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Parameter pattern discovery in nonlinear dynamic model for EEGs analysis

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We propose a nonlinear dynamic model for an invasive electroencephalogram analysis that learns the optimal parameters of the neural population model via the Levenberg–Marquardt algorithm. We introduce the crucial windows where the estimated parameters present patterns before seizure onset. The optimal parameters minimizes the error between the observed signal and the generated signal by the model. The proposed approach effectively discriminates between healthy signals and epileptic seizure signals. We evaluate the proposed method using an electroencephalogram dataset with normal and epileptic seizure sequences. The empirical results show that the patterns of parameters as a seizure approach and the method is efficient in analyzing nonlinear epilepsy electroencephalogram data. The accuracy of estimating the optimal parameters is improved by using the nonlinear dynamic model.

Keywords: Epileptic seizure; nonlinear dynamic model; neurons population; electroencephalogram; parameter changes.

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1. Introduction

The analysis of electroencephalogram (EEG) signals is both fascinating and challenging for computer scientists, neuroscientists, and physicists because new discoveries can be made from brain signals by using tools based on nonlinear dynamics, chaos theory, and information theory. EEG signals collect brain activity during various events and under a wide range of conditions, such as from an event-related potential (ERP), an epileptic episode, sleep, or as a result of Parkinsons disease (Acharya *et al.*, 2005; Carrubbaa *et al.*, 2006; Vossen *et al.*, 2010; Yuvaraj *et al.*, 2014). These signals primarily exhibit irregular and complex wavy patterns. They are not only chaotic, but also multivariate, nonlinear, unstable, and non-stationary. EEG signal analysis has the potential for a variety of applications, including disease diagnosis and prediction, rehabilitation robot, game control, automobile navigation, etc. (Xing *et al.*, 2014).

EEG signals obtained during epileptic episodes are critical to properly diagnose epilepsy as well as to detect and predict seizures. It is possible to diagnose epilepsy if abnormal EEG signals can be accurately distinguished from normal signals; for this, pattern extraction is important since it allows interictal brain activity during healthy intervals to be distinguished from ictal activity during seizures. The ultimate goal is to be able to forecast seizures as early as possible. Typical forecasting methods use linear methods, such as the auto-regressive moving average (ARMA) (Kim *et al.*, 2013a), and usually fail if the data exhibit nonlinear characteristics that are constantly changing. To solve such problems, nonlinear techniques have been widely applied for seizure detection and prediction in EEG signal analysis (Marshall, 2014; Khoa *et al.*, 2012).

Nonlinear dynamic models can be used to represent complex physiological phenomena that exhibit chaotic behavior (Acharya *et al.*, 2005). Babloyantz *et al.* (1985) first demonstrated that brain waves during sleep have chaotic characteristics of a low-dimension. Several nonlinear dynamic analysis methods, such as fractal dimensions and Lyapunov exponents (LEs) (Shayegh *et al.*, 2014), have been applied to verify these properties of brain waves. Subsequently, the use of nonlinear dynamic models has increased in EEG signal analysis. Nonlinear models offer improvements over linear methods when analyzing the intrinsic nature of EEG signals. However, unfortunately, when nonlinear dynamic models are used to analyze data with complex characteristics, the initial parameter settings and parameter estimations often need to be provided. These problems are difficult but important matters.

In this paper, we propose a nonlinear dynamic model for an invasive EEG analysis, based on a neural population model (NPM) and the Levenberg–Marquardt (LM) algorithm. This model reduces some of the burden of using nonlinear models since the chaotic behavior of the differential equations is combined with a parameter estimation algorithm that determines the optimum parameters. In this model parameter patterns are discovered with crucial windows according to a seizure onset. We then evaluate the proposed method and the corresponding optimization techniques by using an invasive EEG signal that exhibits chaotic behavior.

The remainder of this paper is organized as follows. Section 2 presents the proposed method and Sec. 3 describes the experimental results. Section 4 discusses existing methods and compares them to the proposed method. Finally, the conclusions are drawn in Sec. 5.

2. Materials and Methods

2.1. Neural population model

The brain is comprised of neural networks that are interconnected via synapses, and information is transferred through bioelectricity. EEG provides a physiologic signal that measures the electrical activity in the brain through invasive or noninvasive methods. An understanding of the oscillations in the neuronal population is essential for neuroscience because neuronal oscillations are correlated with the dynamic behavior of the interaction between cellular and synaptic domains. Neuronal population models provide an effective approach to describe the dynamic properties of the neuronal population (Ma *et al.*, 2011). Temporal fluctuations in neuronal population activity are mainly caused by the interactions of groups of neurons with each other. These groups include both excitatory and inhibitory neurons with synaptic connections [Fig. 1(a)] (Sole & Goodwin, 2000).

