Synchronization and desynchronization in a biological neural network

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Abstract: In the present paper, we will focus on the characterization of the biological network behaviour, in terms of synchronization and desynchronization of the measured signals by Micro Electrode array. We evaluate a easy calculable estimator that implies de/synchronization property of the biological neural network.

1. Introduction

Forward the classic picture of information processing based solely on firing rates (the average number of action potentials for unit time, a "rate code") of a neuron, or at least a little group of neurons, the extension of the analysis of the temporal dynamics of neuron network beyond the ordinary scale of milliseconds, discovered evident complex oscillatory and periodic behaviour, based on the precise timing of single action potentials. The resultant system is intrinsically non linear and in some conditions chaotic.

Our goal is to show how the description of a complex biological neural network, under the signal processing viewpoint can be performed at high abstraction level using the synchronization analysis of a coupled array of oscillators.

Moreover the problem of non linear network synchronization might treat the synchronization as the result of network stimulation, and any network data processing capability as the reduction of dynamics dimensionality.

2. Design

The biological system is composed by a network of neurons cultured *in vitro*. Using a microelectrode array (MEA), network can be kept alive for a long-term recording. Studying how the network processes and encodes informations, we utilize the following experimental set-up (based on the tools for elettrophysiological studies)

A Micro Electrode Array (MEA) composed of 64 (8 × 8 grid) ITO electrodes on silicon substrated (figure 3a,b) was placed in a faraday cage to avoid electromagnetic interference. Electrodes were 50μm × 50μm (250μm distance) for electrical stimulation and 30μm × 30μm (150μm distance) for recording. Signals were costantly monitored by a real time oscilloscope.

Long term acquisition instrunmentation: a BioLogic DTR-1802 Digital Tape Recorder with a maximum of 8 recording channels, at the sampling frequency of 12kHz, and a GPIB Interface. 8 channels amplifier and filtering stage (gain=100).

The set up was completed by:

- Systems for network electrical stimulation (scanner, stimulation interface, and isolator).
- PC for off-line data management, equipped with National Instruments AT-MIO device.

The biological part of the MEA was composed by in vitro culture of spinal cord neurons from chick embryo (7-8 days old). Cells yield by this procedure were about 1.5×10^6 cells per embryonic cord and plating density was 4×10^5 - 5×10^5 cells/cm^2. The cultured was maintained at 37°C in an atmosphere of 5% Co_2 and 95% of air saturated with water vapour. Cultured medium was changed every 3-4 days.

3. System simplification

The neural network activities were recorded by amplifiers and A/D converters producing a real-time signals.

The activities were measured at all the available microelectrodes. It was evaluated the non linear cross-correlation index between the all measured signals, and afterwards the three globally less correlated were identified and selected. In Figure 1 we report the recorded activity of the network in absence of stimulation.

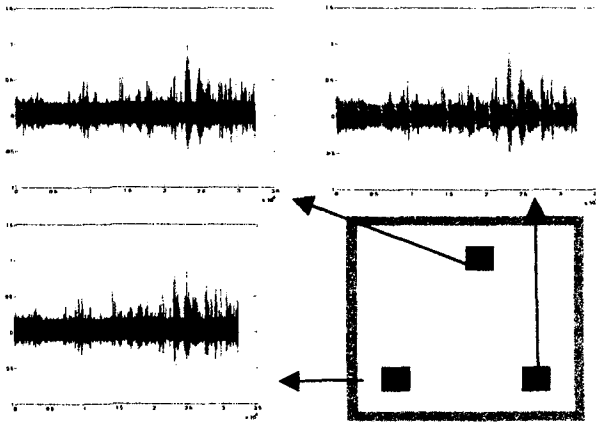


Figure 1: Three channels reordered activity of the network

We can observe that the behaviour of the different output signals is characterized by a synchronized activity, i.e. highly correlated. We suppose that the system in this status performs a significant distributed processing. This status depends on both the topological connections between the neurons and the stimuli given to the network.
Biological neural network can be seen at a coarse grain, as a cluster system where each cluster consists of multitude of neurons, the number of cluster is fairly small, and the connection among the clusters results from the interpolation of many intercluster synapses at the neuron level. Therefore the oscillatory activities are a function of the connectivity (excitatory or inhibitory), at the cluster level [5][6]. From now we will consider each cluster as a formal neuron.

