The Creutzfeldt-Jakob disease in the Hierarchy of Chaotic Attractors

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1. Introduction

Until recently model construction was the main tool for the understanding of the long time dynamic behavior of complex systems\(^1\). If the experimental measurement of a property of the system exhibits some regularity of behavior such as for example periodic oscillations, this behavior was often formulated in terms of a set of coupled nonlinear differential equations. The solutions to these equations were compared with the experimental data. However most often models fit the data only qualitatively and do not account for the variabilities seen in the actual measured time dependent variables. Today we realize that the variabilities cannot be ignored as they may indicate the presence of dynamics radically different from the assumed models.

In other instances, the behavior of a system may appear quasi-random, thus difficult to cast in terms of deterministic differential equations. However the recent advances in the theory of nonlinear dynamics tell us that such random behavior may stem from deterministic systems described with only few degrees of freedom\(^2,3\).

With the introduction of the notion of deterministic chaos, and the evaluation of dimensions of chaotic attractors, today we are in a position to extend the theory of nonlinear systems into areas not explored before. We are also able to assess the dimensions from experimental data\(^4\). These dimensions quantify the system's dynamics and must be compared with the values obtained from theoretical models thus imposing constraints to model construction.

Several definitions are provided for the characterization of attractor dimension and various algorithms are proposed for their evaluation. The most practical and the most widely used algorithm was proposed by Grassberger & Procaccia\(^4\). They introduce the correlation dimension \(D_2\) which may easily be computed from time series.

However in order to implement such an algorithm, there is a need to resurrect all the pertinent variables describing the dynamics from the experimental measurements. In most cases only a single parameter followed in time (time variables) or the temporal evolution of the system is measured simultaneously on several sites of the system (space variables).

Phase space portraits could be constructed from experimental data following four different procedures. With the help of Takens' theorem\(^5\), one shows that \(m\) variables can be reconstructed from a single time series by introduction of \((m-1)\) time lags \(\tau\). Also one could use the Eckmann-Ruelle's conjecture\(^3\) in which a measurement in each site of the system is regarded as a new variable. Singular systems analysis\(^6\) is another promising way to construct phase spaces using either a single time series or measurements from various sites of the system.

In the second section of this paper, we use all four techniques for the construction of the phase portrait from experimental data. The time series were obtained from the electroencephalographic (EEG) recording of a patient suffering from a neurological disorder known as "Creutzfeldt-Jakob disease". In section three, Takens’ theorem and Eckmann-Ruelle conjecture are used to evaluate the correlation dimension of the attractors. This dimension is compared with the previous studies of beta waves, alpha waves, sleep stages two, four, REM sleep and "petit mal" type of epileptic seizures. Section four is devoted to some considerations about the reliability of algorithms.
2. Phase Portraits of the Creutzfeldt-Jakob Disease

In this section, we shall illustrate the various techniques for the construction of the phase space which will be illustrated with the help of the EEG recorded during the terminal state of the Creutzfeldt-Jakob disease in which it is believed that a virus attacks and destroys gradually the nerve cells. After a first stage of dementia, the patient enters in a terminal coma with myoclonus. The EEG is then very coherent (like the "Burst Suppression Pattern" seen after administration of barbiturates) and regular patterns of stable slow waves reminiscent of the "petit mal" type of epileptic seizures appear. However, the phenomenon is of much longer duration and shows a remarkable stationarity. Twenty minutes of EEG are shown in Fig. 1 taken from a single lead and twelve of such leads were recorded simultaneously.