Excitatory neurons send inputs to other neurons by triggering excitations through bursts of activity; inhibitory neurons behave in the opposite manner by suppressing the activity of other neurons. The states of such neurons can be represented as $e_k(t)$, $k = 1, \ldots, N_e$ for excitatory neurons [see the small circles in Fig. 1(a)] and as $i_l(t)$, $l = 1, \ldots, N_i$ for inhibitory neurons [see the small squares in Fig. 1(a)]. The dynamic interactions in the neuronal population can be described by means of the neuronal



Fig. 1. Neural network for the oscillatory cortex: (a) Neural population comprised of the "E" and "I" neuron sets, where E is the set of excitatory neurons and I is the set of inhibitory neurons) and (b) simplified network in which E and I neurons interact with strengths C1, C2, C3, C4, and P.

dynamical system shown in Eqs. (2.1) and (2.2):

$$\frac{de_k}{dt} = -e_k + S\left(\frac{1}{N_e}\sum_{l=1}^{N_e} u_{kl}e_l - \frac{1}{N_i}\sum_{l=1}^{N_i} v_{kl}i_l - \theta_k^e + p_k\right), \quad k = 1, \dots, N_e, \quad (2.1)$$

$$\frac{di_k}{dt} = -i_k + S\left(\frac{1}{N_e}\sum_{l=1}^{N_e} w_{kl}e_l - \frac{1}{N_i}\sum_{l=1}^{N_i} z_{kl}i_l - \theta_k^i\right), \quad k = 1, \dots, N_i,$$
(2.2)

where t denotes time, and p_k denotes the external inputs into the excitatory neurons (see (Sole & Goodwin, 2000) for details). The parameters u, v, w, and z are the strengths of the connections between the populations. The neuronal population models exhibit several types of interactions that involve self- and cross-interactions expressed by u_{kl}, v_{kl}, w_{kl} , and z_{kl} . θ^e and θ^i are the firing thresholds for the excitatory and inhibitory neurons, respectively. The θ^e_k and θ^i_k thresholds should be sufficiently large (Schuster & Wagner, 1990).

S represents the sigmoid function $S(x) = [1 + \exp^{-x}]^{-1}$. The mutual influence of the population model is described through a sigmoidal function. In general a sigmoid function is real-valued and differentiable with either a non-negative or a non-positive first derivative. Often, the sigmoid function refers to a special case of the logistic function, when the logistic functions are sigmoidal and are characterized as solutions to the differential equation (Han & Moraga, 1995). This sigmoid function produces a nonlinear behavior that is critical to the model and for understanding neuronal activity.

2.2. Nonlinear dynamic model

Since the NPM is rather complicated, in the case of the neural networks that generate the MEG/EEG signals, a simplified model is usually more viable as a neural mass model (David & Fristion, 2003). This model consists of a network of coupled neuronal populations that use one or two steady-state variables to indicate the mean activity of the population. This procedure efficiently determines the steady-state behavior of the neuronal systems. The average activity of these neuron sets as measured in terms of their firing rates can be described well with respect to a simple compartment set of two equations. This so-called mean-field model defines the average activity of each group as follows:

$$E(t) = \frac{1}{N_e} \sum_{j} e_j(t),$$
 (2.3)

$$I(t) = \frac{1}{N_i} \sum_{l} i_l(t).$$
 (2.4)

Equations (2.1) and (2.2) can be expressed by simply using a mean-field model [in Eqs. (2.3) and (2.4)] (Sole & Goodwin, 2000). The dynamics of these variables can be described by using a two-dimensional system defining a network. Figure 1(b) shows the basic topology corresponding to the mean-field model. While this model exhibits oscillations as activity, it is not difficult to obtain more complex patterns by coupling

several of these modules to reproduce patterns that occur in the cerebral cortex (Sole & Goodwin, 2000).

Given an average activity $E_r(t)$ of the excitatory neurons at location r and an average activity $I_r(t)$ of the inhibitory neurons at the same location at time t, this can be represented with Eqs. (2.5) and (2.6) as:

$$\widehat{E}_{r}(t) = -E_{r}(t) + S_{\mu}(C1 \cdot E_{r}(t) - C2 \cdot I_{r}(t) - \Theta^{e} + P), \qquad (2.5)$$

$$\widehat{I}_{r}(t) = -I_{r}(t) + S_{\mu}(C3 \cdot E_{r}(t) - C4 \cdot I_{r}(t) - \Theta^{i}), \qquad (2.6)$$

where $\Theta^e = \sum \Theta_k^e / N_e$, $\Theta^i = \sum \Theta_k^i / N_i$, and $P = p_k / N_e$. This simple model captures the activity in terms of the oscillations. The excitatory and inhibitory neurons are connected through self-interactions [C1 and C4 in Fig. 1(b)] and through crossinteractions [C2 and C3 in Fig. 1(b)] where the excitatory neurons have an external input. P refers to the external input, and Θ^e and Θ^i are the firing thresholds for the two neurons with large values.

In this paper, the mean-field model is combined with the LM algorithm to estimate the parameters of the model. It uses differential equation modeling for population dynamics to generate the new signal $\hat{X}(t)$ that is similar to the observed signal X(t). The initial values for $E_r(0)$ and $I_r(0)$ are set to 0 to generate the new signal by using Eqs. (2.4) and (2.5). The parameters for the proposed method are obtained through a learning process as follows: 9.9, 14.9, 14.9, -4, and 3 for C1, C2, C3, C4, and P, respectively. It uses nonlinear least-square fitting to minimize the sum of the squares of the residuals between observed signals and generated signals. In addition, the Θ^e and Θ^i thresholds are set to 2 and 3.5, respectively, according to Schuster and Wagner (1990).

 $\widehat{E}_r(t)$ and $\widehat{I}_r(t)$ obtained by using Eqs. (2.5) and (2.6) are considered as the new activities for the excitatory and inhibitory neurons at time t. In the sigmoid function $S_{\mu}(\cdot)$, the control parameter, μ is set to 1. Finally, the output of the model is obtained by using Eq. (2.7) (Wilson, 1999).

$$\widehat{X}_r(t) = \widehat{E}_r(t) - \widehat{I}_r(t).$$
(2.7)

The proposed method starts at t(0) with initial pre-defined values, and gains a new activity $\hat{E}_r(0)$ with Eq. (2.5) and $\hat{I}_r(0)$ with Eq. (2.6). The neuron activity for \hat{E}_r and \hat{I}_r obtained from t(0) is applied to Eq. (2.7).