4. Modelling

4.1 General formulation

Starting from these observations, we consider a *formal neuronal network* as a coupled of chaotic oscillators.
Let there be N chaotic oscillators. Let x_i be the m-dimensional vector of dynamical variables of the ith node. G is the *connection matrix* that brings information about geometry and the weights of the connections and subject to $\sum_j g_{ij} = 0,\ \forall i$. $H : \Re^m \to \Re^m$ is an arbitrary function of each node's variables that is used in the coupling.
Let the isolated (uncoupled) dynamics be $\dot{x}_i = F(x_i) + \sum_j g_{ij} H(x_j)$.
This kind of coupled oscillators, studied by Pecora [1] [2], can be modelled by the following equation:

$$\dot{x} = F(x) + G \otimes H(x) \qquad (1)$$

where:

- $x = (x_1, x_2 \cdots x_n)^T$ is a vector that contains all the neuron state variables, where x_i is the state variable of the i-th formal neuron
- $F(x) = (F(x_1), F(x_2), \ldots F(x_n))$, $H(x) = (H(x_1), H(x_2), \ldots H(x_n))$
- $\otimes$ is the direct product, defined as

$$A \otimes B(x_i) = \begin{bmatrix} A_{11}B(x_1) & \cdots & A_{1n}B(x_n) \\ \vdots & \vdots & \vdots \\ A_{n1}B(x_1) & \cdots & A_{nn}B(x_n) \end{bmatrix}$$

In determining the stability of the synchronous states, we follow the method suggested by Carrol *et al* [1][2].
We evaluate the variational equations of (1), considering ξ_i be the variations on the ith node, and $\xi = (\xi_1, \xi_2, \ldots \xi_n)$ be the collection of variations. Then we get the following equations:

$$\dot{\xi} = [1_n \otimes Df + G \otimes DH]\xi . \qquad (2)$$

By diagonalizing G (remark that the transformation does not affect the first term since it acts only on the matrix 1_n), we obtain block diagonalized variational equations, with each block being as following:

$$\dot{\xi}_k = (DF + \lambda_k DH)\xi_k . \qquad (3)$$

Since that DF and DH are evaluated on the synchronization manifold (defined by the constraints $x_1 = x_2 = \cdots x_n$)), they are the same for each block. We can get the Master Synchronization Function by computing the largest Lyapunov exponents of the generic variational equation as following:

$$\dot{\psi} = (DF(x) + \lambda DH(x))\psi \qquad (4)$$

for each λ being a non zero eigenvalue of G.
After Carrol *et al* [1][2], when the largest Lyapunov exponent of a single generic variational equation (4) is negative, the synchronization of the coupled array of oscillators (1) occurs.

4.2 System model

For the *formal neuronal network*, we assume the following hypothesis:

1. Oscillators are identical and they are coupled according to the same pattern
2. The synchronization manifold exists (defined by the N-1 constraints $x_1 = x_2 = \cdots x_n$) and it is an invariant manifold.
3. The $i-th$ formal neuron can be approximately modelled as the following Röessler-like oscillator

$$\begin{aligned} \frac{dx_i^1}{dt} &= -k(ax_i^1 + bx_i^2 + cx_i^3) \\ \frac{dx_i^2}{dt} &= -k(x_i^1 + fx_i^2) \\ \frac{dx_i^3}{dt} &= -k(x_i^3 - g(x_i^1)) \end{aligned} \qquad (5)$$

where the non-linear function $g(x_i^1)$ is replaced by:

$$g(u) = \begin{cases} 0 & if\ u \le L \\ (u-L)^2 & if\ u > L \end{cases}$$

where $u(x_i^1) = \alpha x_i^1 - (1-\alpha)V_{ref}$ with L, V_{REF}, α are parameters of the system.
In order to apply the above model, we have first to specify the G and H matrices for a minimal number of formal neurons. There are many reasons for considering not less than three neurons, e.g. the possibility of having partial synchronization in the system (say oscillator 1 and 2, and *not* 3) *in addition to total synchronization /* desynchronization. More than three is not required here.
The matrix G for three coupled oscillators can be taken, as suggested by Pecora *et al* [1][2] for a universal probe of the synchronization properties:

$$\Gamma(\varepsilon,\delta)=\begin{bmatrix} -2\frac{\varepsilon}{3} & \frac{\varepsilon}{3}+\frac{\delta}{\sqrt{3}} & \frac{\varepsilon}{3}-\frac{\delta}{\sqrt{3}} \\ \frac{\varepsilon}{3}-\frac{\delta}{\sqrt{3}} & -2\frac{\varepsilon}{3} & \frac{\varepsilon}{3}+\frac{\delta}{\sqrt{3}} \\ \frac{\varepsilon}{3}+\frac{\delta}{\sqrt{3}} & \frac{\varepsilon}{3}-\frac{\delta}{\sqrt{3}} & -2\frac{\varepsilon}{3} \end{bmatrix} \quad (6)$$

