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On Utilizing Nonlinear Interdependence Measures for Analyzing Chaotic Behavior in Large-Scale Neuro-Models

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Abstract. In this paper we present a comparison between a nonlinear measure (the Nonlinear Interdependence, S) and a linear measure (the Cross Correlation coefficient, CC) for analyzing nonlinear dynamical systems. To do this, we consider a biologically-realistic neural network (NN) model of the piriform cortex. Our previous work studied the EEGs obtained from two components of this network. In this current work, we increase the system's granularity and replicate the exploration using the membrane potentials of our neurons to study the measures S and CC. To be more specific, even though the properties of a nonlinear dynamical system are best analyzed in the natural framework described by its state space, they may be undetectable in the time domain of the system's output, e.g., in the EEG tracing. Rather, a phase space representation may reveal the salient features of the nonlinear structure which are hidden or occluded to standard linear approaches. Nonlinear Interdependence, (S), proposed by Quiroga, is said to occur when the trajectories reconstructed in the phase-space of one time series, experimentally predict the evolution of the phase space trajectories of the second time series. This measure of predictability has the advantage over linear measures, of being sensitive to interdependence between dissimilar types of activity. In many cases where one analyzes nonlinear signals, CC is a measures that well describes the synchronization or the desynchronization between two signals. In other cases, S is introduced in addition to CC in order to describe the nonlinear signals. We thus investigate here the synchronization of these types of signals using the membrane potentials using both linear measures (i.e., CC) and nonlinear measures (i.e., S). Our results clearly prove that utilizing *both* these measures is effective in analyzing and understanding real-life chaotic systems.
Keywords: Chaotic Behavior, Large-scale Neuro-Models, Nonlinear Interdependence (S) Measure.

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1 Introduction

From the theory of nonlinear dynamics [7], we understand that nonlinear dynamical systems can be aptly and best described and quantified by a state space. This is also the natural framework to characterize its underlying phenomena. However, while their properties may be undetectable in the system's time domain output (e.g., in the EEG tracing), they can be studied in the phase space. A phase space representation may reveal the salient features of the nonlinear structure which are hidden or occluded to standard linear approaches [11]. In this context, Nonlinear Interdependence is said to occur when the trajectories reconstructed in the phase-space of one time series experimentally predict the evolution of the phase space trajectories of the second time series [10]. This measure of predictability has the advantage over linear measures, of being sensitive to the interdependence between *dissimilar* types of activity [3].

Often, in the analysis of nonlinear signals, a linear measure (the Cross Correlation coefficient, CC) is a measure that aptly describes the synchronization or the desynchronization between two signals. In other cases, the Nonlinear Interdependence, S, is introduced in addition to CC in order to describe the nonlinear signals. In this paper we present a comparison between S and CC. We shall demonstrate that whenever we are dealing with signals with a "dominant" nonlinear behavior and with a very small linear component, neither S nor CC, by themselves, can provide the same information as the pair $\langle$S, CC $\rangle$.

To demonstrate this hypothesis, we shall investigate a biologically realistic Neural Network (NN) model of the piriform cortex. In our previous work [4], we studied the EEGs obtained from two components of this network. In this current work, we increase the granularity of our approach and replicate the exploration using some previously unexplored criteria, i.e., the *membrane potentials* of our neurons. We thus investigate here the synchronization of these types of signals using the membrane potentials, wherein we utilize both a typical linear measure (i.e., CC) and a typical nonlinear measure (i.e., S). We also compare the synchronization identified between the potentials in this manner, with the one identified between the EEGs.

The issue of neuro-modeling is not merely theoretical. Indeed, is has been motivated by a desire to better understand specific neural circuits, particularly those whose failures could possibly trigger human illnesses. Depression, Anxiety, Schizophrenia, Alzheimer's disease, memory impairment, paralysis, Epilepsy, Multiple Sclerosis, Parkinson's disease, etc. are areas in which intense research efforts have been (and are being) made to better understand and treat these conditions. In this respect, from a modeling perspective, the analysis of the *connections* between the neurons is fundamental to understanding and treating these illnesses. Such an analysis also leads to a better understanding of the development and function of the normal brain.

