei}(h_i) = \left[ N_i^\beta S_i(h_i) + p_{ee} \right] G_i \gamma_i e + \Gamma_3,
\]

\[
(\frac{\partial}{\partial t} + \gamma_i) I_{ii}(h_i) = \left[ N_i^\beta S_i(h_i) + p_{ee} \right] G_i \gamma_i e + \Gamma_4,
\]

\[
\left[ \frac{\partial}{\partial t} + \tilde{\Lambda}_{ee} \right]^2 \phi_e = \tilde{\Lambda}_{ee} N_{ee}^\alpha \left( \frac{\partial}{\partial t} + \tilde{\Lambda}_{ee} \right) S_e(h_e),
\]

The subscripts e and i denote excitatory and inhibitory neuron populations, respectively. In this manner, the variable \(h_e\) is the excitatory mean soma potential for a neuronal population and \(h_i\) is the inhibitory one. The variable \(I_{ee}\) is the postsynaptic activation of the excitatory population due to inputs from the excitatory population, the variable \(I_{ei}\) is the postsynaptic activation of the inhibitory population due to inputs from the excitatory population, the variable \(I_{ie}\) is the postsynaptic activation of the excitatory population due to inputs from the inhibitory population, and the variable \(I_{ii}\) is the postsynaptic activation of the inhibitory population due to inputs from the inhibitory population. Finally, the variables \(\phi_e\) and \(\phi_i\) are corticocortical inputs to excitatory and inhibitory populations, respectively. The \(\Gamma_i\) terms employed in Equations (3–6) are stochastic inputs. In this paper, it is assumed that the implanted electrodes are fixed at their position so spatial derivatives are vanished in Equations (7) and (8). The second-order terms (Equations (3)–(8)) can be converted into the first-order equations and a simpler system of 14 first-order ordinary differential equations (ODEs) is yielded as follows (Kramer, Lopour, et al., 2006):

\[
\tau_e \frac{d h_e}{dt} = (h^\text{rest}_e - h_e) + \psi_{ee}(h_e) I_{ee} + \psi_{ie}(h_e) I_{ie},
\]

\[
\tau_i \frac{d h_i}{dt} = (h^\text{rest}_i - h_i) + \psi_{ei}(h_i) I_{ei} + \psi_{ii}(h_i) I_{ii},
\]

\[
\frac{d I_{ee}}{dt} = J_{ee},
\]

\[
\frac{d I_{ie}}{dt} = -2 \gamma_e I_{ee} - \gamma_i^2 I_{ee} + \left( N_e^\beta S_e(h_e) + \phi_e + p_{ee} \right) G_e \gamma_e e + \Gamma_1,
\]

\[
\frac{d I_{ei}}{dt} = J_{ei},
\]

\[
\frac{d I_{ii}}{dt} = -2 \gamma_e I_{ei} - \gamma_i^2 I_{ei} + \left( N_i^\beta S_i(h_i) + \phi_i + p_{ee} \right) G_i \gamma_i e + \Gamma_2,
\]

\[
\frac{d I_{ie}}{dt} = J_{ie},
\]

\[
\frac{d I_{ii}}{dt} = -2 \gamma_i I_{ii} - \gamma_i^2 I_{ii} + \left( N_i^\beta S_i(h_i) + p_{ee} \right) G_i \gamma_i e + \Gamma_3,
\]

\[
\frac{d I_{ee}}{dt} = J_{ee},
\]

\[
\frac{d I_{ei}}{dt} = -2 \gamma_e I_{ie} - \gamma_i^2 I_{ie} + \left( N_e^\beta S_e(h_e) + \phi_i + p_{ee} \right) G_e \gamma_i e + \Gamma_4.
\]
\frac{d\phi_e}{dt} = \chi_e, \\
\frac{d\chi_e}{dt} = -2\bar{v}\Lambda_{ee}\chi_e - (\bar{v}\Lambda_{ee})^2 \phi_e \\
+ \bar{v}\Lambda_{ee}\psi_{ee} (\frac{d}{dt} + \bar{v}\Lambda_{ee}) S_e (h_e), \\
\frac{d\phi_i}{dt} = \chi_i, \\
\frac{d\chi_i}{dt} = -2\bar{v}\Lambda_{ei}\chi_i - (\bar{v}\Lambda_{ei})^2 \phi_i \\
+ \bar{v}\Lambda_{ei}\psi_{ei} (\frac{d}{dt} + \bar{v}\Lambda_{ei}) S_i (h_i),

