Seizure Prediction with a Single iEEG Electrode Using Non-linear Techniques

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Abstract – **A novel method to predict epilepsy seizures using a single iEEG (Invasive Electro Encephalogram) channel is presented in this paper. This method can potentially facilitate surgeries performed on epileptic patients by avoiding the insertion of grid or stripe electrodes. Both surgery complications and cost would become more acceptable. Also, using a single electrode would significantly reduce the computational effort and; consequently, the power consumption of the Bluetooth implant that will be designed in a later phase. Since epileptic seizures are characterized by a change in the EEG entropy, the signal is processed through a combination of linear and non-linear techniques to determine the seizure signature and to perform its prediction process. Nonlinear techniques allow therefore describing, in a suitable way, the output dynamics of the IEEG channel and then the different evolution stages of oscillatory states. Stability could be characterized by appropriate tools like Lyapunov exponent and phase diagram.**

Moreover, we describe the proposed Bluetooth implant design to give more insight about how we process the seizure detection.

Keywords: Seizure, EEG, Non-Linear Computing, Neural Implant, Chaos theory.

I. Introduction

Epilepsy is a nervous disorder that affects approximately 1% of the world population. Most of the cases can be treated pharmaceutically but nearly 30% of the patients are drug resistant. In this paper, our technique is based on a combination of statistical approaches and chaos theory to predict the occurrence of critical states in the nervous system.

II. State-of-the-Art and Background

Our seizure prediction algorithm relies on non-linear techniques where the signal correlation and entropy are being monitored. EEG signals are broken down into Delta (0-4Hz), Theta (4-8Hz), Alpha (8-15Hz), Beta (15-30Hz) and Gamma (higher than 30Hz) sub-bands. It has been proven in a previous publication [1] that a temporal seizure is preceded by an increase of both the amplitude and the cross-correlation in the Delta sub-band along with a convergence in the Gamma sub-band from a chaotic behaviour to a more synchronized pattern. The algorithm is trained for the specific values of each patient in order to depict interictal, preictal and ictal states. In this experiment, Gamma frequencies stop at 128 Hz due to the 256 Hz sampling frequency used in the current Database.

In the context of using a single electrode, Greene et al. [2] proposed a neonate seizure detection system based on a single surface EEG channel. They extracted a certain number of EEG features and used a classifier to learn the onset signature. Their work was based on training their algorithm on several channels before detecting the most accurate among them. The approach was rather generic than patient specific and no prediction time was provided. Conradsenabd et al. [3] worked on a single surface electromyogram (sEMG) channel to detect the approach of tonic-clonic seizures. They waited until the patient reaches a convulsion state to measure the muscle nervous voltage instead of the EEG signal itself. The target application was far from the seizure anticipation. To the best of our knowledge, no other studies were performed on a single invasive EEG channel for seizure anticipation.

The literature witnessed a certain number of prediction approaches based on non-linear techniques. Iasemidis and Sackellares [4] were the pioneers in predicting seizures through this approach in the 1980s. They first started using the Principal Lyapunov Exponent (PLE) then the Short-Term Lyapunov Exponent (STL). In the last decade, non-linear approaches were used by several researchers to obtain better sensitivity, lower False-Positive (FP) and higher prediction time. Iasemidis *et al.* [5 and 6], Maiwald *et al.* [7], Chaovalitwongse *et al.* [8] and D'Alessandro *et al.* [9].

Other combined techniques were used as well and obtained similar results. Netoff *et al.* [10, 11, 12, 13, 14, 15, 16, 17, 18, and 19] experimented a patient specific classification algorithm on 9 patients from the Freiburg database [20]. Shiau *et al.* [21, 22, and 23] proposed an Automated Seizure Prediction Algorithm (ASPA) based on non-linear techniques (STL) and adaptive transition thresholds according to the current state of dynamical interactions among brain sites. Senger *et al.* [24] used Cellular Nonlinear Networks (CNN) or 'brain like computing' to work on 2 patients having 10 seizures. Duman *et al*. [25] used the Hilbert Huang Transform. Zandi *et al*. [26] worked on a patient specific variational Bayesian Gaussian mixture model of zero-crossing intervals and, finally, Zheng *et al.* [27] developed a Seizure Prediction Model Based on a method of Common Spatial Patterns and Support Vector Machine (CSSVM) to establish a Support Vector Machine (SVM) classifier.