1.1 The Platform: GENESIS and the Computational Model

The platform for our research is the so-called GENESIS (GEneral NEural SImulation System) framework [2] proposed by Bower *et al.* This simulation software

The GENESIS simulation software is free and can be downloaded from `http://www.genesis-sim.org/GENESIS/`.

was initially developed in a CALTECH (California Institute of Technology) laboratory by Wilson [13] as an extension of efforts to model the olfactory cortex. It was designed to allow for the multi-scale modelling of a single simulation system and, until now, is the only simulator possessing this capacity. Indeed, in this context, the Wilson model of the piriform cortex is generally accepted as a realistic model, since it is based on the anatomical structure, apart from which it also contains physiological characteristics of actual biological networks. The model has been cited in more than 100 refereed papers, and a review of large scale brain simulations is found in [5].

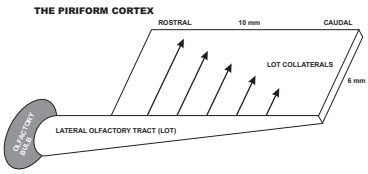

Fig. 1. The model of the piriform cortex.

One of the ultimate objectives of Wilson's model was to understand the role of the piriform cortex in olfactory object recognition. Further, one motivation of the research due to Wilson and Bower was the assumption that this cortex computationally represents a type of associative memory. The model has been used to explore a wide range of cortical behaviors [13], including associative memory functions [12].

The computational model which we present can be viewed as a nonlinear system. Simulation of the piriform cortex requires the numerical solutions of *systems* of differential equations that describe the states of the neurons as a function of time and space. These numerical techniques describe how the system advances the state variables of the simulation (e.g., the potential of the membrane) from time i to time $i+1$, through numerical integration of the differential equations that appropriately describe the system. The computational model of the piriform cortex is treated as a loosely-coupled system of ordinary differential equations. The evaluation of a state of any neuron in the system requires only the information of the previous states from other neurons, and it can be solved for each neuron at every time step. It is well known that such equations can be solved using straightforward numerical integration techniques.

The initial architecture consists of three 15 $\times$ 9 arrays of 135 nodes. Each array has only a *single* type of neuron, being either of the pyramidal cells, of the feedforward inhibitory cells (K^+ mediated inhibition), or of the feedback inhibitory cells (Cl^- mediated inhibition). The array is proposed to represent the whole piriform cortex, which falls within an area of approximately 10 mm $\times$ 6 mm. The pyramidal cells consist of five compartments, with each compartment receiving a distinct kind of synaptic input. The inhibitory cells are modelled using the differences between the exponential functions. The model also contains 10 cells representing the excitatory input from the olfactory bulb to the cortex.

Numerous models of brain circuitry have focused on simulating the macroscopic functionality of systems containing simplified neuronal units. The in-

crease in computational power in the last decade has permitted simulations to include models with considerable complexity, namely those comprising of *realistic* large scale NNs. The goal of a modeling phase is to generate patterns that are similar to EEGs, and to explore their possible physiological basis.

2 Problem of Connectivity

The **Problem of Connectivity** is motivated from the following clinical considerations. In spite of intensive research conducted over the last decades and the discovery of effective medication, the cause and the mechanisms leading to Schizophrenia are still unclear. It is widely agreed that Schizophrenia is most likely based on fundamental neuronal changes of the brain. Unfortunately, physiological methodologies have not been able to contrive reliable tests beside the current assessments. Perhaps the high complexity of the human brain is what renders it vulnerable to diseases such as Schizophrenia, because animals do not develop the same types of diseases [6].

This problem involves investigating the modification of local connectivity within the piriform cortex. More specifically, we analyze the dependence of the level of chaos as a function of the density of the synapses (i.e, the number of synapses generated between the neurons). In addition, we investigate the variation of the maximum Nonlinear Interdependence, S, of two sub-systems embedded in a larger system. Thus, we consider how the coupling of two interconnected sub-systems of the same underlying system would change as a function of the connectivity of the synapses. We believe that the levels of local connections between the neurons can be used as a hypothesis for the mechanism to explain underlying illnesses such as Schizophrenia.

Prior Work on the Problem of Connectivity: In our prior research [4], we have performed modifications to the number of connections between the pyramidal neurons. By changing the connectivity, we proposed to simulate the level of pruning to be excessive or insufficient. We chose to describe the effect of pruning on the level of chaos and the degree of synchronization between the two sub-systems embedded in the piriform cortex model, using three measures: the LLE, S, and CC. These three measures were chosen based on two hypotheses. First of all, schizophrenic symptoms, like thought disorder, hallucinations and delusions, are assumed to be dependent on the level of chaos in the brain. Secondly, the symptoms are triggered by the existence of false attractors near "good" attractors, which suggests that areas from the brain could be highly correlated in an unhealthy manner. To our knowledge, the investigation of the two theories, namely excessive and insufficient pruning, based on these three measures, is new.

