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Intermittency analysis and point processes in biological networks

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1 Data analysis

Prof. J. Soriano Fradera is the leader of a research group mainly focused on the experimental investigation of *in vitro* neural networks. Such neural networks are neural cultures that are posed on a biological substrate. The neurons in the culture spontaneously develop connections (axons and synapses), and the particular network topology depends on the different laboratory conditions (nutrients, possibility of moving or not, external stimulations, presence of drugs

inhibiting or exciting the formation of synapses, etc.). The experimental data are given by the sequences of neuron firings. When the neuron are sufficiently far from each other, the electrical activity of single neurons can be observed and recorded. In more detail, a fluorescence substance is introduced in the neural cultures. This substance is sensitive to the electrical activity of the underlying neurons, so that the fluorescence signal is used as a marker of the electrical activity of the neurons [1]. The neural culture is typically posed in a observation chamber that is mounted on a Zeiss Axiovert inverted microscope equipped with a high-speed CMOS camera. This is used to record the fluorescence signal over all the culture, thus obtaining a sequence of time frames[1].
The collaboration with the host institute has been focused on the statistical analysis of data coming from a particular experiment, where the neural culture was left free to develop spatial clusters [1]. In this experiment, the more connected neurons had the tendency to approach each other as they were left free to move over the substrate. Then, the clustering of the neurons was observed, but the spatial accuracy of the camera did not allow to identify the activity of single neurons, but the activity of the clusters. Thus, in the particular experimental trial here considered, the neural culture developed 30 clusters, whose spiking activity was recorded as described above. In Fig. (1) the raster plot is reported. The red dots represents the occurrence time of a firing (given in units of the frame sampling time) for a given cluster, whose label is indicated in the y-axis by means of a integer number.

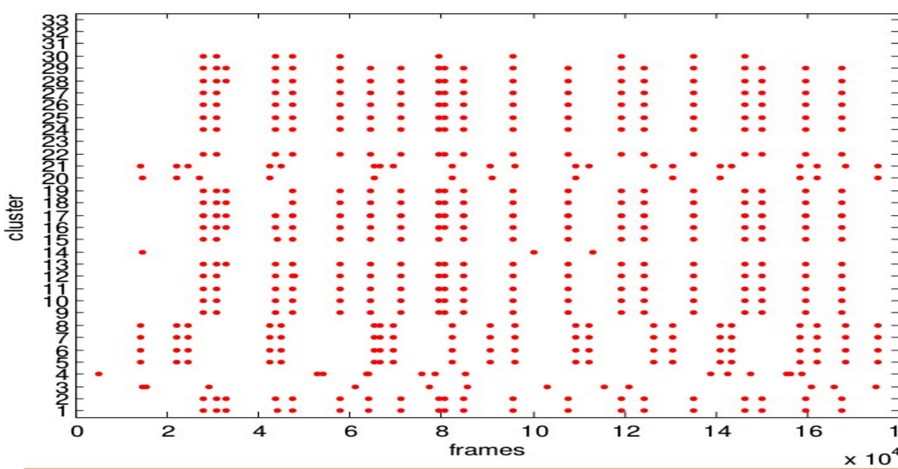

Figure 1: Raster plot of the electrical activity of clusters formed in a neural culture. In x and y axes the frame number and the cluster label are reported, respectively.

It is easy to see that there's an extended subset with many clusters firing to-

[1] It is worth noting that the excitation of the fluorescence substance can be seen only when there's a burst of firings (spike train) with a few spike (about 10), otherwise the ratio signal/noise is too low.

gether, while some other clusters seem to display a substantially different, perhaps independent, firing activity.
For each cluster of neurons, the firing events were collected and described as sequences of event occurrence times. For each cluster, the sequence of inter-event times (or Waiting Times) were derived by simply applying the formula:

$$\tau_n = t_n - t_{n-1}(n = 1, 2, ...) \ .$$

Note that, by convention, $t_0 = 0$, so that $\tau_1 = t_1 - t_0 = t_1$. As well-known, the emergence of self-organization in a complex network is often related with so-called *fractal intermittency* or *Temporal Complexity*, which is essentially described as sequences of critical events with a power-law decay in the distribution of inter-event times [7][2]. In our case, the histogram of all inter-event times is reported in Fig. (2)[3]. A well-defined power-law decay cannot be seen from the