We used the LM algorithm (Gavin, 2013) to automatically find the optimal values for parameters C1, C2, C3, C4, and P. LM is a popular alternative to the Gauss– Newton method to find the minimum of a sum of squares of nonlinear functions. LM repeatedly updates the parameter values to minimize the error value between the observed data and the generated data by Eqs. (2.5), (2.6), and (2.7). The error function of the LM algorithm can be defined as the following:

$$E(\beta) = \sum_{i=1}^{N} [X_i - f(X_i, \beta)]^2, \qquad (2.8)$$

where X_i is the observed data, and $f(X_i, \beta)$ is the predicted data by using function f with parameters β (C1, C2, C3, C4, and P). To minimize $E(\beta)$, β is obtained by updating iteratively as in Eq. (2.9).

$$\beta_{k+1} = \beta_k - (J^T W J + \lambda_k \operatorname{diag}(J^T W J))^{-1} J^T W E(\beta_k), \quad k \ge 0,$$
(2.9)

where the weight matrix W is diagonal with $W_{ii} = 1/w_i^2$, and λ is the Levenbergs damping factor. J is the Jacobian matrix that differentiates E from β as follows:

$$J(\beta) = \begin{bmatrix} \frac{\vartheta E_1(\beta)}{\vartheta \beta_1} & \cdots & \frac{\vartheta E_1(\beta)}{\vartheta \beta_m} \\ \vdots & \ddots & \vdots \\ \frac{\vartheta E_n(\beta)}{\vartheta \beta_1} & \cdots & \frac{\vartheta E_n(\beta)}{\vartheta \beta_m} \end{bmatrix}, \quad E(\beta) = \begin{bmatrix} E_1(\beta) \\ E_2(\beta) \\ \vdots \\ E_n(\beta) \end{bmatrix} = \begin{bmatrix} X_1 - f(X_1, \beta) \\ X_2 - f(X_2, \beta) \\ \vdots \\ X_n - f(X_n, \beta) \end{bmatrix}. \quad (2.10)$$

To optimize parameters β , the order of the LM is as follows. First, we designate the initial parameter values and select λ . In this paper, we would start with a small value such as 0.1. Second, we compute the Jacobian matrix and compute the changing value of the parameters using Eq. (2.9). In other words, when we update the parameters β with λ , if $E(\beta)$ increases, then we increase the λ continually until $E(\beta)$ decreases. Through this process, LM iteratively adjusts the estimates for β , and for each iteration step the set of parameters β is replaced by a new set of estimates for those parameters as β . In this paper, β is an *n* parametric vector that includes *C*1, *C*2, *C*3, *C*4, and *P*. The parameters in the proposed model are adjusted along with time *t*, and the evolving time length generated by the model is limited to 512 time points, which were determined empirically as shown in Table 1. When the signal-generation process for the model has completed, we obtain the adjusted optimal parameters.

3. Experimental Results

In this section, we present the experimental results for the parameter estimation along with the parameter pattern discovery as seizure occurrences. The stability with chaotic behaviors are depicted with vector field simulator. It is also measured the similarity of the generated signals to the observed signals.

3.1. Data description

We performed the experiments on the datasets obtained from the University of Freiburg (http://epilepsy-database.eu/). Epilepsy EEG data were recorded at the Epilepsy Center at the University Hospital of Freiburg, Germany. The data contained 21 patient datasets with medically intractable epilepsy that were obtained through the use of invasive methods. The EEG data were acquired by using an EEG system to sample six signals at a rate of 256 Hz. Electrodes 1–3 were focal electrodes inside of the seizure region, and electrodes 4–6 were extra-focal electrodes, as seen in

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Fig. 2. (Color online) Electrode positions. The red circles indicate the focal areas, and the blue circles indicate the extra-focal areas. (a) Depth-electrode positions for measured signals S1, S2, and S4 from patient P6, (b) strip-electrode positions for the S3 and S6 signals from P6, (c) grid-electrodes of the S5 signal from P6, (d) depth-electrode positions for the S1 to S6 signals for patient P2 (http://epilepsy-database.eu/fspeeg/download/).

Fig. 2. Of the 21 patients, 11 have the epileptic focus located within the neocortical brain structures. The epileptic focus was located in the hippocampus in eight patients, while it was located in both regions for the remaining two patients. Intracranial grid-, strip-, and depth- electrodes were used to record directly from the focal areas in order to obtain a high signal-to-noise ratio and to reduce artifacts. As seen in Fig. 2, the signals obtained from the sixth patient (P6) were recorded by using grid-, strip-, depth- electrodes while the signals obtained from the second patient (P2) were recorded only from the depth- electrodes. Each patient experienced 2–5 epileptic seizure activities. The interictal signals were recorded for a period of at least 24 h without any seizure.