This paper combines statistical and non-linear approaches to form an integral technique aiming at defining a unique seizure signature for each patient using a single electrode. This signature will be used to 'train' the implant to predict seizures with an acceptable rate and a reliable false positive. Theoretical background is presented in section 3. Section 4 describes the adopted methodology. Section 5 presents the proposed Bluetooth implant and, finally, section 6 details the obtained results and compares them with the previously described techniques.

III. Non-Linear Techniques

Two methodologies were used herein to determine the stability of an oscillatory state in a chaotic system: the Lyapunov exponent [28] and phase plan methodologies [29]. Both are efficient to determine either stable or unstable states of a system close to a periodic trajectory or an equilibrium point as described in the following.

A. System dynamics

The human brain is one of the most non-linear and complex systems in nature. Its systems' dynamics can be described as a set of discrete time equations of the form:

$$X_{n+1} = f(X_n) \qquad (1)$$

Where n is the number of samples. If the dynamic system is discrete time, it can be described through a set of first order differential equations $X(t)$ as in equation (2):

$$\frac{dX(t)}{dt} = F\big(X(t)\big) \qquad (2)$$

Non-linear system dynamics can be characterized by monitoring its outputs (state vector components) within the phase plane.

System behaviour is studied for the following control parameters describing: $\beta = 14.87$, $m_0 = -1.27$, $m_1 = -0.68$ and α represents the control parameter. Using a bifurcation diagram, it is possible to predict all the oscillating states generated by this system.

The bifurcation diagram is shown in Fig. 1. Increasing the α values from the initial value of 6 yields to a bifurcation around the value of $\alpha = 6.75$. The same phenomenon is replicated through an infinity of bifurcations afterwards yielding to an infinity of frequency components in the EEG signal.

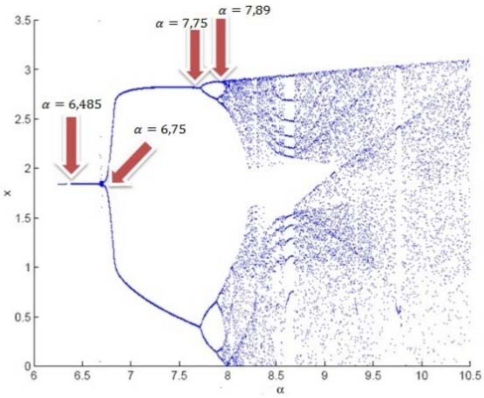

Fig.1: Chua system bifurcation diagram.

B. Use of Lyapunov method in detecting chaotic behaviour

The use of the Lyapunov index constitutes another powerful tool to detect and characterize both chaotic and regular dynamic systems [30].

For a given signal, the Lyapunov index λ is used to obtain a measure of the very sensitive dependency to initial conditions, which is typical to all chaotic systems. Let us consider a function:

$$X_{n+1} = f(X_n) \qquad (5)$$

Considering $X_0$and Y_0 as two initial points in the phase space and considering n such as:

$$X_n = f^n(X_0) \text{and } Y_n = f^n(Y_0) \qquad (6)$$

In a dynamic system, sensitivity to initial conditions can be expressed as a distance separating two trajectories that is growing exponentially in time until equalizing the attractor diameter as seen in Fig. 1. Consequently, supposing that n is big enough, the approximation of the separation between the two points is:

$$|X_n - Y_n| = |X_0 - Y_0|e^{\lambda n} \qquad (7)$$

If n becomes very big $(n \to \infty)$ λ value would be:

$$\lambda = \lim_{n\to\infty} \frac{1}{n} ln\left|\frac{X_n - Y_n}{X_0 - Y_0}\right| \quad (8)$$

Knowing that n cannot tend indefinitely to infinity, λ would be:

$$\lambda = \lim_{n\to\infty} \frac{1}{n} ln\left|\frac{df^n(X_n)}{dX_0}\right| \quad (9)$$

And finally:

$$\lambda = \lim_{n\to\infty} \frac{1}{n} \sum_{k=0}^{n-1} ln\left|\frac{df(X_k)}{dX_k}\right| \quad (10)$$

In periodic cases, the starting point X_0 does not have a lot of importance. The situation is completely different in chaotic cases.