The uniqueness of our research is strengthened by the fact that the pairs of signals being compared belong to the same system. Other authors [8–10], have considered two initially independent systems and partially coupled them; subsequently, they have analyzed the synchronization of the signals obtained from the two systems. In contrast to previous models that evaluate relationships between two different systems (or rather, two partially coupled systems), we have proposed a new approach where the investigation is conducted using

two sub-systems which are embedded within the context of a larger system, namely, two coupled sub-systems of the same system.

2.1 Current Work: Problem of Connectivity

To present our current work in the right perspective, it is appropriate for us to mention how the readings and measurements are taken and recorded. Recordings from the array are averaged to produce the EEGs as below:

$$EEG(t+1) = \frac{1}{m}\sum_{i=1}^{m}[\Phi_i(t)], \tag{1}$$

where m is the number of electrodes, and $\Phi_i(t)$ is the field potential depending of the output of the pyramidal neurons, $X^p(t)$ for $p = 1 \cdots N$. We assume that the influence of the inhibitory neurons is marginal in the process of the EEG computation, and that it can thus be omitted.

The relation between the field potential, $\Phi_i(t)$, recorded from the electrode i and the output of the pyramidal neurons $X^p(t)$ is:

$$\Phi_i(t) = \frac{1}{4\Pi}\sum_{p=1}^{N}\frac{X^p(t)}{d_{pi}}, \tag{2}$$

where N is number of pyramidal neurons, and d_{pi} is the distance of the p^{th} pyramidal neuron from the recording site (the electrode i).

By examining the above equations, the reader can see that the synchronization of the EEGs implies the evaluation of the *aggregated* signals, which is achieved by computing the averages of a certain number of fields (in our setting the number is 8). These fields are, in turn, obtained by weighting the membrane potentials with the inverses of the distances between the electrodes and each neuron, which is considered as a contributor in the EEG. However, prior to the averaging phase, one observes that the computational model of the piriform cortex yielded access to the raw data in and of itself, namely the *original* membrane potential of each neuron. From the perspective of understanding the efficiency of the CC and S measures, in our current work we disaggregate the signals and explore the behavior of the raw data (i.e., the membrane potentials) itself. To accomplish this for a *prima facie* study, we perform a careful selection of only *four* neurons as follows:
i. Two of them (V_1-V_2) were involved in the previous EEG_1 computation;
ii. One of them (V_{135}) was involved in the computation of the EEG_2;
iii. The last (V_{15}) was not involved in the previous computations.
Using these selection criteria, we now investigate all the possible synchronization scenarios (i.e., the intra-EEG and the inter-EEG electrode readings).

2.2 The Settings

In our research, we considered two zones of the piriform cortex as depicted in Figure 1. For each zone, which was treated as a sub-system, we analyzed the artificially generated EEGs, each of them being computed with a fixed number of electrodes, and at a suitable frequency.

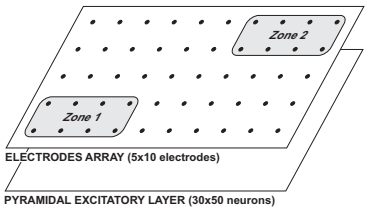

Fig. 2. The distribution of the electrodes in Zone1 and Zone2.

We considered the density of the synapses corresponding to the pyramidal neurons as a control parameter, and explored the effect of modifying the initial values suggested by the Wilson model [13]. This, in turn, involved:

1. The computation of the EEGs as function of the number of electrodes for each sub-system.
2. The determination of the optimum value for the embedding dimension for the phase space reconstruction using the FNN method *for the density of the synapses*.
3. The computation of the CC and S measures *between* the EEGs and for the membrane potentials.

2.3 Results for this Problem

We conducted numerous simulations over an ensemble of settings. However, we merely report here some representative results.

First of all, we mention that the time series used to describe the systems are the EEGs and membrane potentials. To obtain these, we used an array of n evenly spaced electrodes on the surface of the simulated cortex. Recordings from the array were then averaged to produce the EEGs. In our experiments, we set $n = 50$.

We investigated the level of chaos and the synchronization between these two zones of the piriform cortex, when the efficiency of the pruning was higher or smaller than 50%, implying that we decreased, and also increased the connectivity between the pyramidal cells. The level of connectivity was described by the maximum number of possible connections between the pyramidal neurons, where the possible values were $p = 0.1$, 0.2, 0.5, 1, 2, and 10. The case of the healthy brain, when the efficiency of pruning is 50%, corresponds to the setting when $p = 1$.