Remark that other kind of interconnection matrix can be chosen to describe the possible interconnections between the *formal neurons.*

For simplicity we will also assume, without loss of generality, the following linear coupling matrix H:

$$H(x)=\begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad (7)$$

Under the general requirement that G is 3×3 diagonalizable_real-valued matrix with zero-row sum, its eigenvalue λ can assume the values $\{0,\varepsilon+i\delta,\varepsilon-i\delta\}$ [3]. By eqn. (1), (6), (7) the formal

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{bmatrix} = \begin{bmatrix} F(x_1)+\begin{bmatrix} g_{11}x_1^1+g_{12}x_2^1+g_{13}x_3^1 \\ 0 \\ 0 \end{bmatrix} \\ F(x_2)+\begin{bmatrix} g_{12}x_1^1+g_{22}x_2^1+g_{23}x_3^1 \\ 0 \\ 0 \end{bmatrix} \\ F(x_3)+\begin{bmatrix} g_{31}x_1^1+g_{32}x_2^1+g_{33}x_3^1 \\ 0 \\ 0 \end{bmatrix} \end{bmatrix} \quad (8)$$

neuronal network can be expressed by the following:

The model in (5) can be easily implemented as an electronic circuit as shown in Figure 2:

Figure 2: ***Rössler-like oscillator circuit***

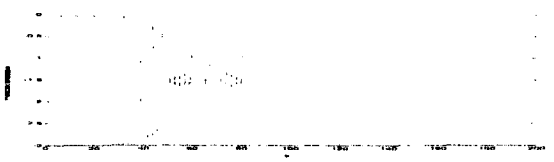
4. Simulations

In our simulation, first we derive the syncronization conditions for the theorical model reported in (1), and afterwards we compute the property of syncronization from the signals measured by the biological neural network.

We evaluate the Master Stability Function, valuing the value of ε and keeping δ=0.

Figure 4 represents an average over N steps to obtain a prediction of Lyapunov exponents of the variational equations with parameters $\varepsilon=-1,\delta=0$. In our three variables system the basic condition to reach stability (which coincides with the synchronization of the coupled array of oscillators) is to have one Lyapunov exponent equal to zero and the others negative [4].

Figure 3: ***: Iterative estimate of Lyapunov exponents with***



$\varepsilon=-1,\delta=0.$

Significant values are at the end of period

As shown in fig 4, the behaviour of the whole system is synchronized. This result is provided by the value (less than zero) of the greatest Lyapunov exponent. This value is caused by the chosen interconnection, depending on the selected parameters.

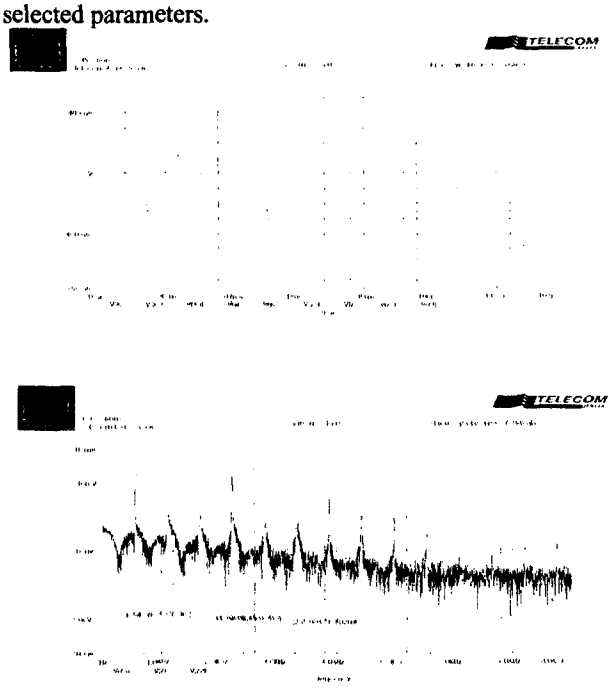


Fig 4: a) x_1^3, x_2^3, x_3^3 **temporal behaviours**

b) Power spectrum

Fig. 5 shows estimation of Lyapunov exponents of the variational equations with parameters $\varepsilon=3,\delta=0$. Desynchronization of the circuit arises because the greatest Lyapunov exponent is greater than zero.

