SMGroup

Mathematical Complexity in Three Dimensions to Help to Interpret Long Term EEG in Children Epilepsy

Ricardo Zavala-Yoe[1], Ricardo A Ramirez-Mendoza[1]* and Luz M Cordero[2]

[1]Escuela de Ingenieria y Ciencias, Tecnologico de Monterrey, Mexico

[2]Instituto Nacional de Pediatria, Mexico

***Corresponding author:** Ricardo A Ramirez-Mendoza, Escuela de Ingenieria y Ciencias, Tecnologico de Monterrey, Mexico, Email: ricardo.ramirez@itesm.mx

Published Date: May 20, 2016

ABSTRACT

It is well known that severe children epilepsy requires numerous EEG studies to provide a di erential diagnostic when possible. In addition, sometimes it is necessary to order long term EEG. Typical cases of such severe affections (formerly called intractable) are Doose syndrome (DS) and Lennox-Gastaut syndrome (LGS) which are especially difficult to deal with. In this document we propose to comprise the long term EEG in- formation in a complexity-based surface (three dimensional complexity plot). Moreover, this 3D plot will be animated computationally in order to observe long term evolution of an epileptic syndrome in a single (or multiple) EEG channel. Thus, minutes or hours of EEG records can be observed and interpreted shortly, graphically and objectively by 3D surfaces. A set of 80 time series which corresponds to four EEG records were investigated. They were obtained from a little patient which has suffered a time-varying disease, which started as DS but has been evolving as a LGS. Instead of studying long rolls of EEG which correspond to 4 years in a subjective way it is shown here how to interpret complexity surfaces to provide conclusions about massive-multiple-long term EEG in severe children epilepsy.

INTRODUCTION

Severe epilepsies demand to collect a lot of EEG studies from a patient. However, giving an objective interpretation from the massive data is a challenge.

One way to deal with this is by entropy plots of EEG. These graphs are drawn in the time-complexity plane. Nevertheless, putting together a set of these figures define a complexity surface. It has been shown that these plots are quite useful to specify objectively the most affected zone of the brain from a historic collection of EEG. Moreover, it is possible to determine the worst year (the year where more damaging seizures appeared) from this huge data set [1], [2]. In this notes, we show how to interpret massive EEG by means of these surfaces which in addition are computationally animated to produce a movie. This 3D-movie exhibits dynamically the evolution of an EEG activity per channel.

MATERIAL AND METHODS

Subject

A little patient which was 11 years old in 2013 was chosen as subject of study. This child was attended at Instituto Nacional de Pediatria (National Institute of Pediatry) in Mexico City. Since the very beginning, providing a di erential diagnostic for this child was a challenge. Moreover, the medical treatment was almost useless as a result of being a severe case of children epilepsy [3]. The affection has been changing from a Doose syndrome (DS) to a Lennox-Gasteaut syndrome (LGS). Neurologists have definitely given up there.

The reason of considering only one child is that such a case is rather weird [4-6] and we wished to investigate it as a sort of a pilot study.

EEG Records Description

A collection of four EEG were used. These records provide the evolution of such affection from 2008 to 2013. Each of them are composed by 20 time - voltage channels. They were recorded in 2008, 2010, 2011 and 2013 so they are referred to as EEG1, EEG2, EEG3 and EEG4, respectively. The entire set of the four EEG clearly shows typical features of DS although some clinical manifestations are not consistent with a typical DS (overlapping). The EEG were recorded according to the international 10-20 system [7]. To simplify notation, our electrode positions: Fp1, F3, F7, T3, C3, T5, P3, O1, Fp2, F4, F8, T4, C4, T6, P4, O2, FZ, CZ, PZ, Oz were renamed as $X_i = 1::20$. The sample frequency was 200 Hz. EEG1, EEG2, EEG3 and EEG 4 lasts 1, 1.5, 1.5 and 2.5 hours, respectively. The epileptic seizures stages considered in our study are preictal, ictal and postictal. The interictal phase was left out because this stage resulted of relative low voltage with respect to the other three phases.