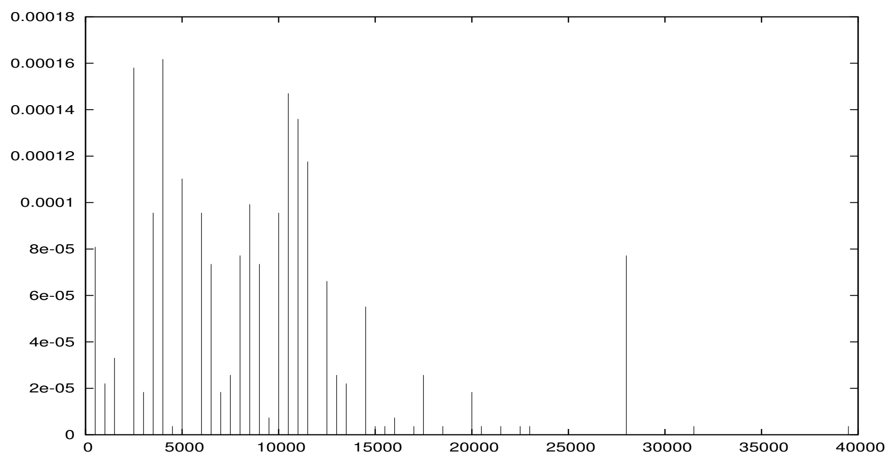

Figure 2: Distribution density of inter-event times τ_n of all clusters.

plot, but this could be due to the blurring effect of noisy events (not related to the self-organized metastable states). Consequently, useful information cannot be extracted from the inter-event time distribution.
For this reason, we applied the EDDiS method [7] for the estimation of the diffusion scaling [3, 4, 5, 6]. When the renewal assumption is verified [2], then the complexity index μ associated with fractal intermittency can be also evaluated. A preliminary investigation of the self-similarity index δ of the inter-event time distribution and of the second moment scaling H has been carried out during the sojourn period. The results of this preliminary data analysis are reported in Fig. 3: Detrended Fluctuation Analysis (DFA) for the scaling H; and Fig. 4: Diffusion Entropy (DE) analysis for the scaling δ.

[2]These crucial events describe the rapid transitions among the birth and death of metastable, self-organized states.

[3]The inter-event times are derived for the single clusters. Then, the histogram is computed mixing together the inter-event times of all the clusters

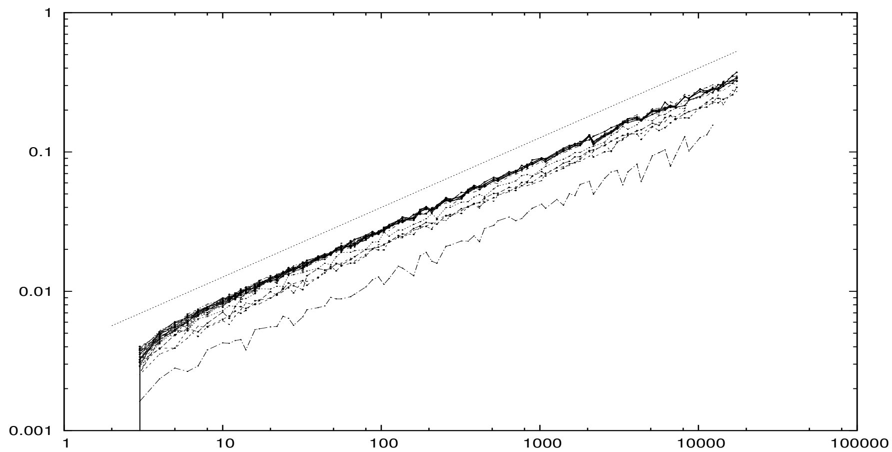

Figure 3: Results of the DFA applied to the event sequences of each cluster of the neural network. The dotted line is a guide to the eye for the scaling $H = 0.5$. x-axis: time; y-axis: DFA function (essentially the square root of the fluctuation variance).