(19) \quad (20) \quad (21) \quad (22)

where \psi_{jk}(h_k) \quad (j, k \in \{e, i\}) \text{ are weighting factors for } I_{jk} \text{ inputs. Also, } S_e(h_e) \text{ and } S_i(h_i) \text{ are sigmoid functions mapping the soma potential to the firing rate. These terms are defined as follows:}

\psi_{jk} = \frac{h_{jk}^{\text{rev}} - h_k}{h_{jk}^{\text{rev}} - h_k^{\text{rest}}} (j, k \in \{e, i\}),

(23)

S_e(h_e) = \frac{s_{e, \text{max}}}{1 + \exp \left[-g_e(h_e - \theta_e)\right]},

(24)

S_i(h_i) = \frac{s_{i, \text{max}}}{1 + \exp \left[-g_i(h_i - \theta_i)\right]},

(25)

A complete description of model state variables and parameters are provided in Tables 1 and 2, respectively.

### 2.1. Numerical values for state changes

Some of the previous papers in the literature have been converted from the present dimensional form of the CM into the dimensionless form (Kramer, Lopour et al., 2006; Kramer, Szeri et al., 2006; Lopour & Szeri, 2010). This transition between the normal and epileptic states occurs based on the changes in two parameters; \( P_{ee} \) and \( \Gamma_e \). These parameters are known as pathological parameters (Kramer, Lopour et al., 2006; Lopour & Szeri, 2010). Numerical values for these parameters are provided in papers which have been utilized as the dimensionless form of the CM.

| Symbol | Description | Typical value | units |
|--------|-------------|---------------|-------|
| \( \tau_e, \tau_i \) | Membrane time constant | 0.04, 0.04 | s |
| \( h_{ee}, h_{ii} \) | Resting potential | -70, -70 | mV |
| \( h_{ee}^{\text{rev}}, h_{ii}^{\text{rev}} \) | Reversal potential | 45, 90 | mV |
| \( p_{ee}, p_{ii} \) | Subcortical spike input to excitatory population | 1100, 1600 | s\(^{-1}\) |
| \( p_{ei}, p_{ii} \) | Subcortical spike input to inhibitory population | 1600, 1100 | s\(^{-1}\) |
| \( \Lambda_{ee}, \Lambda_{ei} \) | Corticocortical inverse-length scale | 0.04, 0.065 | (mm)\(^{-1}\) |
| \( \gamma_e, \gamma_i \) | Neurotransmitter rate constant for excitatory, inhibitory postsynaptic potential | 300, 65 | s\(^{-1}\) |
| \( G_e, G_i \) | Peak amplitude of excitatory, inhibitory postsynaptic potential | 0.18, 0.37 | mV |
| \( N_{ee}^{\beta}, N_{ei}^{\beta} \) | Total number of local synaptic connections | 3034, 3034 | – |
| \( N_{ii}^{\beta}, N_{ee}^{\beta} \) | Total number of synaptic connections from distant excitatory populations | 536, 536 | – |
| \( N_{ii}^{\alpha}, N_{ee}^{\alpha} \) | Total number of synaptic connections from distant excitatory populations | 4000, 2000 | – |
| \( \bar{v} \) | Mean axonal conduction speed | 7000 | mm\(s\)^{-1} |
| \( s_{e, \text{max}}, s_{i, \text{max}} \) | Maximum value for sigmoid function | 100, 100 | s\(^{-1}\) |
| \( \theta_e, \theta_i \) | Inflection-point potential for sigmoid function | -60, -60 | mV |
| \( S_e, S_i \) | Sigmoid slope at inflection point | 0.28, 0.14 | (mV)\(^{-1}\) |

Table 2. Parameters of the ODE electrical CM.

So the corresponding values in the dimensionless form of the model must be calculated. Definition of the \( P_{ee} \) and \( \Gamma_e \) in the dimensionless form of the model are as follows:

\[ P_{ee} = \frac{P_{ee}}{S_{e, \text{max}}} \]

\[ \Gamma_e = \frac{G_e e S_{e, \text{max}}^{\text{max}}}{\gamma_e \left| h_{ee}^{\text{rev}} - h_{ee}^{\text{rest}} \right|^{\gamma_e}} \]

(26) \quad (27)

thus, corresponding parameters in the dimensional form of the CM are as follows:

\[ p_{ee} = S_{e, \text{max}} P_{ee} \]

and

\[ G_e = \frac{\gamma_e \left| h_{ee}^{\text{rev}} - h_{ee}^{\text{rest}} \right|^{\gamma_e}}{e S_{e, \text{max}}^{\text{max}}} \]