Methods

The EEG records show the electric activity of the brain and as known, this organ is the most complex system to deal with. The EEG plots represent the brain as a system in terms of numbers (voltage amplitudes) which vary according to one affection to the other. In general, a non-seizure brain activity is complex with respect to a seizure activity (it is characterized by a lot of oscillations). But, what is complexity? One way to de ne complexity of a dynamical system is by means of its entropy. In time series context, entropy is the rate of information production [8]. Pincus [8] developed the theory for a measure of regularity, the rate of generation of new information that can be applied to clinical data. This statistic was called *approximate entropy*, ApEn. It had as a goal to measure systems complexity (the terms complexity and entropy are used interchangeably [8-10]). This statistic has been evolving and it has taken new names depending of the improvements: *sample entropy* [11], *multiscale entropy, MSE* [10], *bivariate MSE* [2] and some others [2]. A collection of four entropy measures were evaluated in [2] showing that MSE was the more convenient to use under certain circumstances.

Worked out example about how to compute MSE

MSE is calculated according to the following algorithm [10], [2]:

Algorithm 1

1. Define a time series from an EEG channel as: $X = \{X(1), X(2), X(3), ..., X(l)\}$, l =Total number of EEG samples.
2. Define q sub time series from an EEG channel as: $X_1 = \{X(1), X(2), ..., X(l/q)\}, ..., X_q = \{X(l - q), ..., X(l)\}$.
3. For each sub time series do the following steps:
4. Fix the length m of a set of vectors (run set of data) formed from X and r a threshold.
5. Form a sequence of vectors $u(1), u(2), ..., u(N - m + 1)$ each of length m as $u(i) = [X(i)\ X(i + 1) \cdots X(i + 1 - m)]$.
6. Use the sequence $u(1), u(2), ..., u(N - m + 1)$ to find the number of $u(j)$ whose distance to its adjacent vector $u(i)$ is smaller than the given threshold

   r, i.e., $d(u(i), u(j)) \leq r$ for i ≠ j. This distance is given by $d(u(i), u(j)) = max\ |u(i) - u(j)|$
7. Divide the latter number by N - m + 1.
8. For each i, define $C_i^m(r)$ as the latter result.
9. Once with the set of C_i^m at hand, we compute its logarithmic average:

$$\Phi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln(C_i^m(r)) \qquad (1)$$

10. We determine $S = \Phi^m(r) - \Phi^{m+1}(r)$. So, we obtain this value for each subtime series.

11. Finally, we determine the average of all S and name it Multiscale Entropy, MSE.

Assume that we want to analyze the complexity of a 51 samples long signal given by X = :::; 11.74, 1.25, −4.55, 11.74, 1.25,-4.55; 11.74, 1.25, -4.55, ...(milivolts), *N* = 51. Assume that *m* = 2; *r* = 3. In this case the sequence of sub vectors *x(i), i* = 1,...,N - *m + 1* of length *m* (see algorithm 1) is given by *x*(1) = [11.74 1.25], *x*(2) = [1.25 – 4.55], *x*(3) = [-4.55 11.74], *x*(4) = [11.74 1.25]. Now, the distances are evaluated in such a way those vectors which satisfy the constraint *d* = max| x(l), x (j) | ≤ r = 3 will be counted. Observe that *d(x*(1), *x*(2)) = max| 1.25- | (-4.55) |, 11.74 – 1.25| =11:74 - 1:25| =10.49 > 3 (not counted). Similarly, *d(x*(1); *x*(3)) = 16.29 > 3 (not counted either) and *d(x*(1); *x*(4)) = 0 < 3 (counted). Proceeding this way, we realize that vectors which satisfy *d(x*(1); x(j)) < 3 are *x*(1); *x*(4); *x*(7),..., *x*(49) (seventeen elements). Next $\Phi(m)$, will be constructed as

$$\Phi^m(r) = \frac{1}{N-m+1}\sum_{i=1}^{N-m+1}\ln(C_i^m(r)) \qquad (2)$$

The first term of equation 2 is $C_1^2(3)$ = 17/50. Continuing this way $\Phi^2(3)$ will be

$$\Phi^2(3)\frac{1}{50}\sum_{i=1}^{50}\ln(c_i^2(3)) \approx 0.334 \qquad (3)$$

Analogously for Φ^{m+1} we obtain

$$\Phi^{m+1}(3)\frac{1}{49}\sum_{i=1}^{49}\ln(c_i^2(3)) \approx 0.334 \qquad (4)$$

Finally, $ApEn = \Phi^2(3) - \Phi^3(3) \approx 0$. Hence, this periodic signal (or at 2 3least, the part considered here) is not complex. A complex signal has entropy values equal or above 1 [2]. If we repeat this process down sampling the time series which represent an EEG channel for τ = 2, 3, 4, ..., $\tau_{\max}$, we will obtain complexity plot in terms of τ the down sampling rate. Notice that this example was worked out for τ = 1 (contiguous data). In this form, the average of all channels of all the EEG was plotted per year in figure 1. Observe average MSE plus/minus one standard deviation in all figures. 2010 is the worst year because it combines the lowest entropy with high variability in voltage amplitude (seizures). Contrary, 2008 (EEG1) was the best year because the average complexity plot lies above 1 with low variation (measured by the standard deviation).