2 Discussion and open problems

DFA analysis gives a well-defined scaling, given by the normal scaling $H = 0.5$ (see Fig. (3)) . This scaling is usually a signature of non-cooperation, associated with absence of self-organization in the time interval between two events, which are typically distributed according to a Poisson process. However, this apparent absence of self-organization could be due to the joint effect of two contributions: (i) the presence of short-time noise and (ii) the shortness of the time series, which is related with the low number of critical events.

In Fig. (4) the results about the DE time behavior is not well defined, as DE is more sensitive to the presence of noise. This is also clear considering the large variability of the DE behavior depending on the particular cluster under consideration. This reinforces the hypothesis that the event sequences are probably too short for the scaling analysis based on the concept of renewal fractal intermittency.

During several meetings with Prof. Soriano and his collaborators we also discussed theoretical and modeling approaches for the interpretation of the experimental data. The group is facing these aspects by means of neural network models, thus with a basic approach, very near to the primitive equations of the single neurons. It would be interesting to carry out a collaboration on the emergence of self-organized metastable states. In particular, further investigations are needed to understand what are the basic features in a network model that are responsible for the emergence of self-organization and, in particular, of anomalous (non-poissonian) intermittency. It is not clear which are the most important aspects, the topological or the dynamical ones or the most important aspect lies in a particular combination of the two aspects.

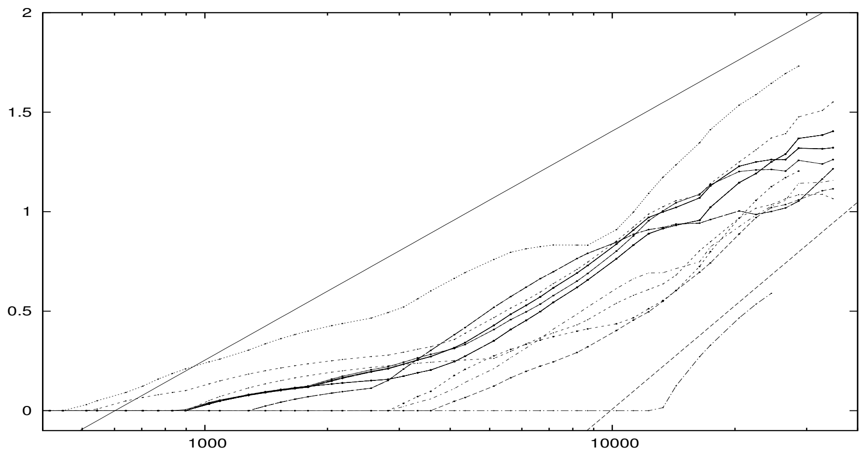

Figure 4: Results of the DE analysis applied to the event sequences of each cluster of the neural network. Continuous line: $\delta = 0.5$; dashed line: $\delta = 0.75$. x-axis: time; y-axis: diffusion entropy.

2.1 A note on renewal theory, fractal and Poisson intermittency

It is worth noting that a Poisson model is typically associated with some critical events in the dynamics of the system under observation. A kind of Markovian dynamics is typically associated with the inter-event evolution of the system, thus corresponding to the emergence of exponential decays in memory kernels and in auto-correlation functions. Then, a Poisson model and, more in general, a Continuous Time Markov Chain, can predict a single exponential decay or a finite sum of exponential decays with different decay rates. However, even in the case of a finite sum, the asymptotic decay of the distribution is associated with a exponential decay, that is, the slowest exponential corresponding to the smallest decay rate.

Thus, the presence of a slow power-law decay is not in agreement with the prediction of a Poisson model and some kind of strong non-linear interaction among single component of the system must be assumed in the time slices between two consecutive critical events. This is a typical condition of cooperative complex systems, characterized by the emergence of self-organized or coherent structures (see, e.g., Refs. [5, 6]). As intermittent behavior of such self-organized structures is usually observed, a particular approach to the modeling of cooperative complex systems is given by the theory of stochastic point processes, which is the theory describing the dynamics of a sequence of critical events occurring randomly in time, whatever independent or statistically dependent they could be.

References

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