We used the dataset that consists of interictal signals and one epileptic seizure signal as the learning data in order to discover the patterns of seizures from normal functions. For the learning dataset, the window size included 512 time points, and the

Num. Patient		Windo	ow Size		Num. Patient	Window Size			
	256	512	768	1024		256	512	768	1024
P1	0.2259	0.2562	0.1932	0.1826	P12	0.0300	0.0082	0.0241	0.0414
P2	0.0582	0.0596	0.0700	0.0580	P13	0.4385	0.4426	0.3682	0.4333
P3	0.4132	0.1758	0.4658	0.4717	P14	0.0172	0.0465	0.0217	0.0556
P4	0.0998	0.0887	0.0893	0.1146	P15	0.0064	0.0337	0.0157	0.0068
P5	0.1721	0.0885	0.0417	0.0819	P16	0.1255	0.1173	0.1350	0.1043
P6	0.0814	0.0427	0.0834	0.0571	P17	0.0008	0.0007	0.0303	0.1489
$\mathbf{P7}$	0.0555	0.0216	0.0323	0.0513	P18	0.3314	0.3072	0.2688	0.3180
P8	0.0852	0.0958	0.0532	0.1163	P19	0.1031	0.0946	0.1121	0.0715
P9	0.1614	0.1346	0.1441	0.1471	P20	0.0560	0.0336	0.0132	0.0218
P10	0.1092	0.0462	0.0848	0.0985	P21	0.0429	0.0341	0.0359	0.0382
P11	0.0382	0.0468	0.0315	0.0536	Average	0.1263	0.1036	0.1102	0.1273

Table 1. RMSE by window length in seizure signal.

experimental data from a single patient had 50 window sets. Window size was selected through empirical experiments by considering the sampling rate of the data. That is, window size was selected as the lower root mean square error (RMSE) between the recorded signal during a seizure and the signal generated by the model. Table 1 shows the RMSE per window size, and a window size of 512 shows a lower error rate than the other window sizes. In this paper, we use the notation P1S3W16 to indicate window W16 from signal S3 for patient P1.

3.2. Stability with chaotic behavior

In this paper, we used a nonlinear dynamic model based on a NPM and the LM algorithm to estimate the values of neurophysiological parameters using a biophysical model of brain dynamics. The biophysical model about the neurophysiological brain function model was incorporated with a cortical function including axonal transmission delays, synapto-dendritic rates, range-dependent connectivities, excitatory and inhibitory neural populations. NPMs can describe the macroscopic neural activity that can be clinically recorded by an EEG. In addition, it is relevant to the investigation of many pathological neurological phenomena including epilepsy and Parkinsons disease because the models are operated on the same scale as the recorded data. Although several models exist in the neuroscience literature, none has leveraged the systematic approach of optimal control theory to design stimuli to treat such neurological conditions (Ruths *et al.*, 2014).

A nonlinear dynamic model consists of differential equations involving the derivatives of a function. The parameters of these equations are unknown and must be extracted. The proposed method is a nonlinear dynamic model with a set of differential equations that estimate the optimal parameters from the observed EEG data including the chaotic behavior. We applied a vector field method to prove the stability of the differential equations in the proposed model. The vector fields can be visualized in the phase space of a dynamic system that exhibits extremely



Fig. 3. (Color onlline) Screen shot of the vector field simulator. The vector field of the phase plane for the damped pendulum is on the left, and the activity of excitatory neurons (black line), activity of inhibitory neurons (green line), and signal generated for the activity of the excitatory and inhibitory neurons (red plus symbol) are on the right.

complicated and chaotic behavior (Krauskopf & Osinga, 1999). The challenge is to find stable and unstable manifolds of the equilibria and periodic orbits because these organize the global dynamics of the system. The global bifurcations and routes for chaos can be identified by tracing the changes in the stability and instability of the manifolds as the parameters vary.

Figure 3 shows the phase space and the flow for a damped pendulum (left) as well as the signal generated by using Eqs. (2.5) and (2.6) (right). A two-dimensional phase space provides a qualitative picture of the behavior in the dynamic system including its orbit and flow. In the vector field plot (left), the red curve indicates an orbit or trajectory in a phase space that is obtained by solving the equation. The blue arrows of the vector field are tangential to all of the trajectories in the phase space. Some points in the phase space approach a stable fixed point as $t \to \infty$. In summary, if all trajectories approach a fixed point, stability is guaranteed in the analysis. In other words, if all of the trajectories diverge through an infinite series, then the system becomes unstable. In the proposed model, the vector field converged on a fixed point. That is, it can be considered to be very stable according to vector field theory. The vector field or structure of the phase space depends on the given parameters, and small changes in the values of the parameters can produce larger qualitative changes in the phase space. Therefore, nonlinear dynamic systems require the use of a parameter fitting method that considers the stability and reflects the conditions for the chaotic behavior.

3.3. Parameter estimation for best fitting

We used the LM method, which is a popular method for finding the minimum of a function to solve the parameter estimation problem. This method can automatically detect the optimal parameter values through an iterative process, to minimize the

sum of squares of the differences between the input and output data of the model. The nonlinear differential equation is critically dependent on either the initial values for the parameters or the initial conditions. Therefore, to obtain the initial parameter values in nonlinear dynamic models, we used the LM learning process to determine the initial values for the parameters that could guarantee the best performance. The suitability of using LM to estimate the parameters was verified by measuring the accuracy of the signals that were generated. We then compared the optimal parameters obtained with LM with those obtained with other state-of-the-art methods, such as genetic algorithms (GAs) and Markov chain Monte Carlo (MCMC) methods (Chen & Wang, 2009; Cowles, 2013).