(28) \quad (29)
According to Kramer, Lopour, et al. (2006) and Lopour and Szeri (2010), typical values for these two pathological parameters in normal and epileptic states are as in the following; the normal state has occurred when $p_{ee} = 11$ and $G_e = 0.18 \text{mV}$, and hyperexcited “epileptic” state occurs when $p_{ee} = 548$ and $G_e = 0.8 \times 10^{-3}$. Thus, corresponding values for these two typical values in the dimensional CM are: $p_{ee} = 1100(\text{s}^{-1})$ and $G_e = 0.18(\text{mV})$ for normal state, and $p_{ee} = 54,800(\text{s}^{-1})$ and $G_e = 0.1(\text{mV})$ for the epileptic state which are calculated using Equations (28) and (29).

3. Chaotic behavior of the model

Analysis of transition between the epileptic and normal states plays an important role in designing an effective controller with good performance. In previous researches such as Kramer, Lopour, et al. (2006) and Lopour and Szeri (2010), examination of the designed controller was just performed for typical values of pathological parameters. However, the present paper considers the variation of pathological parameters in different states. Moreover, based on variations of the pathological parameters, we have investigated the occurrence of the transition between the different states.

A physiological aspect of the normal state is having a lower level of excitation in mean soma voltage of excitatory neuron population ($h_e$), which is similar to a damping behavior. While in the epileptic state, we have hyperexciting large amplitude oscillations in the $h_e$ signal. Figures 1 and 2 illustrate typical behavior of the normal and epileptic states, respectively.

Transition from a healthy to the epileptic state results in increased amplitude and more periodic waveform of the $h_e$. Based on the CM, transition between the states occurs through changing two pathological parameters which are $p_{ee}$ and $G_e$. Figure 1 illustrates $h_e$ in the case of typical healthy values for pathological parameters, $p_{ee} = 1100(\text{s}^{-1})$ and $G_e = 0.18(\text{mV})$. Transition from the epileptic to a healthy state occurs while $p_{ee}$ increases and $G_e$ decreases (Kramer, Lopour, et al., 2006; Lopour & Szeri, 2010). Required percentage of change in $p_{ee}$ is much greater than $G_e$. Moreover, from the physiological aspect, the increased rate of $p_{ee}$ is more allowable than the decrease rate of $G_e$ (Kramer, Lopour, et al., 2006). Increasing $p_{ee}$ and simultaneously decreasing $G_e$ results in the transition from the normal to the epileptic state. However, continuous increase in $p_{ee}$ and decrease in $G_e$ will eventually cause the brain’s dynamics to go back to the healthy state. These transitions will be proved through analyzing chaotic behavior of the CM. This is done by utilizing two chaotic criteria which adopts the model to the chaotic behavior of the human brain.

According to physiological aspects of normal brain activity, the neuronal activities show less organized behavior and greater chaos. On the contrary, during the epileptic state, the behavior of the neuronal population becomes much more organized and the amount of disorder is very small. Adeli, Ghosh-Dastidar, and Dadmehr (2007), Ghosh-Dastidar, Adeli, and Dadmehr (2007), Mirzaei, Ayatollahi, and Vavadi (2011), Vavadi, Ayatollahi, and Mirzaei (2010). In this research, we have utilized two chaotic criteria; The LLE (Adeli et al., 2007; Ghosh-Dastidar et al., 2007) and Entropy (En; Mirzaei et al., 2011; Vavadi et al., 2010) to investigate chaotic behavior of the CM. The subsequent subsections are devoted to these chaotic criteria.

3.1. Analysis of LLEs

For the system to be chaotic, at least one of its Lyapunov exponents should be positive, i.e. the LLE has to be greater than zero (Adeli et al., 2007). Thus, it can be concluded that the measure of LLE in healthy subjects is greater than in epileptic subjects (Adeli et al.,
The LLE measures of the $h_e$ signal for different values of pathological parameters are calculated and presented in Table 3 for the following intervals: $1.1 \times 10^3 < p_{ee} < 187 \times 10^3$ (s$^{-1}$) and $0.18 < G_e < 0.087$ (mV). It should be noted that the CM for $p_{ee} < 1.1 \times 10^3$ (s$^{-1}$) and $G_e > 0.18$ (mV) is in the healthy state.

