Stabilization of Epileptic Seizures Over Unknown Cortex Dynamics

Meric Cetin
Dept. of Computer Eng.
Pamukkale University
Denizli, Turkey
mcetin@pau.edu.tr

Bedri Bahtiyar
Dept. of Electrical and Electronics Eng.
Pamukkale University
Denizli, Turkey
bedribahtiyar@pau.edu.tr

Selami Beyhan
Dept. of Electrical and Electronics Eng.
Izmir Democracy University
Izmir, Turkey
selami.beyhan@idu.edu.tr

***Abstract*—The simulation of cortical electrical activity of the cerebral cortex is very important for the treatment of neurological disorders involving seizures such as epilepsy, parkinson and etc. It is assumed that the mathematical model of the brain cortex has been exactly modeled. However, the cortex dynamics are highly nonlinear and chaotic under some conditions. The stabilization of seizures becomes difficult when cortex dynamics are unknown or uncertain. This paper presents design and application of the simple adaptive fuzzy control and proportional-integral-derivative (PID) control to the stabilization of the unknown epileptic dynamics. Assuming that all of the system states are not suitable for the measurement where only the system output is available. An adaptive update rule has been designed to allow the adjustment of the controller parameters. Simulation results show that the desired performance for the stabilization of epileptic seizure is achieved via simple controllers.**

Keywords*—*Epileptic seizures, adaptive fuzzy control, PID control, stabilization.

I. Introduction

The functions of the human brain, which is one of the most complex system, can be investigated by analyzing synaptic transmissions. Uncontrolled seizures can lead to irreversible damages in the brain and various limitations in the patient's life [1]. Therefore, the analyze of brain signals and the investigation of impending epileptic seizure precursors have become very important [2], [3]. Recurrent seizures are recorded by electroencephalography (EEG), which records electrical activity in brain tissues. In the literature, active brain stimulation designs are available to stabilize high amplitude regular spike wave oscillations that cause epilepsy seizures [3]–[5]. An electrical or optogenetic stimulation is required to produce a suitable control signal capable of stabilizing the traumatic membrane potential in the epileptic seizure [6].

Adaptive fuzzy controllers, which based on the feedback linearization rule, are used to control nonlinear systems in diverse areas [7]. Using by this approach, a nonlinear control problem becomes a linear control problem [8]. There are many studies based on adaptive fuzzy approach in the literature. For example, in [9], analysis of the electroencephalogram (EEG) signal with a fuzzy interference system has revealed normal and onset of epilepsy phases. The control of possible future penetration analysis in biological systems with fuzzy controller is examined in [10]. Wang et al. proposed an adaptive fuzzy synchronization method for chaotic systems with unknown nonlinearities and disturbances [11]. In [12], an adaptive fuzzy Kalman filter type was proposed to suppress epileptic spikes in a neural mass model with uncertain measurement noise.

978-1-7281-2420-9/19/$31.00 ©2019 IEEE

In this paper, conventional adaptive fuzzy and PID controllers have been designed to suppress epileptic seizures of the nonlinear cortex model. Thus, unmeasurable cortex dynamics have also been bounded within their limit values. The aim is here to show the applicability of the both controllers not to compare them. If the controller algorithms are embedded into microcontrollers, they can be applied to the patient in the form of electrical or optogenetic stimulation. In this way, mobile devices can be utilized to treat the epilepsy seizure in early phase.

The rest of this paper is organized as follows. The conventional indirect adaptive fuzzy control is revised in Section I-A, respectively. The mathematical dynamics of cortex model is explained in Section II. The computational results are shown in Section III, respectively. Finally, Section IV concludes the paper.