For this experiment, we used both sinusoidal and synthetic signals, as shown in Fig. 4. Figures 4(a) and 4(b) show the original sinusoidal signal and the signals generated by using random and fixed initial parameters. A synthetic input signal of (c) and (d) was created with a nonlinear dynamic model without the LM process by using arbitrarily selected parameters as follows: C1 = 3, C2 = 7, C3 = 10,



Fig. 4. Comparison of LM against other state-of-the-art methods. The generated signal was estimated with the proposed method by using random as well as fixed initial parameters, and a comparison was performed by updating the values of the parameters obtained with LM as well as the other state-of-the-art methods for 1000 iterations: (a) Sinusoidal signal generated using random initial parameters, (b) sinusoidal signal generated using fixed initial parameters, (c) synthetic signal generated using random initial parameters.

Data	Sinu	ısoidal Sig	gnal	Synthetic Signal			
Method	MCMC	\mathbf{GA}	LM	MCMC	\mathbf{GA}	LM	
Fixed initial Random initial	$0.3037 \\ 0.30722$	$0.1482 \\ 0.1489$	0.0721 0.3061	$0.20751 \\ 0.20774$	$0.3055 \\ 0.3069$	0.035 0.2177	

Table 2. RMSE of the generated signals is measured from both sinusoidal and synthetic signals using random and fixed initial parameters.

C4 = -5, and P = 1. Also, Figs. 4(c) and 4(d) show the signals generated by LM, GA, and MCMC, respectively. The fixed initial parameters were determined using an LM learning process of 40⁵ by using a synthetic input signal created based on the above arbitrarily selected parameter values [see the original signal of Figs. 4(c) and 4(d)]. The boundary for all parameters during the learning process was configured to have a lower limit at -20 and an upper limit at 20. The optimal values obtained according to the empirical probability for the fixed initial parameter values in Fig. 4 are as follows: C1 = 9.9, C2 = 14.9, C3 = 14.9, C4 = -4, and P = 3. GA requires an initial population in order to start, which can either be randomly generated or pre-defined with starting values that are known to be adequate. The initial values used for the parameters include a population size of 40 and a maximum generation number of 1000.

The RMSE between the original and the generated signal is shown in Table 2. We assumed that the lowest RMSE provides the optimal values for the parameter values. For the sinusoidal signal, the lowest RMSE was exhibited when we used fixed initial parameters for the LM. In addition, we measured the accuracy of synthetic signals that were generated by using the proposed method without LM learning for the input data. In the case of the synthetic signal, the RMSE obtained with LM learning is 0.035 when fixed initial parameters were used. The results of this experiment indicate that the proposed model can guarantee the lowest RMSE between the observed signal and the generated signal when fixed initial parameters for the LM were used.

Table 3 shows the RMSE and execution time to generate signals using the fixed initial parameters on epileptic signals of several patients. In this experiment, we divide the input signal into normal and seizure signals with 512 time points for each patient. We measured the RMSE through parameter estimation methods that used fixed initial parameters. The results indicate that the proposed model with LM parameter estimation obtained the lowest RMSE when compared with other methods. In addition, the execution time of the proposed method was the fastest among the other methods, as shown in Table 3, since it has well-behaved functions and reasonable starting parameters.

3.4. Signal estimation

The performance of the proposed method was measured to ensure it provides a correct estimation for the signal compared with an auto-regressive (AR) model and

		MCMC	$\begin{array}{c} 0.0125\\ 628.61\\ 0.0219\\ 247.60\end{array}$
tter set.	P17	GA	$\begin{array}{c} 0.0152 \\ 49.281 \\ 0.0207 \\ 49.047 \end{array}$
uai param		ΓM	0.0087 3.4320 0.0094 5.8812
g a nxeu mu		MCMC	$\begin{array}{c} 0.1463\\ 253.91\\ 0.2473\\ 244.05\end{array}$
THOUS USING	P11	GA	$\begin{array}{c} 0.1391 \\ 48.704 \\ 0.0875 \\ 48.875 \end{array}$
ng une mei		ΓM	0.0241 4.2900 0.0664 2.4960
erate signais, comparit		MCMC	$\begin{array}{c} 0.1505\\ 238.74\\ 0.1172\\ 542.06\end{array}$
	P6	GA	$\begin{array}{c} 0.0849\\ 49.265\\ 0.1335\\ 87.844\end{array}$
(sec) to ge		LM	0.0761 3.7596 0.0791 3.9780
TADIE 9. NIVIJE AND EXECUTION UNITE		MCMC	$\begin{array}{c} 0.1438\\ 235.17\\ 0.3009\\ 214.38\end{array}$
	P1	GA	$\begin{array}{c} 0.1494\\ 49.1091\\ 0.3010\\ 48.594\end{array}$
		ΓM	0.0062 2.7456 0.0223 5.8968
	ient	hod	RMSE Time RMSE Time
	Pati Metł		Normal Seizure

+05 frod initial n athods th, - low ----+ rution RMSE and e Table 3

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Fig. 5. Comparison of the observed signal against the signals generated with the proposed method, the AR method, and the nonlinear Gaussian kernel regression method: (a) Normal signal for P5S1W15 and (b) seizure signal for P18S1W45.

the nonlinear Gaussian kernel method (Yuan *et al.*, 2009; Chisci *et al.*, 2010). The AR model has been extensively applied in prediction problems, and is known to be a good model for linear prediction. The nonlinear Gaussian kernel method is a nonlinear regression analysis that produces predicted signals in a smoothing fashion. The parameters for each model were set for this experiment, with the order of the auto-regression p = 2 and the nonlinear Gaussian kernels constant h = 5. Figure 5(a) shows part of signal S1 from patient P5 during normal activity. The results indicate that the proposed method generated a more accurate signal relative to the observed signal than the AR model and the nonlinear Gaussian kernel method. Figure 5(b) shows the seizure signal S1 from patient P18. In this case, the P18S1 signal can be seen to have a much higher frequency than the P5S1 signal. The proposed method generates a new signal that can trace the observed signal, including complex frequencies.

