Chapter 1

Introduction

This chapter introduces the reader to the basic fundamentals of *Self-Organized Criticality* (SOC) Theory applied in Neuroscience and tries to put in clear light the most important aspects of the matter, based on the knowledge that modern Neuroscience has acquired so far. Furthermore, it explains the main purposes of the thesis project along with the description of its organization.

SOC Theory has been initially introduced by Bak et. al [1] and defined as a tendency of dynamical systems that share both temporal and spatial degrees of freedom to rearrange themselves towards a critical state independently from their initial conditions, i.e., the system's behaviour is attracted to a critical state[1]. Such systems are "just barely stable with respect to further perturbations" that are likely to alter it both at its least scale length – causing local changes, typical of very stable states – and at its greatest scale length – causing avalanches, typical of very unstable states.

But how can we define a critical state? The term "critical" has been firstly used in physics to indicate the point at which a system is at the edge of two clearly different behaviours – think about the critical point of CO_2, defined as the pair of critical temperature and pressure above which the substance cannot coexist in liquid and vapour phase but changes it to liquid, gas or super critic fluid.

From a dynamical point of view, we may say that a system is in a critical state depending on some parameter I when, if I is subjected to small perturbations with respect to some value I_C, no matter how small they are, the system will jump between two topologically different phase portraits, each one of which puts it in the circumstance of *potentially* showing two qualitatively different behaviours, depending on its initial conditions; in other terms, when the system expresses a *bifurcation* [2].

The system that is going to be studied is a network of dissociated cultures of rat's neurons manifesting spontaneous activity, i.e., no inputs are given. Such system is dynamical, since it can be modelled as a set of N interacting units – the neurons – whose behaviour is determined by N-tuples of time-dependent variables, each one capturing the state of the single unit. Any healthy and mature neuronal network typically, though not always, exhibits prolonged periods of silent activity characterized by few units undergoing action potentials (also known as *spikes*) and sudden moments of bursts of widespread activity that expands throughout all the network inducing a considerable amount of units to spike in a quasi-simultaneous fashion [3], [4], [5]. The latter phenomenon is called *neuronal avalanche*.

1- Do not confuse the critical state towards which a system may be attracted to with its attractor(s), namely, the equilibrium point(s) of the system where its state variable(s) remain constant in time. The definition of critical state will be given just ahead.

The importance that SOC theory's role plays in these surroundings is that it let us differentiate the network's activity into three different dynamical states, named *subcritical*, *critical* and *supercritical* and sustains the idea that a neural network's optimal performances to storage and process information arise when it operates in a critical state [6], [7].

By studying the avalanche size and lifetime distributions, namely, the number of neurons recruited in each avalanche and their temporal duration, as well as other parameters that are descriptive of the avalanches' dynamics, it is possible to discern the three aforementioned states. As firstly introduced by Beggs and Plenz [8] in the context of critical branching processes, avalanche size distributions share a tendency to follow power law trends whose exponents are linearly dependent with their branching parameter. Moreover, a critical branching parameter of 1 has been found for exponents close to $-3/2$ [8], [9].

Another key topic we are going to deal with is the concept of *functional connectivity* (FC). Functional connectivity measures a statistical dependence between neurophysiological events located at different points of a neural network [10] without giving any clue about causal effects, that is, any sign of influence that one point may exert to another and any information about the *anatomical connectivity*, namely, how different points of the network are connected together by means of structural links between them. Many studies have proposed that FC may be fundamental to understand how different cortical brain areas – often called modules – cooperate together in order to exert a precise function [11], [12] and that it can reveal, though not generally speaking, the presence of anatomical connectivity between them [13].

Usually, FC measures are evaluated amongst all possible pairs of signals coming from a simultaneous, multi-sites recording system, be it the one used in electroencephalography or a micro-electrode array (MEA), by means of cross-correlation statistics [14], [15], but recent studies have accessed FC also by adopting multivariate approaches in order to infer all the possible direct and indirect effects that neurons or groups of neurons may exert on others [16], as well as other measurements that go by the name of synchronization measures [17] and spike metrics [18] that don't require the hypothesis of wide sense stationarity to be true.

It is necessary to specify, moreover, that functional dependencies may exist for some short intervals of time and disappear soon after [19] and that what they can tell us is just an approximate description of the network, for the activity of every single unit composing the network has to be detected during a prolonged period of time in order to access a full mapping of its functional connections [20].

In this work, we will try to evaluate FC by making use of a variety of methods – most of which are model free methods, i.e., no assumptions about the processes that have generated the data are given – amongst pairs of spike trains recorded from spontaneous activity, so we may assume that the function wielded is a "resting state function" and try to link it with SOC

Project's Objectives

This thesis project has born as a mutual collaboration between Politecnico di Torino and DIBRIS Genoa's faculty of engineering (Dipartimento di Informatica, Bioingegneria, Robotica e Ingegneria dei Sistemi) under the superintendence of Professor Luca Mesin and Paolo Massobrio. Its main purpose is trying to correlate the emergence of dynamical states with functional connectivity techniques, a work sustained by the perspective – and the hope – of finding some good answers to the fundamental question: "Which functional connectivity measure can better distinguish the three dynamical states?". To move in response of this query we are going to make use of both experimental and simulated data, to-develop and pre-existing algorithms and past knowledge brought to light by researchers' experiences.
All the computational operations and algorithm scripts have been executed and developed on a Notebook PC with clock rate of 2.60 GHz and 16 Gb RAM, by means of Matlab 2018b software (MathWorks, Natick, MA, USA).

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