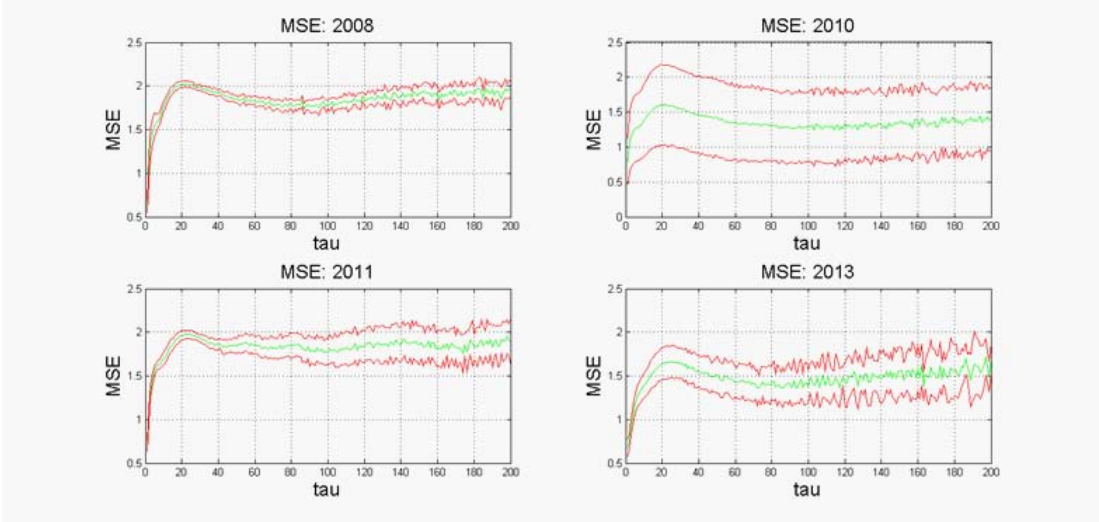

Figure 1: MSE averaged for all channels of all EEG. These gures clearly indi- cates that 2010 (EEG2) was the worst one for the kid. The big values of the standard deviation means high variation.

RESULTS: BIVARIATE MSE

Bivariate MSE or M SE (t, τ). An interesting 3D plot was obtained by plotting t, the time scale factor, the time axis t, and MSE (t, τ). This figure was generated by placing together complexity MSE plots calculated for continuous periods of time forming so slices which define the structure of the surface (Figures 2, 3 and 4).