Variations of LLE values versus $p_{ee}$ and $G_e$ in this process are illustrated in Figures 3 and 4, respectively. It is clear from Figures 3 and 4 that the measure of the LLE decreases with a slow rate from $p_{ee} = 1100$ (s$^{-1}$) and $G_e = 0.18$ (mV) to $p_{ee} = 22,000$ (s$^{-1}$) and $G_e = 0.159$ (mV), while the $h_e$ signal shows normal cortical behavior. The measure of LLE values show an extreme reduction from $p_{ee} = 22,000$ (s$^{-1}$) and $G_e = 0.159$ (mV), resulting in seizure-like events. By decreasing LLE values, the amplitude of the $h_e$ signal increases and shows more fluctuations thus becoming more periodic.

Figures 5–7 show the behavior of the $h_e$ signal in this range. Figures 5 and 6 show the results for $p_{ee} = 1100$ (s$^{-1}$) and $G_e = 0.18$ (mV) and for $p_{ee} = 21,000$ (s$^{-1}$) and $G_e = 0.162$ (mV), respectively. In this case $p_{ee}$ has higher value and $G_e$ a lower value compared with the case in Figure 5, and it seems that the amplitude of $h_e$ has increased and its oscillations commence. Figure 7 illustrates the $h_e$ for $p_{ee} = 22,000$ (s$^{-1}$) and $G_e = 0.159$ (mV).

It is clear from Figure 7 that hyperexcited oscillations emerge in these pathological parameters, and seizure-like events occur. In this case, $h_e$ is periodic with a larger amplitude (as in epileptic state) compared with the healthy state.

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### Table 3. LLE measures of the $h_e$ dynamic variable of the CM for different values of pathological parameters.

| $p_{ee} \times 10^{-3}$ (s$^{-1}$) | 1.1 | 5.5 | 11 | 16.5 | 22 | 33 | 44 | 55 | 60.5 | 88 | 110 | 121 | 132 | 170.5 | 187 |
|-----------------|-----|-----|----|------|----|----|----|----|------|----|-----|-----|-----|-------|-----|
| $G_e$ (mV)      | 0.18| 0.175| 0.172| 0.168| 0.159| 0.139| 0.12| 0.1 | 0.099| 0.097| 0.095| 0.094| 0.093| 0.089| 0.087 |
| LLE $\times 10^{-3}$ | 0.784| 0.781| 0.771| 0.767| 0.659| 0.647| 0.643| 0.637| 0.64 | 0.653| 0.665| 0.671| 0.674| 0.714| 0.717 |

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Figure 3. Variation of LLE versus $p_{ee}$ values.

Figure 4. The variation of LLE versus $G_e$ values.

Figure 5. Typical normal state with $p_{ee} = 1100$ (s$^{-1}$) and $G_e = 0.18$ (mV).

Figure 6. Prior to epileptic state, with $p_{ee} = 21,000$ (s$^{-1}$) and $G_e = 0.162$ (mV).
dynamics. From the values illustrated in Table 3, it can be concluded that by increasing \( p_{ee} \) and decreasing \( G_e \), and consequently decreasing LLE values, the patient’s state is going to be epileptic, and its symptoms appear. These epileptic seizures continue until the pathological parameters reach \( p_{ee} = 170,500 \text{s}^{-1} \) and \( G_e = 0.089 \text{mV} \). By completely finishing epileptic seizures, \( p_{ee} \) starts to decrease and \( G_e \) to increase and consequently LLE measures will increase. Thus, the patient would be back to the normal state.

### 3.2. Analysis of the entropy

The second chaotic criterion that is investigated is entropy. The concept of entropy in information theory was first introduced by Shannon (Mirzaei et al., 2011; Vavadi et al., 2010). It is a criterion of information theory that concludes the condition of regularity or irregularity. Moreover, Entropy (En) is considered as a chaotic criterion in researches. The definition of Entropy is expressed in terms of a discrete set of probabilities \( p_i \). Assume that \( X \) is a set of discrete samples \( x_i (i = 1, 2, \ldots, n) \), then the Entropy measure of this set is defined as follows:

\[
En(X) = -\sum_{i=1}^{n} p(x_i) \log p(x_i)
\]  

in which \( n \) is the number of samples, and \( p(x_i) \) is the probability of the \( x_i \) occurrence. The more regular the signal, the greater the value of \( En \). In our research, when the system transfers to the epileptic state, it shows a regular curve like a periodic waveform. Thus, we expect to have greater entropy values in the epileptic state in comparison with the healthy state. Table 4 shows En values of the \( h_e \) versus different values of \( p_{ee} \) and \( G_e \). Behavior of the \( h_e \) signal can be explained by variations of \( p_{ee} \) and \( G_e \) in different states. It is clear from Table 4 that increasing \( p_{ee} \) and decreasing \( G_e \), results in increasing value of the \( En \). So we conclude that, the system transfers from a healthy to epileptic state.