The most popular phase space construction results from a theorem shown by Takens. This theorem states that for a dynamical system of $n$ variables $X_1 \ldots X_n$, the space spanned by the variables

$$\{ X_1(t), X_1(t+\tau), X_1(t+2\tau), \ldots, X_1(t+(m-1)\tau) \}$$
is at least topologically equivalent to the original phase space and therefore represents many of its dynamic properties. Moreover $m$ is restricted by the relation $m \geq 2d+1$ where $d$ is the lowest integer greater than the dimension of the attractor. In this section we refer to such procedures as Takens' construction. Recently it was conjectured that the space spanned by several simultaneous measurements of an observable at various sites of the system is at least topologically equivalent to the original phase space and therefore represents many of its dynamical properties. Moreover $m$ is restricted by the relation $m \geq 2d+1$ where $d$ is the lowest integer greater than the dimension of the attractor. In this section we refer to such procedures as Takens' construction. Recently it was conjectured that the space spanned by several simultaneous measurements of an observable at various sites of the system

$$\{ X_1(t_1), X_1(t_2), X_1(t_3), \ldots, X_1(t_m) \}$$

may also yield a phase portrait which is topologically equivalent to the portrait obtained from the variables $X_1, \ldots, X_n$ of the system. Such constructions may be obtained via electrocardiograms as actually simultaneous measurements up to 256 leads may be recorded. In the Eckmann-Ruelle construction, the lag $\tau$ disappears from the construction and is replaced by another subjective quantity namely the inter-electrode distance which is bounded by a minimum length imposed by the physical reality. A more recent technique for phase space construction was introduced by Broomhead & King. It is based on singular value decomposition which may be a noise reduction procedure. In essence in this technique, one diagonalises the covariance matrix constructed from the phase space vectors of the previous constructions and one obtains orthogonal eigenvectors that may be used to reconstruct a phase portrait and evaluate its correlation dimension.

![Figure 2. Phase portraits of the Creutzfeldt-Jakob attractor. A similar structure is seen from four different three-dimensional constructions: (A) Takens' construction from one lead, (B) Eckmann-Ruelle's construction from simultaneous leads. (C) and (D) are respectively the (A) and (B) portraits constructed using the singular eigenvectors.](image)

Figure 2 shows the phase portrait of the Creutzfeldt-Jakob pathology constructed using all four techniques outlined above. It is interesting to note that the constructions of Takens, Eckmann-Ruelle and Eckman-Ruelle with singular decomposition, yield very similar three-dimensional phase portraits. On the contrary, the portrait obtained with the help of the singular eigenvectors and from a single lead time series (Fig.2) looks different and is more flat and is smoother as noise and also some of the finer twists of chaotic trajectories has been eliminated from the portrait.
3. Dimensional Analysis

Once the variables spanning the phase space become available, the Grassberger & Procaccia algorithm could be used for the evaluation of the correlation dimension $D_2$. We have computed $D_2$ for all four phases of Fig.2. Such a comparative study is in the process of completion for beta waves, alpha wave sleep stages 1, 2, 4, REM sleep, and "petit mal" epilepsy (Destexhe, Sepulchre & Babloyantz, in press).

In the case of the Creutzfeldt-Jakob attractor, all four approaches give remarkably comparable results. We report here only the dimensions computed from the usual Takens' construction such as to compare them with the $D_2$ values already reported for other stages of brain activity. If the correlation dimension computed from a single lead (Takens' construction), we find $D_2 = 3.8 \pm 0.1$. In the case of the Eckman Ruelle construction, the phase space was obtained from 12 EEG leads covering the entire scalp and a value of $D_2 = 3.8 \pm 0.2$ was seen. The concordance between these two values is remarkable.

Although at first sight, the signal appears as extremely coherent with obvious periodicities, we find surprisingly high value for the correlation dimension as compared with the low value of $D_2 = 2.05 \pm 0.1$ observed for the "petit mal" type of epileptic seizure. This finding may stem from the fact that the typical phenomenon of the epileptic seizure was of 5 sec. duration whereas the Creutzfeldt-Jakob disease was analyzed over 8 minutes (from a total phenomenon lasting several hours). The analysis of 1 min recording gave the same result as 8 minutes whereas a 8 sec. time series gave an underestimated dimension of $3.1 \pm 0.2$.