A. Adaptive Fuzzy Control (Indirect Formulation)

An n^{th} order nonlinear system can be described as

$$\begin{aligned} \dot{x}_1 &= x_2, \\ \dot{x}_2 &= x_3, \\ &\vdots \\ x^{(n)} &= f(x) + g(x)u \\ y &= x_1 \end{aligned} \tag{1}$$

where f and g are unknown functions, $u \in R$ and $y \in R$ are the input and output of the plant respectively. Let $\boldsymbol{x} = (x_1, x_2, \ldots, x_n)^T = (x, \dot{x}, \ldots, x^{(n-1)})^T$ is state vector of the system that is assumed to be measurable. It must be noted that $g(\boldsymbol{x}) \neq 0$ to (1) be controllable. Beside without loss of generality it is assumed that $g(\boldsymbol{x}) > 0$. Since it is assumed that $f(x)$ and $g(x)$ are unknown, a collection of fuzzy IF-THEN rules, that describe the input-output behavior of the system, can be employed to construct the fuzzy system if some plant knowledge is available. These rules can be shown that

$$\begin{aligned} &IF x_1 is F_1{}^r and \ldots and x_n is F_n{}^r THEN f(x) is C^r \\ &IF x_1 is G_1{}^s and \ldots and x_n is G_n{}^s THEN g(x) is D^r \end{aligned} \tag{2}$$

where ${F_i}^r$, C^r, ${G_i}^s$ and D^s are fuzzy sets and $r = 1, 2, \ldots, L_f$ and $s = 1, 2, \ldots, L_g$. If a reference signal y_m and its derivative are known and bounded, to the plant output y to follow the reference signal, firstly, let the tracking error $e = y_m - y = y_m - x$, $\boldsymbol{e} = (e, \dot{e}, \ldots, e^{(n-1)})$ and $\boldsymbol{k} = (k_n, \ldots, k_1)^T$ which is the coefficients of the Hurwitzian polynomial $\lambda^{n-1} + k_{n-1}\lambda^{n-2} + \ldots + k_1$ and then control law can be chosen as

$$u^* = \frac{1}{g(\boldsymbol{x})}\big[-f(\boldsymbol{x}) + {y_m}^{(n)} + \boldsymbol{k}^T\boldsymbol{e}\big] \quad (3)$$

Thus, the plant output converges to reference signal asymptotically as $t \to \infty$. The fuzzy systems $\hat{f}(\boldsymbol{x}|\boldsymbol{\theta_f})$ and $\hat{g}(\boldsymbol{x}|\boldsymbol{\theta_g})$, which are constructed from the rules (2), can be used instead of $f(\boldsymbol{x})$ and $g(\boldsymbol{x})$ in (3) since they are unknown. Here,

$$\hat{f}(\boldsymbol{x}|\boldsymbol{\theta_f}) = \frac{\sum_{l=1}^{p} \bar{y}_f^l\big(\prod_{i=1}^{n} \mu_{A_i}^l(x_i)\big)}{\sum_{l=1}^{p}\big(\prod_{i=1}^{n} \mu_{A_i}^l(x_i)\big)} \quad (4)$$

and

$$\hat{g}(\boldsymbol{x}|\boldsymbol{\theta_g}) = \frac{\sum_{l=1}^{q} \bar{y}_f^l\big(\prod_{i=1}^{n} \mu_{B_i}^l(x_i)\big)}{\sum_{l=1}^{q}\big(\prod_{i=1}^{n} \mu_{B_i}^l(x_i)\big)} \quad (5)$$

which are constructed with using product inference engine, singleton fuzzyfier and center average defuzzyfier. So the fuzzy controller is obtained as

$$u = u_I\frac{1}{\hat{g}(\boldsymbol{x}|\boldsymbol{\theta_g})}\big[-\hat{f}(\boldsymbol{x}|\boldsymbol{\theta_f}) + {y_m}^{(n)} + \boldsymbol{k}^T\boldsymbol{e}\big] \quad (6)$$

If $\bar{y_f}^l$ and $\bar{y_g}^l$ are free parameters so we can rewrite (4) and (5) in a compact form as

$$\hat{f}(\boldsymbol{x}|\boldsymbol{\theta_f}) = \boldsymbol{\theta_f}^T\boldsymbol{\xi}(\boldsymbol{x}) \quad (7)$$

$$\hat{g}(\boldsymbol{x}|\boldsymbol{\theta_g}) = \boldsymbol{\theta_g}^T\boldsymbol{\eta}(\boldsymbol{x}) \quad (8)$$

where $\boldsymbol{\xi}(\boldsymbol{x})$ and $\boldsymbol{\eta}(\boldsymbol{x})$ are can be shown that

$$\boldsymbol{\xi}(\boldsymbol{x}) = \frac{\prod_{i=1}^{n} \mu_{A_i}^l(x_i)\big)}{\sum_{l=1}^{p}\big(\prod_{i=1}^{n} \mu_{A_i}^l(x_i)\big)} \quad (9)$$

and

$$\boldsymbol{\eta}(\boldsymbol{x}) = \frac{\prod_{i=1}^{n} \mu_{B_i}^l(x_i)\big)}{\sum_{l=1}^{q}\big(\prod_{i=1}^{n} \mu_{B_i}^l(x_i)\big)} \quad (10)$$