Variations of the \( En \) with respect to \( p_{ee} \) and \( G_e \) in this process are shown in Figures 9 and 10, respectively. Figure 9 illustrates the variation of \( En \) values with respect to the variation of \( p_{ee} \). Increase and decrease of the \( En \) values in different states of the patient and increasing value of \( p_{ee} \), is clear in this figure. Also Figure 10 illustrates the variation of \( En \) with respect to the variation of \( G_e \). Increase and decrease of the \( En \) values in different states of the patient and increasing value of \( G_e \), is clear in this figure.

As explained above, from a physiological point of view, the measure of \( En \) in healthy subjects is lower than in epileptic ones, and due to chaotic behavior of brain dynamics, the \( h_e \) signal in healthy states would be less regular compared with epileptic ones (Mirzaei et al., 2011; Vavadi et al., 2010). The calculated measures of \( En \) for different values
of pathological parameters, $p_{ee}$ and $G_e$ in different states confirm this behavior of brain dynamics.

From the values that are compiled in Table 4, it can be concluded that by increasing $p_{ee}$ and decreasing $G_e$ results in increasing value of $En$, the $h_e$ signal would be more regular, and the patient would transfer from a healthy to epileptic state and experiences the seizure-like events. These epileptic seizures continue until the pathological parameters reach approximately $p_{ee} = 170,500$ (s$^{-1}$) and $G_e = 0.089$ (mV). By this time, the epileptic state completely passes and $p_{ee}$ value starts to decrease and $G_e$ value increases which results in decreasing value of $En$ measures. Thus, regularity of $h_e$ would be reduced and the patient state would be back to the normal form.

It is shown that the two chaotic analyses are representing the same results. The mentioned values will be used in simulations presented in the next section where we will provide the controller.

### 4. Sliding mode controller

In previous researches, various controllers have been presented by researchers to suppress and control epileptic seizures based on the CM (Dafilis et al., 2001, 2002; Kramer, Lopour, et al., 2006; Lopour & Szeri, 2010). However, the proposed algorithms are not robust against variations of pathological parameters. For example in Dafilis et al. (2002), while the system is in the healthy state, the feedback controller is turned off, and when the system is transferred to the epileptic state, the controller is turned on. So a supervisory controller is needed to discover the epileptic state and to turn the main controller on and off. The controller presented here uses a robust algorithm based on the sliding mode control (SMC) method which is able to suppress and control the seizure-like events in all states despite the changes in pathological parameter values ($p_{ee}, G_e$).

The aim of current research is to halt epileptic seizures and make the controller to be robust against variations of pathological parameters. Here variations of pathological parameters, $p_{ee}$ and $G_e$ are considered as system uncertainties. As explained in Section 3, our focus is on suppressing and controlling hyperexcited oscillations of the $h_e$ known as epileptic seizures. Hence $h_e$ is the output of interest and the control signal $u_{SMC}$ will be applied to the first equation of the CM (Equation (9)) as follows:

$$
\tau_e \dot{h}_e = \left( h_{e,\text{rest}}^\text{rev} - h_e \right) + \psi_{ee}(h_e)I_{ee} + \psi_{ie}(h_e)I_{ie} + u_{SMC},
$$

(31)

It should be noted that application of an electrical signal at the electrode connection point is possible and has been done in previous works (Dafilis et al., 2002; Kramer, Lopour, et al., 2006). Substituting $\psi_{ee}$ and $\psi_{ie}$ from Equation (23) into Equation (31) gives the following:

$$
\dot{h}_e = \frac{1}{\tau_e} \left\{ \left( h_{e,\text{rest}}^\text{rev} - h_e \right) + \left( \frac{h_{e,\text{rest}}^{\text{rev}} - h_e}{|h_{e,\text{rest}}^{\text{rev}} - h_e|} \right) I_{ee} + \left( \frac{h_{e,\text{rest}}^{\text{rev}} - h_e}{h_{e,\text{rest}}^{\text{rev}} - h_{e,\text{rest}}^\text{rev}} \right) I_{ie} + u_{SMC} \right\}.
$$

(32)
Variations of $p_{ec}$ and $G_z$ that are considered as system uncertainty results in variation with the state variables, $h_c, I_{ee},$ and $I_{ie}$ in Equation (32), i.e.