Table 1 explains the meanings of different Lyapunov index values.

Table 1 : λ value meanings

Dynamics type	λ_{max} *value*
Stable point	λ < 0
Limit of stable cycle	λ = 0
Chaos	0 < λ
Noise	λ = ∞

Going back to Fig. 1, it is possible to link the value of the control parameter α with the Lyapunov index λ. Moving α to the right of the bifurcation point would cause a chaotic behaviour and cause λ values to be positive. Similarly, moving α to the left of the bifurcation point would cause the system to be more stable and; consequently, λ to be negative. For each patient, thresholds for both λ and its derivative were determined empirically for the Gamma signals. At the same time, we used the Duffing oscillator to illustrate the frequential behaviour of the Delta signal and the associated Signal–to-Noise Ratio (SNR). Consequently, predicting a seizure is triggered by:

- An increase in the system stability being monitored through a decreasing λ,
- A decrease in the frequential content of the EEG signal.
- An increase in the SNR along with a Delta spike.

These values contribute in determining the epileptic seizure signature.

IV. Methodology

A. Database description

The patients' list used in this work comes from the Freiburg Database [10] and contains EEG signals from 21 patients from different ages and genders. Seizures are signalled by neurologists with a 4-millisecond accuracy. Each seizure is preceded by not less than 50 minutes of preictal time and all patients were monitored for at least a 24-hour interictal period. EEG signals were sampled at a 256 Hz rate. This gives a medium resolution for the basic frequencies; however, it unfortunately prevents the experimental results to explore any ripples occurring above the Nyquist frequency of 128 Hz.

B. Single electrode prediction technique

Experimental results are summarized in Table 2. The technique consists of determining the Delta voltage threshold then finding a relative voltage maximum occurring in the same time window than a relative minimum for the Lyapunov index λ (Fig. 2).

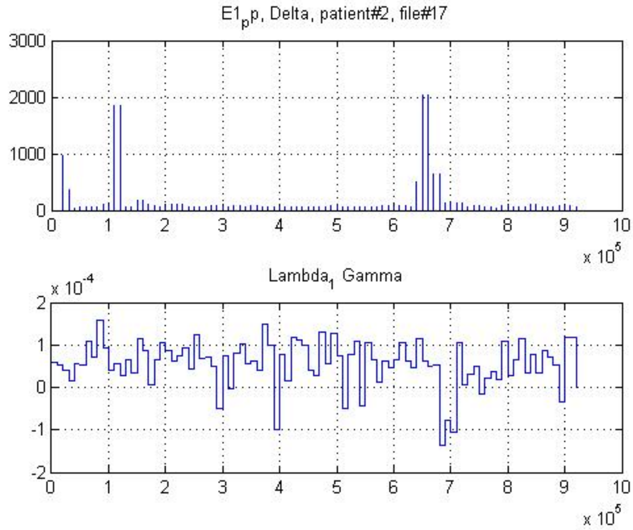

Fig.2: Seizure predicted through a relative Delta maximum voltage along with a relative Lambda minimum. Sample # 680,000

Having more than one focal point would require more than one electrode. On the other hand, seizures that immediately start generalized will not be detected.