Beside $\boldsymbol{\theta_f}$ and $\boldsymbol{\theta_g}$ are the parameter vectors, values of which are chosen randomly, and its dimension is defined by the number of rules. The adaptation laws of the parameters are employed as

$$\dot{\boldsymbol{\theta}}_{\boldsymbol{f}} = -\gamma_1\boldsymbol{e}^T\boldsymbol{P}\boldsymbol{b}\boldsymbol{\xi}(\boldsymbol{x}) \quad (11)$$

and

$$\boldsymbol{\eta}(\boldsymbol{x}) = -\gamma_2\boldsymbol{e}^T\boldsymbol{P}\boldsymbol{b}\boldsymbol{\eta}(\boldsymbol{x})u_I \quad (12)$$

where γ_1, γ_2 are positive constants and the details of $\boldsymbol{P}$ and $\boldsymbol{b}$ can be found in [13].

II. Mathematical Model of Cortex Dynamics

Electrical activity of the brain cortex model is mathematically modeled by stochastic partial differential equations. Some diseases such as epilepsy, parkinson, anesthesia and etc. can be invastigated and treated using electrical stimulation and optogenetic application. The constructed cortex model in SPDEs [14] is converted into ordinary differential equations [15] as

$$\begin{aligned}
\dot{h}_e(t) =& ((h_e^{rest} - h_e) + \psi_{ee}(h_e)I_{ee} + \psi_{ie}(h_e)I_{ie})/\tau_e,\\
\dot{h}_i(t) =& ((h_i^{rest} - h_i) + \psi_{ei}(h_i)I_{ei} + \psi_{ii}(h_i)I_{ii})/\tau_i,\\
\dot{I}_{ee}(t) =& J_{ee},\\
\dot{J}_{ee}(t) =& -2\gamma_e J_{ee} - \gamma_e^2 I_{ee} + [N_{ee}^{\beta}S_e(h_e) + \phi_e + p_{ee}]G_e\gamma_e e\\
&+ \Gamma_1,\\
\dot{I}_{ei}(t) =& J_{ei},\\
\dot{J}_{ei}(t) =& -2\gamma_e J_{ei} - \gamma_e^2 I_{ei} + [N_{ei}^{\beta}S_e(h_e) + \phi_i + p_{ei}]G_e\gamma_e e\\
&+ \Gamma_2,\\
\dot{I}_{ie}(t) =& J_{ie},\\
\dot{J}_{ie}(t) =& -2\gamma_i J_{ie} - \gamma_i^2 I_{ie} + [N_{ie}^{\beta}S_i(h_i) + p_{ie}]G_i\gamma_i e + \Gamma_3,\\
\dot{I}_{ii}(t) =& J_{ii},\\
\dot{J}_{ii}(t) =& -2\gamma_i J_{ii} - \gamma_i^2 I_{ii} + [N_{ii}^{\beta}S_i(h_i) + p_{ii}]G_i\gamma_i e + \Gamma_4,\\
\dot{\phi}_e(t) =& \chi_e,\\
\dot{\chi}_e(t) =& -2\bar{\nu}\Lambda_{ee}\chi_e - (\bar{\nu}\Lambda_{ee})^2\phi_e +\\
&\bar{\nu}\Lambda_{ee}N_{ee}^{\alpha}(\frac{\partial}{\partial t} + \bar{\nu}\Lambda_{ee})S_e(h_e),\\
\dot{\phi}_i(t) =& \chi_i,\\
\dot{\chi}_i(t) =& -2\bar{\nu}\Lambda_{ei}\chi_i - (\bar{\nu}\Lambda_{ei})^2\phi_i +\\
&\bar{\nu}\Lambda_{ei}N_{ei}^{\alpha}(\frac{\partial}{\partial t} + \bar{\nu}\Lambda_{ei})S_e(h_e),
\end{aligned} \quad (13)$$

