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Effects of inhibitory neurons on the quorum percolation model and dynamical extension with the Brette–Gerstner model

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ABSTRACT

The Quorum Percolation model (QP) has been designed in the context of neurobiology to describe the initiation of activity bursts occurring in neuronal cultures from the point of view of statistical physics rather than from a dynamical synchronization approach. This paper aims at investigating an extension of the original QP model by taking into account the presence of inhibitory neurons in the cultures (IQP model). The first part of this paper is focused on an equivalence between the presence of inhibitory neurons and a reduction of the network connectivity. By relying on a simple topological argument, we show that the mean activation behavior of networks containing a fraction η of inhibitory neurons can be mapped onto purely excitatory networks with an appropriately modified wiring, provided that η remains in the range usually observed in neuronal cultures, namely $\eta \lessapprox 20\%$. As a striking result, we show that such a mapping enables to predict the evolution of the critical point of the IQP model with the fraction of inhibitory neurons. In a second part, we bridge the gap between the description of bursts in the framework of percolation and the temporal description of neural networks activity by showing how dynamical simulations of bursts with an adaptive exponential integrate-and-fire model lead to a mean description of bursts activation which is captured by Quorum Percolation.

1. Introduction

Neuronal rhythms are widespread oscillating phenomena, both *invivo* and *in vitro*, which were observed over many temporal scales [1]. Hitherto, the fundamental mechanisms underlying their occurrence is far from being fully understood and is the subject of a significant research activity; it involves several scientific fields, from fundamental biology, information theory [2], physics of dynamical systems and critical phenomena [3] to graph topology [4] and massive parallel computation [5,6]. The human brain is a very complex network, with about 10^{11} neurons [7], each of them connected to 1000–15,000 others. Moreover, it is organized in localized computational units connected according to a well defined hierarchical structure. Thus, although investigation and imaging techniques enabling to record the cerebral activity *in vivo* are making significant progress [8,9], the mere size and complexity of the brain makes its whole description and understanding a far-sighted goal. Complementary to observations and experiments on real brains, *in vitro* experiments on dissociated neuronal cultures are an invaluable tool in investigating the fundamental questions on neuronal dynamics set above. Such cultures

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are usually obtained by seeding dissociated neurons extracted from rodent embryos, or alternatively neuronal stem cells, on a suitable substrate. Though similar monitoring can be performed on brain slices, we will focus on the activity of dissociated cultures, where axons and dendrites grow in such a way that neurons self-organize after a few days into a two-dimensional network exhibiting a high level of randomness [10]. As a matter of fact the connectivity between neurons is described by probability distributions. These neuronal cultures hold between 10^3 and 10^5 neurons with typical densities between 500 and 5000 neurons per mm^2, each of them connected via a number of synapses falling between 20 and 200 [11]. These changes in connectivity and scale compared to a brain could, at first glance, appear as a loss from a neurobiologic point of view; yet, they are a key feature for the complementary approach of *in vitro* experimentation to study neuronal activity and growth. Quantitative measurements of the neural activity inaccessible *in vivo* can be carried out with the help of micro-electrode arrays (MEA) [12], optogenetics, and calcium imaging [13].

Synchronized periodic bursts of spiking activity have been regularly observed in dissociated neuronal cultures [14,15] and appear as a fundamental emergent spatio-temporal property of neuronal populations. Bursts of activity can also be artificially triggered by externally activating a fraction of neurons. The Quorum Percolation model (QP) has been elaborated to describe the initiation of bursts observed in such cultures as a collective phenomenon, from the point of view of statistical physics rather than dynamical systems [16]. Under its original form the QP model does not take into account the presence of inhibitory neurons. However, a general description of collective behaviors in neural networks requires the integration of inhibitory neurons in the QP model, since it has been pointed out that they can play a role in the structure of bursts [17,18]. We devoted recently several studies to extend the original QP model by including additional biological relevant properties and modulation of the neuronal activity: the decay of the neuronal voltage accounting for ions leakage through the neuron membrane [19], variability in the quorum accounting for a modulation of the neuronal excitability threshold [20], finite size scaling and the derivation of a normal form around the critical point together with a preliminary study of the incorporation of inhibitory neurons [21]. In this last paper, we suggested that under specific conditions, the mean characteristics of the burst activation of networks with inhibitory neurons are the same as the ones of purely excitatory networks with different effective connectivity. The first goal of this paper is to provide a deeper investigation of the mapping between the presence of inhibitory neurons and an equivalent purely excitatory reduced connectivity. We point out what should be learned from the mean field approach, we characterize the connectivity features of the purely excitatory network accounting for a fraction of inhibitory neurons, we quantify its equivalence domain and derive a relation between the critical point and the fraction of inhibitory neurons. As inhibitory neurons are commonly assumed to play a modulating role of neuronal activity and spatio-temporal coordination, we investigate the validity of our previous conclusions in a dynamical setting. Thus, the second goal of this paper is to show that the key features of Quorum Percolation captured by the simple, discrete model with inhibition are preserved in a fully dynamical model based on biologically more refined description of neurons and synapses, namely the adaptive Exponential Integrate-and-Fire model [22]. However, it should be noticed that the dynamics of the activity cannot be captured by IQP and QP models, since they deal with equilibrium properties of the short time onset of bursts.

2. The original Quorum Percolation model

The original Quorum Percolation (QP) model is a discrete-time cellular automaton describing the propagation of information on a graph through a minimal set of rules for activation cascades in neuronal populations. Since neuronal communication through synapses is directional, the neuronal population is represented by a directed graph connecting neurons located on the vertices. Specifically introduced to describe the onset of activity bursts observed in small, *in vitro* cultures [16], the model is based on a non spatial graph considering only the node connectivities and constructed by randomly choosing, for each neuron i, k incoming links among the $N-1$ other neurons according to an in-degree probability distribution p_k. It is worth noticing that such a random description of the incoming links probability relevant in the case of cultures of dissociated neurons grown in an *in vitro* environment does not work anymore in the case of neuronal cultures that have grown *in vivo* like brain slices or animal visual cortex [23].

In the QP model, each neuron i is represented by a discrete variable $V_i(t)$ which accounts for the membrane potential, and by a neuronal state – at rest or active – with activation governed by a threshold rule. A neuron is activated between $t - \Delta t$ and t if its potential becomes greater or equal to some activation threshold m; once activated, it sends signals to its outgoing neighbors. As the models represents only one activation wave, an activated neuron remains so and sends no further signals in the following steps. After a time step Δt, each neuron i integrates the signals it received by incrementing its potential $V_i(t - \Delta t)$ by the sum of the inputs from its incoming neighbors activated during the elapsed time interval. All the signals are taken identical and associated to an integer increment equal to +1, which sets the scale for the threshold value m. The network is stimulated at time $t = 0$ by an initial excitation of the network, performed by activating a given fraction f of randomly chosen neurons.

The activity of the network at time t is given by the fraction of active neurons $\phi(t)$, increasing with t, and converging towards a stationary value $\Phi(f, m)$ after a few time steps, dependent on the initial active fraction f and the threshold m. As first reported by Cohen et al. [16] the surface $\Phi(f, m)$ (noted simply Φ in the following) defines a phase diagram as shown on Fig. 1, where two regimes can be distinguished depending on m. Below some critical value m_c, Φ presents a discontinuity at some value $f^*(m)$ when the control parameter f is varied, whereas it remains continuous above m_c. The sudden jump occurring at $f^*(m)$ is associated with a percolation phenomenon on the network, where a very small variation of f results in the appearance of a giant cluster, whose normalized size is given by the difference between the lower and upper values of Φ