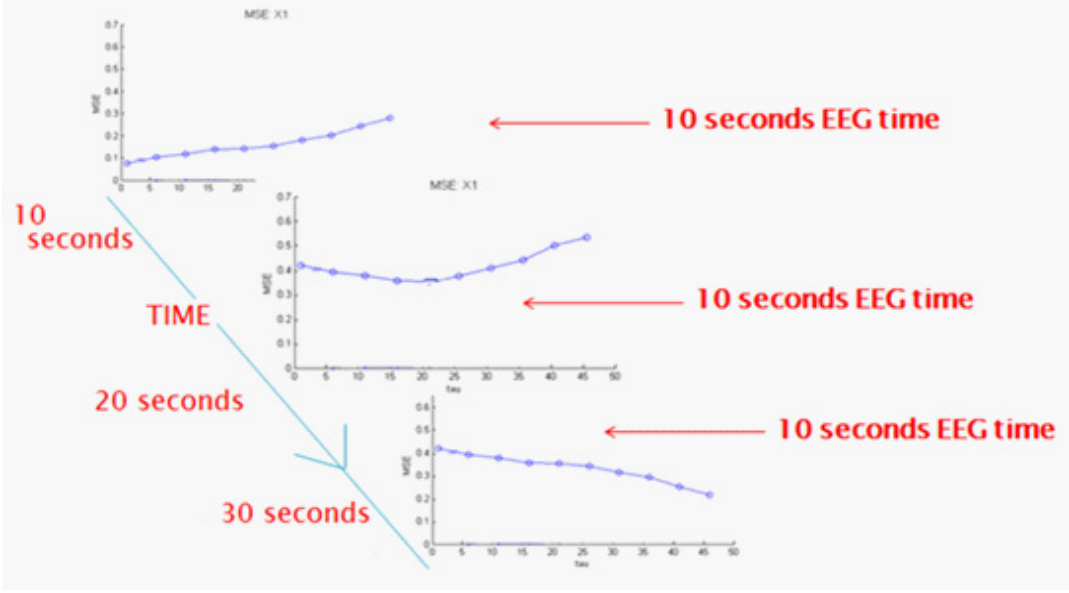

Figure 2: Slices to construct a 3D complexity surface; i.e., a BMSE surface.

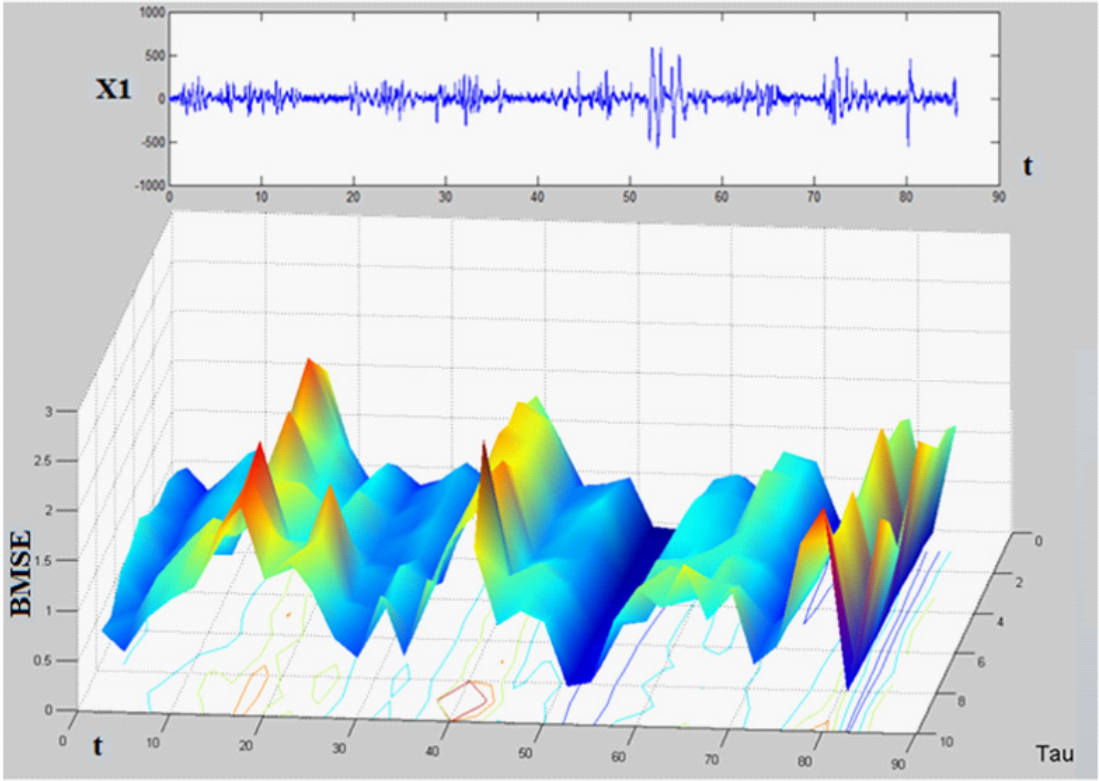

Figure 3: Comparison between an EEG channel with its corresponding 3D complexity surface during 90 seconds time.

A 3D surface has been obtained from a traditional 90 seconds-long Fp1 plot (2013) in Figure 3. Notice the zones with high peaks in the EEG corresponds to low-blue zones in the surface, indicating so that these are low complexity zones. In contrast, observe low amplitude activity in the EEG which correlates with red-high zones in the surface which means high complexity periods. The τ axes gives information about regularity (low/high entropy) and time axes t, evolution.

Next, in Figure 4 the evolution of channel X9=Fp2 (2013) is shown for 9000 seconds time (about 2.5 hours). In opposition to figure 3 this new surface is plenty of ripples which show the varying activity of this channel. However, observe that red/yellow regions predominate over the blue ones, indicating so, that in general, this EEG is quite good with respect to the others (not shown).