where the indices e and i indicate the excitatory and inhibitory neuron populations. The states $h_e(mV)$ and $h_i(mV)$ imply the excitatory and inhibitory mean soma potential for a neuronal population, respectively. $I_{ee}(mV)$ is the postsynaptic activation of the excitatory population and $I_{ei}(mV)$ is the postsynaptic activation of the inhibitory population due to inputs from excitatory population. Similarly, $I_{ie}(mV)$ is the postsynaptic activation of the excitatory population and $I_{ii}(mV)$ is the postsynaptic activation of the inhibitory population due to inputs from inhibitory population. $\phi_e(s^{-1})$ and $\phi_i(s^{-1})$ are corticocortical inputs to excitatory and inhibitory populations, respectively. The variables Γ_i are the stochastic inputs. In addition, $\psi_{jk}(h_k)(j,k \in e,i) = \frac{h_j^{rev} - h_k}{|h_j^{rev} - h_k^{rest}|}, (j,k \in e,i)$ terms are weighting factors for I_{jk} inputs. The sigmoid functions mapping to the soma potential to the firing rate are expressed as $S_e(h_e) = \frac{S_e^{max}}{1+exp[-g_e(h_e - \theta_e)]}$ and $S_i(h_i) = \frac{S_i^{max}}{1+exp[-g_i(h_i - \theta_i)]}$.

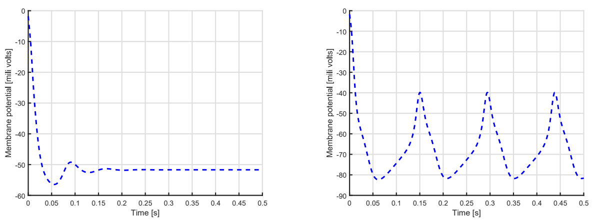
The P_{ee} and Γ_e parameters in the dimensionless form of the cortex model are

$$P_{ee} = \frac{p_{ee}}{S_e^{max}}, \quad \Gamma_e = \frac{G_e e S_e^{max}}{\gamma_e|h_e^{rev} - h_e^{rest}|}. \quad (14)$$

In fact, these parameters provide the transtions between the epileptic and normal states. According to [16], the "normal state" occurs when $p_{ee} = 1100$ and $G_e = 0.18$mV with $\Gamma_e = 1.42 \times 10^{-3}$. Also, the "epileptic state" occurs when $p_{ee} =$

54800 and $G_e = 0.1$mV with $\Gamma_e = 0.8 \times 10^{-3}$. Figure 1 illustrates these phases. The parameters of the cortex model are shown in Table I.

The normal and epileptic behaviors of the cortex dynamics are illustrated in Figure 1, respectively. The normal state is assumed that there is no complex brain activities. However, the epileptic seizure has an known ossilatory behavior which is an undesired situtation for the patients. In order to stabilize the epielptic seizures, it is assumed that the beginning of the seizure is detected by EEG signals or heart rate activities. Then, using these detection signal, the designed controllers are applied to stabilize the epileptic behavior of the brain cortex.



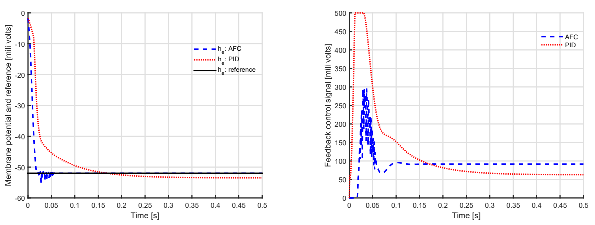
(a) Normal state. (b) Epileptic state.

Fig. 1. Uncontrolled normal and epileptic states.

III. Computational Results

Consider that the nonlinear cortex model is assumed in the form of

$$\begin{aligned} \dot{\hat{h}}_e(t) &= \hat{f}(h_e) + \hat{g}(h_e)u(t), \\ \hat{y} &= \hat{h}_e, \end{aligned} \tag{15}$$



(a) h_e stabilization. (b) Control signal.

Fig. 2. Stabilization results: adaptive fuzzy and PID controllers.