In Table 4, the RMSE was calculated between the observed signal and the generated signal for all patients. All of the signals from each patient are composed of 35 normal window sets and 15 seizure window sets. We measured the accuracy without discriminating between the normal and the seizure signals. The results indicated that the proposed method performed well and was more accurate for all patients than the AR model and the nonlinear Gaussian kernel method. With these results, we can infer that the parameters used for this model are optimal, providing the lowest RMSE between the observed signals and that generated with the proposed model.

We obtained the optimal parameters for each window set from the 21-patient dataset. For example, as shown in Table 5, the P5S1 signal obtained from the focal areas of the seizure has optimal values for C1 and C3, which minimize the error between the obtained signal and the generated signal and remain positive. C4 and P are largely represented by negative values, and the values for C2 are obtained in both

Table 4. RMSE between the observed and generated signals compared to the non-parametric methods.

_	Proposed	Auto-	Nonlinear Gaussian	_	Proposed	Auto-	Nonlinear Gaussian
Patients	Method	Regressive	Kernel Method	Patients	Method	Regressive	Kernel Method
P1	0.0605	0.3017	0.3533	P12	0.0310	0.0519	0.3744
P2	0.0737	0.0754	0.3504	P13	0.1092	0.2098	0.6570
P3	0.1647	0.4106	0.4082	P14	0.0130	0.0348	0.0995
P4	0.0259	0.0383	0.4267	P15	0.1331	0.0428	0.1161
P5	0.0485	0.1383	0.1095	P16	0.0196	0.0471	0.2617
P6	0.0097	0.1522	0.3495	P17	0.0031	0.3169	0.1901
$\mathbf{P7}$	0.0029	0.0435	0.3922	P18	0.2269	0.1356	0.4992
P8	0.1110	0.1031	0.4136	P19	0.0364	0.0693	0.2854
P9	0.0036	0.2664	0.2723	P20	0.0672	0.0932	0.3246
P10	0.0240	0.1013	0.2926	P21	0.0589	0.1086	0.2169
P11	0.1030	0.1235	0.1879	Average	0.06313	0.1364	0.3133

Table 5. Optimal parameters and the RMSE in epilepsy datasets.

Data	Signal	C1(In)	C2(EI)	C3(IE)	C4(Ex)	P(External)	RMSE
P5S1	Win10	1.6584	4.6344	9.2528	-10.795	-0.0669	0.0153
	Win20	1.7529	3.3868	8.8478	-9.9731	-0.3820	0.0118
	Win30	7.2258	-3.5894	20.4022	-11.182	0.0190	0.0168
	Win40	10.5626	-8.5043	18.7538	-10.642	2.1763	0.0140
	Win50	7.9316	-5.3095	23.4701	-12.336	-0.0347	0.0184
	Average	5.8263	-1.876	16.145	-10.985	0.3423	0.0153
P15S2	Win10	7.5133	-3.2195	11.3329	-10.200	-5.0000	0.0075
	Win20	1.5096	7.3552	7.6501	-8.7523	-2.9654	0.0054
	Win30	2.7999	11.587	7.6701	-8.4490	-2.0864	0.0062
	Win40	5.5442	-7.7407	21.4605	-11.614	-1.2936	0.0250
	Win50	5.1276	-9.7190	18.1164	-8.8721	-2.9284	0.0060
	Average	4.4989	-0.3474	13.2460	-9.5775	-2.8548	0.0100
P15S2	Win10	1.5900	2.9130	8.4830	-11.7220	-0.7010	0.0224
	Win20	2.2060	14.4590	9.7800	-11.3220	-4.8140	0.0131
	Win30	9.7970	-6.0800	9.8810	-11.0060	3.1640	0.0088
	Win40	6.3210	-4.7520	20.5250	-10.8080	-0.0300	0.0174
	Win50	8.3970	-3.5830	19.2070	-10.4010	0.1260	0.0137
	Average	5.6622	0.5914	13.5752	-11.052	-0.4510	0.0151

positive and negative ranges. The average RMSE for the P5S1 data was 0.0153. For P15S2 and P18S3, the average RMSEs were 0.01 and 0.0151, respectively. Each window of the other patients provided a similar result to that of P5S1. Thus, the proposed model provides a high rate of accuracy when the new signals are generated. In this experiment, we can discover patterns that were obtained from the optimal parameters of the entire dataset. We can use these parameters to distinguish between normal and seizure signals. We provide further detail on how patterns present the approaching of seizure onset in Sec. 3.5.

3.5. Parameter changes as seizures

We discovered special patterns in terms of the values of the parameters that allow for the signals to be classified into either normal or abnormal. Most normal signals had a C1 < 5 and seizure signals had C1 > 5. C3 had positive values, where C3 < 10 was normal and $C_3 > 10$ indicated a seizure. C_2 is the most important parameter because signals can be classified into positive for normal function and negative for seizures. During the training process described by Kim *et al.* (2013b), we observed a consistent pattern where the parameters allow the signals to be distinguished between normal and seizure. For example, the majority of healthy signals exhibited positive values for C1 and C2 with C1 < 5 and C2 > 0, while the majority of the seizure signals produced C1 > 5 and C2 < 0. Therefore, we discretionally define the parameter regions by using a statistical distribution of the parameter values. The results of the observations provided by Kim *et al.* (2013b) are used as the parameter region for the normal and seizure behaviors. We assume that the parameters for the normal signals appear inside a consistent area that depends on the above-mentioned parameter distribution region. We introduce the proposed method phase plot as a visualization tool shown in Fig. 6. The proposed method phase plot is a scatter plot of C1 vs. C2, for each window W_i ($i = 1, \ldots, 50$) for a given patient P and signal S. Figure 6 shows two carefully chosen parameters (viz., C1 and C2) to discriminate seizure onset.