\[ \begin{align*}
    h_c &= h_{en} + \Delta h_c, \\
    I_{ee} &= I_{een} + \Delta I_{ee}, \\
    I_{ie} &= I_{ien} + \Delta I_{ie},
\end{align*} \]

where $h_{en}, I_{een},$ and $I_{ien}$ are nominal values. Considering these variations in Equation (32) yields:

\[ \dot{h}_c = f_n + \Delta f + \frac{1}{\tau_c} u_{SMC}, \]

where

\[ 
    f_n = \frac{1}{\tau_c} \left( h_{rest}^f - h_{en} + \frac{h_{rev} - h_{en}}{|h_{rev} - h_{rest}^f|} (I_{een}) + \frac{h_{rev}^f - h_{en}}{|h_{rev}^f - h_{rest}^f|} (I_{ien}) \right) \]

and

\[ \Delta f = \frac{1}{\tau_c} \left\{ -\Delta h_c + \frac{h_{rev}^f - h_{en}}{|h_{rev}^f - h_{rest}^f|} ( \Delta I_{ee} ) \\
    + \frac{h_{rev} - h_{en}}{|h_{rev} - h_{rest}^f|} ( \Delta I_{een} ) \\
    + \frac{h_{rev} - h_{en}}{|h_{rev} - h_{rest}^f|} ( \Delta I_{een} ) \\
    + \frac{-\Delta h_c}{|h_{rev}^f - h_{rest}^f|} ( I_{ien} ) + \frac{-\Delta h_c}{|h_{rev}^f - h_{rest}^f|} ( \Delta I_{een} ) \right\} \]

The control signal in this approach, $u_{SMC}$, includes two terms:

\[ u_{SMC} = u_c + u_{eq}, \]

$u_c$ guarantees that states reach the sliding surface and is considered to cope with the effect of uncertainties. This term is defined as follows:

\[ u_c = -k \text{ sign}(s), \]

where $k$ is a positive constant and \(\text{sign}(\cdot)\) denotes the sign function:

\[ \text{sign}(u) = \begin{cases} 
    1, & u \geq 0, \\
    -1, & u < 0,
\end{cases} \]

$s$ is the sliding surface which is defined here to be the tracking error:

\[ s = e = h_c - h_{ed}, \]

In this equation, the state $h_{ed}$ is the healthy mean soma potential, and the state $h_c$ is the epileptic one.

The second term in Equation (39), $u_{eq}$ guarantees that states are remaining on the sliding surface. This term will be introduced in the following theorem.

**Theorem** For the uncertain system (36) where it is assumed that the variations are bounded by $M$

\[ \Delta f < M, \]

with the controller that is given by Equation (39) in which:

\[ u_{eq} = \tau_c \dot{h}_{ed} + \left( \frac{h_{rest}^f - h_{en}}{|h_{rev} - h_{rest}^f|} - \frac{h_{rev} - h_{en}}{|h_{rev} - h_{rest}^f|} \right) I_{een} + \left( \frac{h_{rev} - h_{en}}{|h_{rev} - h_{rest}^f|} \right) I_{ien} \]

and $u_c$ is defined as Equation (40) with

\[ k > (M + \eta) \tau_c, \]

where $\eta$ is a positive constant (the design parameter), then the error signal vanishes in finite time given by

\[ \tau(e = 0) < \frac{|e(t = 0)|}{\eta}. \]

**Proof** Consider the following Lyapunov function candidate:

\[ V = \frac{1}{2} e^2, \]

which is a positive definite function. The time derivative of $V$ is obtained from

\[ \dot{V} = e \dot{e} \]

and is a derivative of the error signal:

\[ \dot{e} = \dot{h}_c - \dot{h}_{ed} = f_n + \Delta f + \frac{1}{\tau_c} u_c + \frac{1}{\tau_c} u_{eq} - \dot{h}_{ed} \]

substituting $u_{eq}$ yields:

\[ \dot{e} = \Delta f + \frac{1}{\tau_c} u_c \]

and we have the following:

\[ \dot{V} = e \dot{e} = e \left( \Delta f + \frac{1}{\tau_c} u_c \right) \leq Me - \frac{k}{\tau_c} e \text{ sign}(e) \]

\[ \leq \left( M - \frac{k}{\tau_c} \right) |e| \]

substituting $k$ from Equation (45) yields the following:

\[ \dot{V} < -\eta |e|, \]

thus $V$ is a Lyapunov function, so the system is asymptotically stable and the error of $h_c$ approaches zero as $t \to \infty$. 