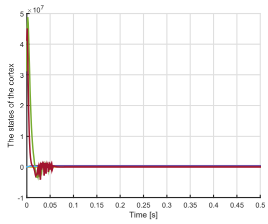
TABLE I. Parameters of the cortex model.

τ_e, τ_i	Membrane time constant	0.04, 0.04 s
h_e^{rest}, h_i^{rest}	Resting potential	-70, -70 mV
h_e^{rev}, h_i^{rev}	Reversal potential	45, -90 mV
p_{ee}, p_{ie}	Subcortical spike input to e population	1100, 1600 s^{-1}
p_{ei}, p_{ii}	Subcortical spike input to i population	1600, 1100 s^{-1}
$\wedge_{ee}, \wedge_{ei}$	Corticotical inverse-length	0.04, 0.065 mm^{-1}
γ_e, γ_i	Neurotransmitter rate constant for e, i postsynaptic potential	300, 65 s^{-1}
G_e, G_i	Peak amplitude of e i postsynaptic potential	0.18, 0.37 mV
$N_{ee}^{\beta}, N_{ei}^{\beta}$	Total number of local synaptic connections of e	3034, 3034
$N_{ie}^{\beta}, N_{ii}^{\beta}$	Total number of local synaptic connections of i	536, 536
$N_{ee}^{\alpha}, N_{ei}^{\alpha}$	Total number of synaptic connections from distant e populations	4000, 2000
$\bar{v}$	Mean axonal conduction speed	7000 mms^{-1}
S_e^{max}, S_i^{max}	Maximum of sigmoid function	100, 100 s^{-1}
θ_e, θ_i	Inflection-point potential for sigmoid function	-60, -60 mV
g_e, g_i	Slope at inflection point	0.28, 0.14 mV^{-1}

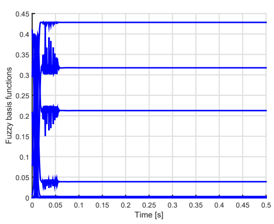
where $h_e(t) \in \Re$ measured membrane potential, $\hat{h}_e$ is the identified membrane potential, $u(t) \in \Re$ is the applied control signal. The $f(.)$ and $g(.)$ are nonlinear fuzzy basis functions. The membrane potential is measured output where in case of epileptic oscillations it is stabilized applying a suitable control signal. For the PID control, the parameters are tuned manually from an interval as $K_p = 50$, $K_i = 20$ and $K_d = 5$, respectively. For the adaptive fuzzy control, the feedback constant K is selected as 100. Then, the membership functions are selected as Gaussian membership functions with centers between $[-60, 10]$ and the standart value 10, respectively. The parameter learning rates are chosen as 100. Using these parameters, the stabilization results are shown in Figure 2. Both stabilization results are successful however the adaptive fuzzy control produces much better results in terms of the stabilization error and applied control signal. Using an offline parameter optimization method for PID, better stabilization results can be provided. Noting that the adaptiveness of the adaptive fuzzy control has an important power for unknown systems control. In Figure 3(a), complete state set are plotted to show their boundedness. Figure 3(b) shows the fuzzy basis functions to see the fired fuzzy membership functions. Figure 3(c) and Figure 3(d) demonstrate the adapted fuzzy parameters to stabilize the system dynamics which are bounded and stable.

IV. Conclusion

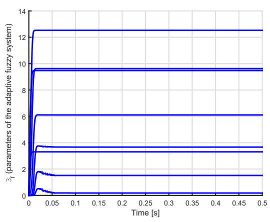
In this paper, two well-known controllers are applied to the unknown cortex dynamics for the stabilization of epileptic seizures. Adaptive fuzzy control can be designed by simple parameter tuning. Using the current results, the adaptiveness of the adaptive fuzzy control method provided much better stabilization results. However, using an offline optimization method or parameter adaptation method, PID control can also be redesigned and better stabilization results can be obtained. The parameter selection of PID controller is needed to satisfy



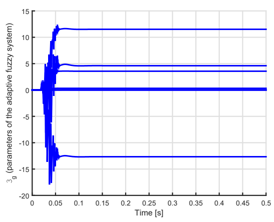
(a) Complete states.



(b) Fuzzy basis functions.



(c) Adaptive parameters $\hat{\boldsymbol{\theta}}_f$.



(d) Adaptive parameters $\hat{\boldsymbol{\theta}}_g$.