Fig 5: Iterative estimate of Lyapunov exponents with $\varepsilon=3,\delta=0.$

Significant values are at the end of period

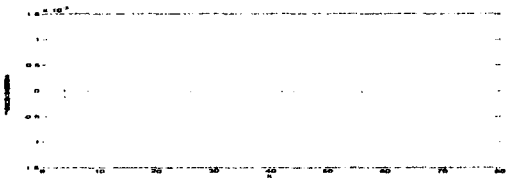


Figure 6 shows the desynchronized behaviour of the coupled array system.

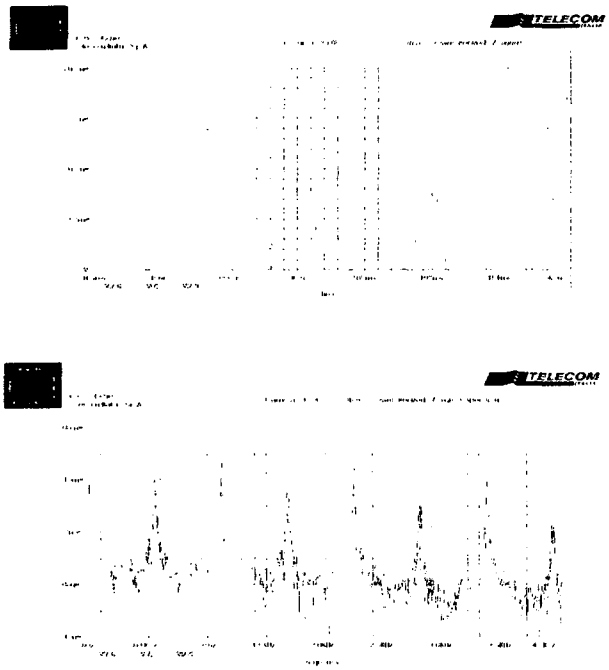


Fig 6: a) x_1^3, x_2^3, x_3^3 temporal behaviours
b) Power spectrum

5. Results

Let us analyse an experimental cultured neuron network at high abstraction level as shown in Fig.1 and described by (8).

Under the hypothesis that the G matrix fulfils the fundamental requirement above and that the choice of the clusters is well balanced, we evaluated the map in Fig. 7.

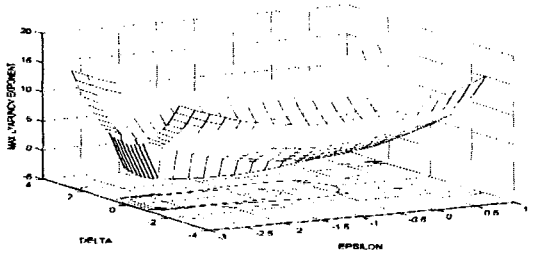


Fig 7: MSF (Master synchronization function)

For some $\varepsilon + i\delta$ we had the possibility to measure the value of the largest Lyapunov exponent from the data measured at the MEA electrodes, evaluating

$$(9) \qquad \min_{\lambda\in\Sigma,\tau\in\Re^+,i=1,2,3}\left\|x^m{}_i(t)-x_i(t-\tau,\lambda)\right\|$$

where x_i^m is the measured signals from the ith microelectrod, τ is a delay-time and Σ is a set of (ε,δ) that implies synchronization or desynchronization evaluated by the theoretical surfaces shown in Fig. 7.

As a furher results, we can evaluate the λ of a specific network over a contour plot of Figure 7, estimated by eqn . (9). We can use the curve in plane (ε,δ) as a map of the change that the network undergoes time after time dued to different stimuli.

In different situations the strength of the interconnections is changing, as well as the network synchronization. This is allowed by the fact that the synapses are far from constant connection weights.

Moreover, it is demonstrated that the analysis of synchronization, according to our approach, is a powerful tool for studying both the processing and the learning of the network and the parameter λ is a straightforward index of the network adaptivness.

6. Future works

In future work the trajectory in the (ε,δ) plane followed by a network will be related to its internal learning process.

Comparing equations (1) and (4) it is straightforward that we have a strong simplification. In equation (4) the role of G is limited to the value of $\varepsilon + i\delta$. In other words solving the synchronous problem, as expressed by equation (4), against each $\varepsilon + i\delta$, any interconnection pattern is also solved. This is a strong result for the study of the synchronous status of biological networks interconnected according to random patterns.

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