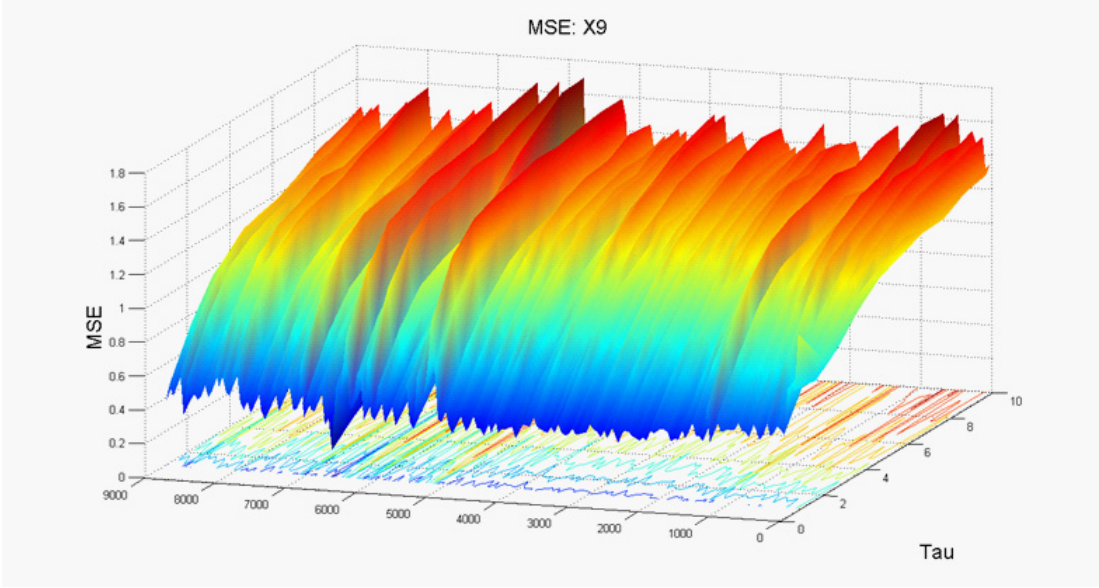

Figure 4: BMSE for channel X9 in EEG4 (2013). Notice red/blue coloured zones which indicate high/low complexity.

Notice as well that the ripples there do not have profound blue regions which would indicate intense seizures. This figure comprises 2.5 hours of EEG activity for channel Fp2. If we put together a set of surfaces like this we can observe a computer animation of even longer periods.

References

1. Zavala-Yoe R, Ramirez-Mendoza R, Jimenez-Botello LC. Mathematical Complexity as Alternative to deal with Multiple Massive Data EEG in Children Epilepsy. Zeitschrift fuer Epileptologie. 2015; 28: 12.
2. Zavala-Yoe, R., Ramirez-Mendoza R, Cordero LM. Novel way to investigate evolution of children refractory epilepsy by complexity metrics in massive information. Springer Plus. 2015; 4: 1–33.
3. Kwan P, Arimazinoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Comission on Therapeutic Strategies. Epilepsia 2010; 51: 1069–1077.
4. Stephani U. The natural History of Myoclonic Astatic Epilepsy (Doose Syndrome) and Lennox Gastaut syndrome. Epilepsia. 2006; 47: 53–55.
5. Kelley S. Doose syndrome (myoclonic-astatic epilepsy): 40 years of progress. Developmental medicine and Child Neurology. 2010; 52: 988–993.
6. Doege C, Kleiss R, Stephani U, von Spiczak S, Myoklonisch- astatische Epilepsie. Zeitschrift fuer Epileptologie. Springer Medizin. 2014; 2: 105–111.
7. Gil Nagel A. Manual de Electroencefalografia. McGraw-Hill- Interamericana, 2001; Mexico City, Mexico.
8. Pincus SM. Approximate entropy as a measure of system complexity. Proc Nat Acad Sci USA. 1991; 88; 2297–2301.
9. Chon KH, Scully CG, Lu S. Approximate entropy for all signals. IEEE Engineering in Medicine and Magazine. 2009; 28: 18–23 .
10. Costa M, Goldberger A, Peng CK. Multiscale entropy analysis of complex physiologic time series. Physical Review. 2002; 89: 068102–10681024.
11. Richman J, Moorman JR. Physiological time series analysis using approximate entropy and sample entropy. Am J Physiol Heart Circ Physiol. 2000; 278: H2039-H2049.