Fig. 6. Phase plot of the proposed method: (a) First "crucial" window, (b) all "crucial" windows before seizure, and (c) all "crucial" windows from the entire signal. An alert can warn of an impending seizure by noticing that C1 and C2 parameters deviate away from the "normal" region. We present a time-plot and a phase-plot stage by stage. Notice that most of the "normal" signal windows fall within the "normal" area of $(0,5) \times (0,10)$. The "crucial" parameters, C1 and C2, are either declared as "seizures" or as possible early alerts.

In the dataset, the seizure begins in the 36th window signal. Figure 6(a) shows the first "crucial" parameters that appear for P4S6W4. In the plot, the square formed by the black dotted line indicates the region that contains a normal parameter. However, the parameter for P4S6W4 is observed to be outside of the square formed by the black dotted line. Figure 6(b) shows the parameters as measured before the onset of an epileptic seizure (i.e., until the 35th window). It presents the patterns in the phase plot of parameters C1 and C2 with the data recordings for 1 min 10 s (35 window set) before seizure onset. For all six windows, the parameters deviate outside of the onset of a seizure. Figure 6(c) shows all the data from the time windows for P4S6. In this plot, only one of the red circles appears inside of the normal window region (in the 36th window signal). During this time window, the patient underwent an epileptic seizure. Except for this single case, however, most windows appeared inside of the red square, which indicates that these windows represented abnormal conditions.

In the epilepsy dataset, the region for the "crucial" windows (red color square) is clearly separated from the region for the normal windows. We use these "crucial" windows to show patterns of a seizure approaches. Before an epileptic seizure commences, a pattern of the onset of a seizure can be utilized by detecting that "crucial" windows have begun to appear outside of the region for normal windows. Table 6 shows the number of seizure approaching signs for five patients where the optimal parameters from the normal signal windows (35 window set) were used before the onset of a seizure. P4S1 had four approaching signals before the onset of a seizure, while P4S2 and P4S3 both had five. P4 shows an average of four alerts for every six signals. Patient P7 had an average of five approaching signs and P14, P16, and P20 had averages of 4, 5, and 7 approaching signs, respectively. These results also indicate that more approaching signs appeared from focal (1–3) electrodes than from extrafocal (4–6) electrodes. Therefore, we establish the hypothesis that a seizure can be detected from the signal of a few focal electrodes.

The receiver operating characteristic (ROC) curve is one of the best-known approaches to provide a reliable indication of overall separability, with regard to sensitivity and specificity, to discriminate between two amplitude distributions

			Signal Number							
Patients		S1 Normal	S2 Normal	S3 Normal	S4 Normal	S5 Normal	S6 Normal			
Signs/No. Window	P4 P7 P14 P16 P20	4 7 5 7 9	$5 \\ 5 \\ 4 \\ 6 \\ 9$	5 8 5 7 8	$\begin{array}{c}3\\5\\4\\4\\6\end{array}$	$5 \\ 3 \\ 3 \\ 6 \\ 6 \\ 6$	$ \begin{array}{c} 6 \\ 4 \\ 4 \\ 5 \\ 5 \end{array} $			

Table 6. Number of approaching signs using a "crucial" window with C1 and C2 parameters.

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	Proposed	l Method	L	E	ECD		
Patients	Sensitivity(%)	Specificity(%)	Sensitivity(%)	Specificity(%)	Sensitivity(%)	Specificity(%)	
P1	82.9	93.3	100.0	93.3	88.6	73.3	
P2	77.1	100.0	94.3	100.0	85.7	73.3	
P3	85.7	100.0	94.3	100.0	88.6	66.7	
P4	88.6	93.3	100.0	100.0	91.4	66.7	
P5	80.0	100.0	97.1	93.3	88.6	93.3	
P6	85.7	93.3	100.0	93.3	88.6	86.7	
$\mathbf{P7}$	80.0	100.0	100.0	100.0	91.4	66.7	
P8	88.6	100.0	100.0	93.3	85.7	80.0	
P9	82.9	100.0	100.0	100.0	88.6	73.3	
P10	82.9	93.3	88.6	100.0	91.4	73.3	
P11	80.0	100.0	100.0	100.0	85.7	60.0	
P12	82.9	100.0	97.1	80.0	85.7	86.7	
P13	88.6	100.0	100.0	100.0	88.6	86.7	
P14	85.7	93.3	97.1	100.0	91.4	86.7	
P15	85.7	100.0	97.1	93.3	94.3	80.0	
P16	80.0	93.3	97.1	93.3	85.7	60.0	
P17	77.1	100.0	100.0	86.7	82.9	86.7	
P18	88.6	100.0	97.1	93.3	91.4	86.7	
P19	85.7	100.0	100.0	86.7	88.6	86.7	
P20	74.3	93.3	97.1	100.0	82.9	60.0	
P21	82.9	93.3	94.3	93.3	88.6	66.7	
Average	83.1	97.5	97.7	95.2	88.3	76.2	

Table 7. Sensitivity and specificity.