For each sub-system we analyzed the artificially generated EEGs, each of them computed with 8 electrodes. We also analyzed the membrane potentials for four neurons: V_1 and V_2 involved in the computation of EEG1 for $Zone_1$, V_{135} involved in the computation for the EEG2 for $Zone_2$, and V_{15} not involved in the computation of EEG1 or EEG2. The EEGs and the membrane potentials were recorded at 5,000 samples/sec for a duration of half of a second.

The first experimental step was to compute the optimum embedding dimension for each zone, using The False Nearest Neighbor (FNN) Statistics. In the interest of brevity, we will not present these results here.

To evaluate the interdependence between the artificially generated EEGs and between the membrane potentials, as mentioned earlier, we used two metrics, namely S and CC. For computing CC we used a lag which ranged between -100 and +100. The absolute value is reported. The evolution of S and CC function of connectivity between pyramidal cells are presented in Table 1, in which we report the averages for 20 experiments, each of them conducted with a different model.

		V_1-V_{15}		V_2-V_{15}		V_1-V_{135}		V_2-V_{135}		EEG1 *vs* EEG2
Weights	CC_{max}	$S(X,Y)$	CC_{max}	$S(X,Y)$	CC_{max}	$S(X,Y)$	CC_{max}	$S(X,Y)$	CC_{max}	$S(X,Y)$
0.1	0.9678	0.2341	0.9668	0.2366	0.9680	0.2439	0.9692	0.246	0.5005	0.2396
0.5	0.6600	0.1094	0.6539	0.1117	0.7300	0.212	0.8032	0.2170	0.6204	0.2870
1	0.1386	0.0797	0.2111	0.0671	0.1380	0.0823	0.1872	0.0680	0.2227	0.1112
1.5	0.1439	0.0234	0.1419	0.0215	0.2526	0.0390	0.2158	0.0330	0.2524	0.2607

Table 1. Nonlinear Interdependence (S) and maximum Cross Correlation Coefficient (CC_{max}) for membrane potentials (V_1-V_{15}, V_2-V_{15}, V_1-V_{135}, and V_2-V_{135}) and for EEG1 and EEG2 function of the value of the connectivity between the pyramidal cells.

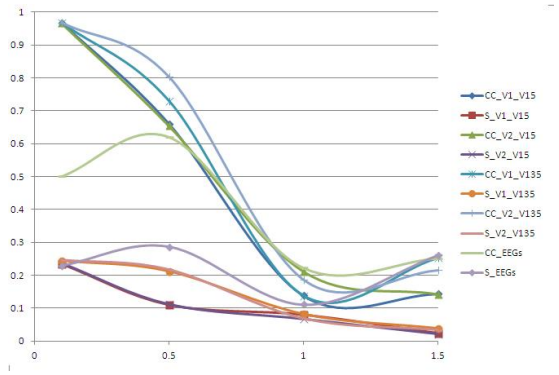

Fig. 3. The evolution of $S(X|Y)$ and CC as a function of the level of connectivity between the neurons (see Table 1.)

2.4 Discussion of Results

Table 1 and Figure 2 are used for analyzing the two behaviors, namely that of increasing and decreasing the connectivity levels. Table 1 contains the averages of the CC and S measures computed with membrane potentials (the first 8 columns) and the averages computed with the EEG signals (reported earlier in [4]). The reader can see that the computation used to obtain the EEG affects the ranges of the CC and S measures, namely it decreases the ranges, compared to the ranges of the CC and S measures computed with the membrane potentials. To be more specific, the CC ranges are 0.8306 for the membrane potentials and 0.3977 for the EEGs , while the S measure ranges are 0.2245 for the membrane potentials and 0.1758 for the EEGs. With regard to the degree of synchronization represented by the Nonlinear Interdependence

S, only a decrease in the connectivity leads to a consistent modification, again as displayed in Figure 2.

3 Conclusions

The analysis of the two behaviors, namely that of increasing and decreasing the connectivity levels, reveals that both of them determine a decrease in the level of chaos in the system, as seen in Figure 2.

From these observations, we can conclude that whenever we are dealing with signals with a "dominant" nonlinear behavior and with a very small linear component, neither S nor CC, by themselves, can provide the same information as the pair ⟨S, CC ⟩.

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