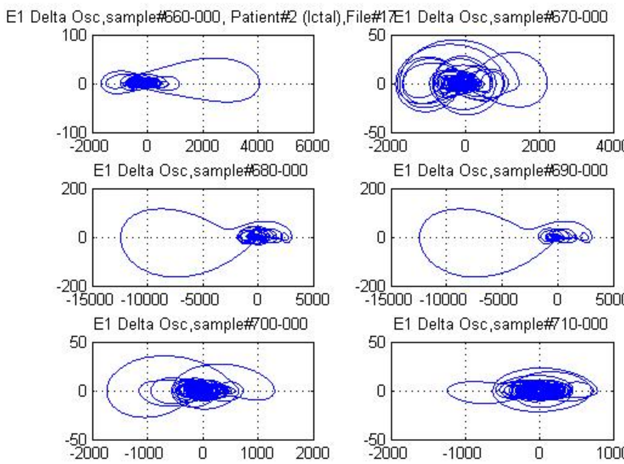

Fig.3: Duffing oscillator around the anticipation point (sample # 690,000)

Delta voltage shows a first peak around the sample # 110,000. Since no drop in the Gamma entropy is noticed at that moment, the required and sufficient conditions for a seizure are not met. A second peak in the Delta voltage appears at the sample # 670,000 and is immediately followed by a decrease in λ_{Gamma} and its derivative. These 2 conditions constitute a seizure warning.

Duffing oscillator was used to simultaneously monitor the behaviour of both Delta signals and their derivative.

Figure 3 clearly shows that, at the moment of the seizure prediction, the oscillator diagram takes a shape of a horizontal ¨8¨ with the two characteristic wells of a Duffing oscillator and that the spectral content of the signal tends to a minimum knowing that a given frequency with its harmonics would be represented with a unique line. It is worth mentioning that the SNR reaches its maximum value at the instant of a seizure detection and that the existing noise may have a DC (Direct Current) component at certain moments.

Table 2 : Experimental result summary

	Detected seizures	**Total seizures**	**Gender**	**Age**	**Recording Duration (Hours)**	**Origin of seizures**
Patient_1	4	4	Female	15	31	Frontal
Patient_2	2	3	Male	38	30	Temporal
Patient_3	4	5	Male	14	33	Frontal
Patient_4	3	5	Female	26	34	Temporal
Patient_5	4	5	Female	16	34	Frontal
Patient_6	3	3	Female	31	32	Tempo/occipital
Patient_7	2	3	Female	42	31	Temporal
Patient_8	2	2	Female	32	28	Frontal
Patient_9	4	5	Male	44	34	Tempo/occipital
Patient_10	4	5	Male	47	35	Temporal
Patient_11	3	4	Female	10	32	Parietal
Patient_12	4	4	Female	42	33	Temporal
Patient_13	2	2	Female	22	28	Tempo/occipital
Patient_14	3	4	Female	41	31	Fronto/temporal
Patient_15	3	4	Male	31	34	Temporal
Patient_16	2	5	Female	50	36	Temporal
Patient_17	4	5	Male	28	39	Temporal
Patient_18	4	5	Female	25	38	Frontal
Patient_19	3	4	Female	28	37	Frontal
Patient_20	4	5	Male	33	39	Tempo/parietal
Patient_21	4	5	Male	13	36	Temporal
Total	68	87			644	
Results	68/87=78.16%				Forecast time	42.40 minute

Table 3: Result comparison with previous works

	Numb. of patients	Tot. mon. hours	Tot. num. of seizures	Sub-bands	Sens. (%)	FP/Hr	Prediction time (min)	Method
D'Alessandro et al. [9]	4	160	ND	5	62.5	0.27	10	Non-linear
Maiwald et al. [7]	21	582	88	5	21-42	0.04-0.15	< 30	Non-linear
Chavoalitwongse et al. [8]	10	ND	ND	5	68-76	0.15-0.17	22.4-135	STL, Non-linear
Iasemidis et al. [5]	2	ND	13	5	81.82	0.12	89+/-15	STL, Non-linear
Shiau et al. [21]	10	2100	120	5	85	0.159	63+/-45	ASPA
Netoff et al. [10]	9	219	45	5	77.8	0	10	CSSVM
Senger et al. [24]	2	201.1	10	5	59-63	ND	30	CNN

Duman et al. [25]	21	582	87	5	89.66	0.49	ND	(*)
Zheng et al. [27]	7	ND	51	5	57	ND	2-20	CSSVM
Zandi et al. [26]	20	561	86	5	88.34	0.155	22.5	(**)
Our previous work [1]	6	200	25	2	72	0	30.29	(***)
Current work	21	644	87	2	78.16	0.136	42.40	(***)

(*) Hilbert-Huand Transform. (**) variation Bayesian Gaussian mixture model of zero-crossing intervals. (***) Statistical and non-linear methods

V. Novel Bluetooth Implant Design

The proposed neural implant integrates the EEG signal acquisition and pre-processing into a circuit that uses a Bluetooth connection with a cellphone.