Table 5. Numerical values used in simulations.

| Healthy state (Figure 11) | Pre-epileptic state (Figure 6) | Epileptic state (Figure 7) |
|---------------------------|-------------------------------|---------------------------|
| $p_{ee}$ ($s^{-1}$)       | 5500                          | 21,000                    | 22,000                    |
| $G_e$ (mV)                | 0.175                         | 0.162                     | 0.159                     |

Now we will prove that the error signal vanishes in finite time given by Equation (46). From Equation (52) we have the following:

$$\dot{e} < -\eta \text{ sign}(e)$$

for the case that $e(t = 0) \geq 0$, we have

$$de < -\eta dt$$

integrating both sides yields

$$-e(t = 0) < -\eta t(e = 0)$$

one would obtain similar result starting with $e(t = 0) < 0$, so we have the following:

$$t(e = 0) < \frac{|e(t = 0)|}{\eta}$$

and this completes the proof. ■

5. Simulation results

In this section, the applicability and performance of the provided control algorithm is verified via simulation. Different states of the patient are considered using different pathological parameters in order to show the ability of the SM controller in controlling epileptic seizures. The error signal of the system and applied control signal are also presented. Finally, the proposed SM controller is compared with the previously presented control methods. As mentioned before the pathological parameters in the CM (Equations (9)–(22)) determine the state of the patient. Numerical values used in simulations are given in Table 5.

The healthy state is plotted in Figure 11. Figure 12 shows three different cases: pre-epileptic state with and without control and the healthy state. It is clear that the pre-epileptic state with the application of the SM controller tracks the healthy state with acceptable accuracy. Comparison between the pre-epileptic state with and without applying the SM controller shows that the controller successfully controls epileptic seizures. Figure 13 shows the healthy and epileptic state with and without applying the control signal. It is clear from this figure that the epileptic state with the applied SM tracks the healthy state with acceptable accuracy and consequently epileptic seizures are controlled. It should be noted that a single controller is applied for different states of patient and there is no need to change the controller characteristics similar to previous researches.

The error between the pre-epileptic state and the applied SM controller and the healthy state, which can be obtained from Equation (42) is illustrated in Figure 14. The error between the epileptic state and the applied SM controller with the healthy state is also shown in Figure 15. The applied control signal which is obtained from Equation (39) is shown in Figure 16. By applying the presented robust control method, the epileptic hyperexcited oscillations are suppressed for different values of pathological parameters in different states.

5.1. Comparison

From Figure 13, it can be seen that the steady-state value of $h_e$ is $-52$ mV and the controller is able to maintain
the steady state at this value. The applied control signal is illustrated in Figure 16. The steady-state value of the control signal is 18.8 mV which is significantly low compared with the 100 mV steady-state value of Kramer, Lopour, et al. (2006) achieved through applying the linear feedback control. This makes the method of the current paper applicable in practice, but the mentioned proportional feedback control would be difficult to implement safely. The chemical processes associated with this type of control algorithm, would damage the cortical tissue (Lopour & Szeri, 2010; Kramer, Lopour, et al., 2006). Furthermore, the presented proportional feedback controller is not robust against variations of pathological parameters (the uncertainties). To improve this proportional feedback controller, the researchers have considered adding a derivative or integral term to the controller, or even using all three components to produce a proportional-integral-differential controller (Lopour & Szeri, 2010). First, we will compare the PD controller with the linear feedback controller, which are both presented in Kramer, Lopour, et al. (2006). The applied voltage delivered by the control signal in differential control method approaches to zero after 1 s which is very good for practical implementation (Kramer, Lopour, et al., 2006). However comparison continues from two points of view: steady-state behavior and robustness. The control signal, presented in Figure 8 of Kramer, Lopour, et al. (2006), approaches to its steady-state value after 1 s. It is clear from Figure 16 that the control signal of the presented method approaches to its steady-state value in 0.2 s. As the required time for approaching the steady-state value increases, the fluctuations around the steady-state value are also increased. These fluctuations can be seen from Figure 16 in the current work and Figure 8 of Kramer, Lopour, et al. (2006).