(Mormann *et al.*, 2005). The sensitivity is the ratio of the true positive classifications to the total number of positive classifications, based on Table 6 and specificity is the ratio of true negative classifications to the total number of negative classifications.

The LE and the effective correlation dimension (ECD) are commonly used to detect seizures (Marshall, 2014; Shayegh *et al.*, 2014). The LEs define the average exponential rate of the divergence or the convergence of nearby orbits in the phase space. The LEs are estimated from data by using the popular Wolf algorithm which detects and quantifies chaos in experimental data by accurately estimating the first few non-negative LEs (Wolf *et al.*, 1985). The dimension of the correlation is used in order to detect the onset of an epileptic seizure in terms of the decrease in dimensionality. That is, a reduction in dimensionality can be indicated during a seizure (Osorio *et al.*, 2001).

In Table 7, the sensitivity indicates the correct classification of normal signals as normal, and the specificity indicates the probability of classifying signals as seizures. In this paper, we demonstrate that using a nonlinear dynamic model with the corresponding optimal parameters provides the patterns of a seizure approache. The approaching sign is provided by using false negatives within the confusion matrix that classify normal signals as seizure signals. Therefore, the proposed method offers the patterns of seizures in advance with a low sensitivity and a high specificity. Table 7 shows that the proposed method and ECD have similar sensitivities, differing

only by 5% on average, while the specificity of ECD appears to be 20% lower on average than the proposed method. A high probability was reported for LE in terms of both sensitivity and specificity. Therefore, the proposed method can present a robust pattern of a seizure approaching when compared to other methods.

4. Discussion

In order to validate a nonlinear model, an important task is to identify unknown parameters from actual data captured from experiments. We used a parametric estimation method constrained with differential equations in order to analyze an epilepsy EEG data. The two methods that are normally used for parametric estimation include least- squares estimation (LSE) and maximum likelihood estimation (MLE) (Johnson & Faunt, 1992). LSE is used to fit a model to the given data by minimizing the sum of squares of the errors between the observed data and the generated data by the model. The Gauss–Newton method can be used for such ends, and an improved version thereof is the LM algorithm. On the other hand, MLE is a standard approach and an indispensable tool for parametric estimation, particularly for nonlinear modeling. A GA and a MCMC method (i.e., Bayesian estimation) are based on MLE and can also be used.

Jansen *et al.* (2001) used a GA to perform a parametric estimation of peri-stimulus EEG activity. Chen & Wang (2009) estimated the kinetic parameters for the hydrogenation reaction in DNA. A GA was employed for parametric estimation problems (Goldberg, 1989), and the GAs have since been applied in various disciplines (Nougues *et al.*, 2002), (Milani & Milani, 2012). With respect to EEG data, Valdes *et al.* (1999) reported the first model fitting, and Bremer & Kaplan (2001) and Zhou *et al.* (2011) used a Bayesian approach to perform parametric estimation of EEG models via a marginalized MCMC approach. In this paper, we proposed LM to estimate the parameter set and showed that it outperformed the other state-of-the-art methods.

The proposed method is a nonlinear dynamic model that uses differential equations based on an LM algorithm to minimize the sum of the squares of the deviations between observed data and the data generated by a model. The final goal of our model is to provide the patterns of a seizure approache. Much research has been conducted to this end by using nonlinear, LE, and correlation dimension (CD) methods. Jansen & Rit (1995) proposed a canonical form of the population model adapted to the simulation of spontaneous EEG and evoked the potential for the visual cortex. Gourevitch *et al.* (2006) developed complementary approaches in order to estimate the direction of the coupling between signals by reflecting the external inputs. These methods are based on linear systems and can capture only linear properties of relationships within the time series. However, the epilepsy EEG signals acquired from patients are nonlinear.

Various methods based on nonlinear dynamics have been employed to detect seizures. Sackellares *et al.* (2006) evaluated the performance of an adaptive threshold seizure-warning algorithm that detects the convergence in short-term maximum LE values obtained from critical intracranial EEG electrode sites as seizure precursors. Nesaei and Sharafat (2013) proposed a method to detect seizures by considering the largest LE as the discriminating feature in a discrete wavelet packet transform in segmented EEG signals. Maiwald *et al.* (2004) suggested that the characteristic useful in predicting seizures is a function of the sensitivity and the maximum false prediction rate. It is revealed by assessing and comparing three nonlinear prediction methods by means of the seizure prediction characteristics including the ECD, the dynamical similarity index, and the prospective version of the accumulated energy.

In the present paper, we compared the performance of the proposed method with that of the state-of-the-art methods mentioned above. The proposed method is based on a nonlinear dynamic model and can provide the optimal parameters of model to draw the signal that was most similar with complex epilepsy EEG data.

5. Conclusion

We developed an approach to provide the best parameter values for analyzing epilepsy EEG data. The proposed method also can discover the essential parameters that are able to distinguish the seizure signal from normal data using a nonlinear, dynamic model which is based on a NPM. The proposed method offers the best parameters of the model to generate the data that most closely resembles to the obtained data. Our analysis indicates that the combination of C1 and C2 parameters (i.e., the "crucial" parameters) in the proposed method is sufficient to distinguish windows of normal function from those with seizure activity. Furthermore, the "crucial" parameters present the patterns of the approaching of seizures.

Our model takes into account the chaotic characteristics of the epileptic signals by using a NPM. A nonlinear dynamic model is combined with an LM algorithm to provide the potential for discriminating between healthy activity and seizures. In future studies, we will extend the new parameter estimation method to find a global minimum in order to solve the multi-structure curve-fitting problems.

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