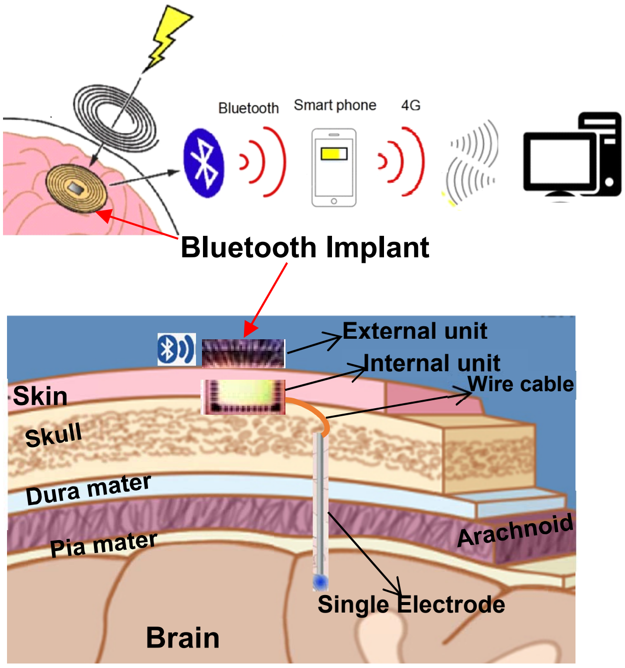

Fig. 4. Novel Implant Design using a Bluetooth connection with the cellphone along with a TCP/IP connection with the server.

Once the connection is established, the phone application communicates, through a TCP/IP link with a server which processes the live EEG signal and compares it against the patient's specific signature (thresholds) as shown in Fig 4. It will then issue a seizure warning signal through the TCP/IP link to the cellphone which will alerts both the patient and a relative.

VI. Experimental Results and Discussion

As depicted in Table 2 above, at the approach of a seizure, an increase in the system stability can be observed through a decrease in λ parameter along with a decrease in the frequency content. This decrease in chaos is also accompanied with an increase in the SNR of the EEG reading.

The use of a single electrode for seizure detection is made possible through simultaneously:

- Performing a deeper analysis of the entropy in the EEG readings focusing on the evolution stages of oscillatory states.
- Investigating the chaos as defined by the Lyapunov index.
- Investigating the Signal-to-Noise Ratio.

Table 2 shows an improved detection time by about 12 minutes at the expense of a slight decrease in both the detection and the false-positive rate.

The study performed on 21 patients shows a 78.16% detection rate with an average latency of 42 minutes. The false positive (FP) rate was very small, around 3 FP/Day. The application of this technique is restricted to seizures that are necessarily mono-focal. Having more than one focal point would require more than one electrode. On the other hand, seizures that immediately start generalized will not be detected.

VII. Conclusion

A novel seizure prediction method using a single iEEG electrode was presented in this paper. The approach was a combination of both linear and non-linear techniques. The peak voltage occurring in the Delta frequencies along with the decrease in entropy in the Gamma sub-bands were determined for each patient to train a detection algorithm on a specific signature. Mid-band frequencies were not taken into consideration during the analysis process due to the lack of information they provide both on the voltage peak level and on the chaos level.

The simplicity of the algorithm makes it implementable in a small device inserted underneath the skin. Restricting the EEG acquisition to a single electrode would make such surgery much easier and much more likely to be operated on medically vulnerable patients where SUDEP (Sudden Death Due to Epilepsy) is still a major threat to their health. Surgery costs would also be fairly alleviated which is a considerable point. Finally, we proposed a novel implant using Bluetooth communication.

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