![Figure 3. Short stretches of some of the most typical episodes of human EEG activity (identically scaled, 12 bit sampling).](image)

In this respect, the Creutzfeldt-Jakob disease may be compared with the normal cardiac activity. At first sight, the electrocardiographic signal appears as periodic however in a recent paper Babloyantz & Destexhe have shown that the normal cardiac activity is governed by deterministic chaos characterized by $D_2 = 4.4 \pm 0.4$.

The values of the correlation dimension of Creutzfeldt-Jakob Disease taken together with the $L$ computed previously for other stages of brain activity give a coherent image of brain dynamics. The values can be represented as a function of the width of the power spectrum (see Fig.4 and Fig.5). The width is estimated by taking the two extreme frequencies of 75% of the spectral energy.
Figure 4. Power spectra of the typical EEG episodes seen in fig.3. The main peaks forming 75% of the spectral energy are underlined with black solid vertical lines. Only for low dimensional systems as (F), the 75% of spectral array is contained relatively few peaks.

Figure 4 shows that the broad spectra corresponds to high dimensional attractors such as eyes open at REM sleep. For these two states we find, by using the Grassberger & Procaccia algorithm\(^9\), extreme high values of \(D_2\). These values were \(D_2 = 9.7 \pm 0.7\) for beta rhythm\(^9\) (Eyes open in fig.3a), \(D_2 = 8.2 \pm 0.4\) for REM sleep\(^10\) (Fig.3c). A word of caution is needed here as we are not sure that the algorithm gives reasonable results for such high dimensional systems. In any case, we can say that beta waves at REM sleep behave like colored noise.

In an awake subject with eyes closed, alpha waves set in (Fig.3b). The dynamics becomes more coherent and switches into a deterministic chaotic activity\(^9\) characterized by \(D_2 = 6.1 \pm 0.5\) confirmed by other laboratories\(^11,12\). As expected, the spectral width also decreases. As the sleep cycle sets in, brain activity enters a chaotic state of \(D_2 = 5.01 \pm 0.03\) for the stage two\(^13\) (fig.3c) and \(D_2 = 4.4 \pm 0.4\) for the stage four or deep sleep\(^10,13\) (Fig.3d). Similar values were obtained from intra-cranial EEG recordings;
from cats and rabbits\textsuperscript{14,15}. As correlation dimension decreases, so does the width of the spectral ban. The sleep stage four is the most coherent stage of the normal brain activity.

In various pathologies, the coherence of the brain dynamics increases further as the correlation dimension decreases. Finally in the "petit mal" type of epileptic seizure (Fig. 3f), the most coherent state reached. Here a near unison is seen in the neuronal activity and the correlation dimension drops to a value of $D_2 = 2.05 \pm 0.09$. Such a low dimensional chaos is seen in three variable differential equations such as the Rössler attractor\textsuperscript{16}. As expected, the width of the power spectrum drops dramatically in this case.

Figure 5. Dimension - Power spectrum plot. The extreme frequencies from 75\% of the spectral energy are drawn for each EEG episode. Active states are broad banded and high dimensional, while pathologies are of low dimension and their spectrum is restricted to a thin band of frequencies.

Figure 6. Dimension - Amplitude plot. The variations of EEG voltage observed in successive stretches of one second are represented for each type of EEG behavior. The synchronization between neurons which occur in pathologies is reflected in high amplitudes and low dimensions.

Therefore we see from fig. 5 a consistent relationship between the correlation dimension and the main energy of the power spectrum. The correlation dimension appears as an increasing function of the spectrum width.

The EEG is the sum over a very large number of neuronal membrane potentials and its magnitude therefore a good measure of the synchrony between neurons. Low amplitude EEG reflects relative
desynchronized states whereas high amplitude waves are an indication of synchrony between neural masses. In Fig.6 the correlation dimension of various stages of the brain activity is plotted against measure of the amplitude of the EEG. To obtain this measure, the signal is computed at one sector intervals. The average value of these local amplitudes is represented by points in Fig.6. The highest and lowest amplitudes are included in the horizontal bar. During normal states of brain activity, the dimension of the chaotic attractors decreases as the amplitude of the waves increases. The reverse situation is seen pathological conditions. The Creutzfeldt-Jakob disease is characterized by a higher amplitude and a high dimension than the epileptic seizure.