Fig. 3. Adaptive fuzzy control results.

the constraints of small tracking error and less control signal power.

ACKNOWLEDGMENT

This paper is supported by Pamukkale University Scientific Research Projects Council under grand number 2019KRM004-059.

REFERENCES

[1] D. G. Fujikawa, H. H. Itabashi, A. Wu, and S. S. Shinmei, "Status epilepticus–induced neuronal loss in humans without systemic complications or epilepsy," *Epilepsia*, vol. 41, no. 8, pp. 981–991, 2000.

[2] B. Litt and J. Echauz, "Prediction of epileptic seizures," *The Lancet Neurology*, vol. 1, no. 1, pp. 22–30, 2002.

[3] L. D. Iasemidis, "Epileptic seizure prediction and control," *IEEE Transactions on Biomedical Engineering*, vol. 50, no. 5, pp. 549–558, 2003.

[4] M. S. Mennemeier, W. J. Triggs, K. C. Chelette, A. Woods, T. A. Kimbrell, and J. L. Dornhoffer, "Sham transcranial magnetic stimulation using electrical stimulation of the scalp," *Brain stimulation*, vol. 2, no. 3, pp. 168–173, 2009.

[5] G. van Luijtelaar, A. Lüttjohann, V. V. Makarov, V. A. Maksimenko, A. A. Koronovskii, and A. E. Hramov, "Methods of automated absence seizure detection, interference by stimulation, and possibilities for prediction in genetic absence models," *Journal of neuroscience methods*, vol. 260, pp. 144–158, 2016.

[6] M. Çetin and S. Beyhan, "Adaptive stabilization of uncertain cortex dynamics under joint estimates and input constraints," *IEEE Transactions on Circuits and Systems II: Express Briefs*, vol. 66, no. 4, pp. 627–631, 2018.

[7] L.-X. Wang, "Stable adaptive fuzzy control of nonlinear systems," *IEEE Transactions on fuzzy systems*, vol. 1, no. 2, pp. 146–155, 1993.

[8] S. Beyhan, Z. Lendek, R. Babuška, M. Wisse, and M. Alcı, "Adaptive fuzzy and sliding-mode control of a robot manipulator with varying payload," in *2011 50th IEEE Conference on Decision and Control and European Control Conference*. IEEE, 2011, pp. 8291–8296.

[9] N. Arunkumar, K. Ramkumar, S. Hema, A. Nithya, P. Prakash, and V. Kirthika, "Fuzzy lyapunov exponent based onset detection of the epileptic seizures," in *2013 IEEE Conference on Information & Communication Technologies*. IEEE, 2013, pp. 701–706.

[10] M. Mahfouf, M. F. Abbod, and D. A. Linkens, "A survey of fuzzy logic monitoring and control utilisation in medicine," *Artificial intelligence in medicine*, vol. 21, no. 1-3, pp. 27–42, 2001.

[11] Y. Wang, Y. Fan, Q. Wang, and Y. Zhang, "Adaptive fuzzy synchronization for a class of chaotic systems with unknown nonlinearities and disturbances," *Nonlinear Dynamics*, vol. 69, no. 3, pp. 1167–1176, 2012.

[12] X. Liu, H.-J. Liu, Y.-G. Tang, Q. Gao, and Z.-M. Chen, "Fuzzy adaptive unscented kalman filter control of epileptiform spikes in a class of neural mass models," *Nonlinear Dynamics*, vol. 76, no. 2, pp. 1291–1299, 2014.

[13] L. X. Wang, *A course in fuzzy systems and control*. London: Prentice-Hall Inc., 1997.

[14] D. T. Liley, P. J. Cadusch, and J. J. Wright, "A continuum theory of electro-cortical activity," *Neurocomputing*, vol. 26, pp. 795–800, 1999.

[15] M. A. Kramer, A. J. Szeri, J. W. Sleigh, and H. E. Kirsch, "Mechanisms of seizure propagation in a cortical model," *Journal of computational neuroscience*, vol. 22, no. 1, pp. 63–80, 2007.

[16] M. A. Kramer, B. A. Lopour, H. E. Kirsch, and A. J. Szeri, "Bifurcation control of a seizing human cortex," *Physical Review E*, vol. 73, no. 4, p. 041928, 2006.