Fluctuations in the control signal, which would be delivered to the patient’s cortex, may damage the cortical tissue. By applying the controller, epileptic seizures are expected
to be halted and the behavior of $h_c$ become similar to the behavior of the healthy state. The presented robust control meets these expectations (Figures 12 and 13). However, the epileptic state after applying the differential controller which is plotted between $t = 1$ s and $t = 3$ s in Figure 8 of Kramer, Lopour, et al. (2006), is not similar to the healthy state shown in Figure 4 of Kramer, Lopour, et al. (2006) or the curve shown in Figure 11.

According to results of the differential control algorithm illustrated in Figure 8 of Kramer, Lopour, et al. (2006), the controller succeeds in halting the seizures, but the mentioned difference in behavior of the $h_c$ signal after applying the controller, compared with a healthy state may cause damages to the cortical tissue. Second, the improvement of the presented method compared with the differential controller of Kramer, Lopour, et al. (2006) is robustness. Robustness in Kramer, Lopour, et al. (2006) is investigated with constraint of the time delay. Moreover, by variations of pathological parameters, the results of the controller are not preserved. To show that the differential controller in Kramer, Lopour, et al. (2006) is not robust against the changes in pathological parameters, numerical solutions of the dimensionless model are computed over the parameter range of $11 < p_{ee} < 1000$ and $0.3 \times 10^{-3} < \Gamma_e < 1.3 \times 10^{-3}$. These ranges of parameters in the dimensionless model are equivalent to $1100 < p_{ee} < 100,000$ (s$^{-1}$) and $0.038 < \Gamma_e < 0.165$ (mV) in the dimensional one. According to chaotic analysis and its corresponding results which are compiled in Tables 3 and 4, the transition from the epileptic to a healthy state commences from approximately $p_{ee} = 170,500$ (s$^{-1}$) despite the fact that this value of $p_{ee}$ was not considered in Kramer, Lopour, et al. (2006). In other words, a healthy state after the epileptic state was not considered.

Although the integral term in the controller presented in Lopour and Szeri (2010) pushes the integral of the control signal to zero, but the control voltage $u$, is applied to all electrodes, where the maximum applied voltage by a single electrode is 60 mV (Lopour & Szeri, 2010) which is greater than the applied voltage compared with the presented robust method (18.8 mV). Moreover, it is not robust against the variations of pathological parameters.

The filter controller is another control strategy which has been presented in Dafilis et al. (2002) to suppress the seizures. It is able to suppress the oscillations in the epileptic state just for a specific value of the controller gain which is a constraint for the control system. So the filter controller is not a robust method due to its limitation in having a particular gain specified for specific values of pathological parameters in healthy and epileptic states (Dafilis et al., 2002). Unlike the filter control approach, the presented robust method could be applied in different states with different pathological parameters without considering any constraint. Comparison of the different control algorithms mentioned above and the presented method is summarized in Table 6.

### Table 6. Comparing results between the different control algorithms and SMC.

| Controller     | Control effort in steady state (mV) | Settling time (s) | Number of electrodes used | Robust |
|----------------|-------------------------------------|-------------------|---------------------------|--------|
| P              | 100                                 | 0.4               | 1                         | No     |
| PD             | 0                                   | 1                 | 1                         | No     |
| PI             | $<60$                               | 1                 | 5                         | No     |
| Filter controller | 60                               | 1                 | 1                         | No     |
| SMC            | 18.8                                | 0.2               | 1                         | Yes    |

### 6. Conclusions

In this paper, control of epileptic seizures is considered and a robust sliding mode controller based on the human CM is provided. First the chaotic behavior of the model is investigated based on LLE and Entropy criteria. Based on the chaotic analysis of the model, proper values of the model’s pathological parameters for transitions between a healthy and epileptic state and then going back to the healthy state are calculated. The second part of the paper was dedicated to design a robust sliding mode controller capable of controlling the behavior of the brain and halting the hyperexcited oscillations in the epileptic state. Comparison between our control algorithm with previous researches was performed from two points of view. (1) Steady-state behavior, i.e. the amplitude of applied control signal across the cortex tissue and settling time, and (2) Robustness. We analyzed and compared the behavior of the delivered control signal based on its steady-state value, oscillations, and settling time. The control signal presented in the current paper shows reduced oscillations around its steady-state value compared with previous researches. Also the robust method shows lower steady-state value compared with P, PI, and filter controller and higher value compared with the PD controller. However, the settling time in the PD controller is much more than the presented method. Regarding the settling time, the presented method shows lower settling time compared with all previous researches. We have also investigated the robustness of the controller against uncertainties. Here, by uncertainties, we mean the variations of pathological parameters in the model. Unlike previous researches, in this research, the robustness has been taken into account and the method is robust to the mentioned variations.

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