4. Reliability of Algorithms

For several years, various algorithms for the phase space construction and dimension evaluation from experimental time series has been used to assess the existence of deterministic chaotic dynamics problems ranging from hydrodynamics\(^ {17}\) to complex biological systems such as electroencephalograms\(^ {7,9-14}\) or electrocardiograms\(^ {8}\). After a first wave of enthusiasm as the range of applications increased and conditions of applicability of the techniques relaxed, skepticism and criticism were arising. In the same time new techniques were proposed which aimed at reducing the few subjective aspects of the methods\(^ {6}\).

Most algorithms are tested on and are shown to give satisfactory results for simple maps or well defined systems described by differential equations involving few variables such as the Rössler attractor\(^ {16}\). Such systems are free of experimental or intrinsic physiological noise. Therefore the success of the algorithm for such simple systems does not guarantee their applicability to real complex physiological processes involving many variables and endowed with experimental as well as physiological noise. On the other hand in the nonlinear world, care must be taken before extrapolating the results from one dynamics to the next. An algorithm could fail for the characterization of one attractor and give good results for another system.

The subjective aspects of the methods are the following: (a) The sampling frequency is a crucial factor for reliable analysis. Biological attractors may have very fine twists which are barely noticeable from background noise. Too fine sampling will incorporate undesirable noise and too wide intervals between samples may wash out some irregularities of the trajectories\(^ {5}\).

(b) Another crucial element is the choice of the time lag \(\tau\). In principle for an infinite set of data points all time lags must lead to the same results. However with finite experimental data sets, a proper range of values of \(\tau\) must be found\(^ {18}\). The Eckmann-Ruelle phase space construction avoids the problem of time lag \(\tau\). However this quantity appears implicitly in the choice of the inter-electrode distance which introduces a subjective element. One does not avoid this subjectivity of choice in singular vector techniques. There also a window must be chosen according to criteria which are empirical.

(c) In biological systems when the stationarity of the data sets is of finite duration, the choice of time length of the data is crucial. We have explained elsewhere how to choose the recording time, the lag \(\tau\) at the sampling frequency in the case of the EEG\(^ {7}\). Our experience in this field shows that if care is taken to eliminate the subjective factors in the implementation of the algorithms, one can get satisfactory results for biological complex systems where no other simple way of access to the system's dynamics exists.

5. Discussion

In several papers\(^ {7,9,10,13}\) we had reported the existence of deterministic chaos in various stages of normal as well as pathological brain activity. Our previous results together with the new values of the Creutzfeldt-Jakob disease as summarized in Figs. 5 and 6, constitute a coherent representation of cerebral activity. In this paper we have shown how from the recording of the brain waves we can have access to the dynamics of the system and quantify various stages of the cerebral activity. From Figs. 5 and 6, we can infer that the brain activity constantly switches between various chaotic attractors loosen gaining coherence as it is needed by the biological functions of the organism.

The fact that brain attractors obey deterministic chaotic activity is not surprising as these objects behave such that they obey to deterministic dynamics nevertheless are unpredictable and are sensitive to the initial condition
Therefore they are endowed with great information processing capability\(^{19}\), a most conspicuous fact of the cerebral activity.

We believe that with all the problems raised regarding the application of the algorithms, the dimension analysis is a powerful tool for the study of complex biological phenomenon which cannot be handled otherwise. It is especially valuable when it is used as a comparative study as in the case in this paper where it follows the evolution of the coherence of the brain waves in various stages of the cerebral activity. The various attractors appear to follow a well defined hierarchy where some key properties, such as the EEG amplitude, the spectral width and the correlation dimension, seem to be intimately correlated. It is expected that this hierarchy could be reproduced by models describing neural networks (work in progress).

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