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# Simple model of complex bursting dynamics in developing networks of neuronal cultures

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**Abstract:** We consider and analyse emergence of spatiotemporal activity patterns in living neuronal cultures. Such patterns are often referred to as neuronal avalanches exemplifying self-organized criticality in living systems. A crucial question is how these patterns can be explained and modelled in a way that is mathematically tractable and yet broad enough to account for neuronal heterogeneity and complexity. Here we propose and analyse a simple model that may constitute a response to this question. A distinctive feature of the model is an energy feedback regulating efficacy of local neural connectivity. Such regulatory mechanism steers the overall dynamics to that of balancing on the edge of network percolation transition. Network activity in this state exhibits population bursts satisfying the scaling avalanche conditions. This network state is self-sustainable and represents an energetic balance between global network-wide processes and spontaneous activity of individual elements.



## 1. INTRODUCTION

Neuronal cultures have been in the focus of attention in physics and neuroscience for many years. Notwithstanding their importance as a convenient and accessible in-vitro model of brain tissues, they are a puzzling physical phenomenon with rich and complicated behavior requiring explanations. One of the striking examples is self-organized criticality (SOC) (Bak, 1997) observed in experimental studies (Beggs & Plenz, 2003, 2004; Pasqualea et al., 2008). The cultures grow autonomously and form synaptically coupled networks of living cells. After a period of initial growth and development the cultures start to generate spontaneous activity patterns in the form of population bursts. These bursts are shown to satisfy the power scaling law and hence are often referred as neuronal avalanches (Beggs & Plenz, 2003, 2004).

Since then a number of mathematical models have been proposed for simulation and analysis of spontaneous burst generation in neuronal networks. The spectrum of network's features linked to emergence of persistent bursts includes, but is not limited to, e.g. re-wiring, delays (Gong & van Leeuwen , 2004, 2007), frequency and spike timing dependent synaptic plasticity (Tsodyks et al., 2000; Izhikevich et al., 2004; Izhikevich, 2006). With regards to neuronal avalanches, models of network's growth (Abbott & Rohrkemper , 2007) and stochastic networks (Benyoun et al., 2010) have been put forward. They substantially advance our understanding of the phenomenon; yet macroscopic physical mechanisms steering living neuronal networks to the burst multiscale dynamics are still unclear.

It has been shown recently (see e.g. (Masquelier & Deco, 2013) and references therein) that population spikes and bursts can be attributed to cell's adaptation and short-time plasticity mechanisms. Effect of growing neuronal connectivity on bursts was studied in (Gritsun et al., 2012). The authors found that network connectivity, expressed e.g. as the number of synaptic connections per

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neuron, may play an important role in spiking and bursting activity in cultures. Additional links between connectivity development, firing activity homeostasis, and criticality are exposed in (Tetzlaff et al., 2010).

In this work we further contribute to the idea that complex dynamics of activity patterns in living neural cultures (super-bursts, periodic and chaotic spiking, and SOC-like behavior) can be explained by just few macroscopic variables capturing local connectivity patterns, neuronal activation dynamics, and a generalized an energy supply. Section 2.1 presents a simple percolation-based geometric model of cells' connectivity. In Section 2.2 we present and analyze mean-field approximation of neuronal activity in cultures and show that in presence of energy-dependent activation network connectivity parameter may be used to describe periodic spiking, irregular dynamics, and population bursts. Section 2.3 presents large-scale simulation of network of agents of which the activation probability depends on their current energy level. In Section 2.4 we compare our results with empirical data, and Section 3 concludes the paper.

## 2. RESULTS

### *2.1 Geometric model*

We start with geometrical arrangement of the network elements. Consider a network of $N$ neurons whose spatial coordinates are randomly and uniformly distributed in the unit square. Each individual neuron is described by two basic elements. The first is the region of reception of inputs represented by a circle of a given radius $R$. The circle models neuron's ability to sense input signals from other neurons, and is referred to as the dendrite region (in biology, dendrite is an input). The second element is an axon (in biology, output), which in our model is simulated by a straight segment of length $H$ (on the mature stage of the network development $H > R$) and whose end point is acting as a transmitter of the neuron's signal. If this point reaches out to the dendrite region of another neuron, a connection is established between these neurons (Abbott & Rohrkemper , 2007). There are three different ways that yield geometrical coupling or connectivity of the network elements:

*Case 1*: cells without axons, i.e. $H = 0$. In this case $N$ circles with radius $R$ are randomly and uniformly distributed in the unit square. If a circle **A** overlaps with a circle **B**, and circle **B** is connected with a circle **C**, then **A** is connected with **C**. Thus, a path between two distant cells can be defined as a chain of overlapping circles joining these cells. Emergence of large groups of connected elements in this network can be analyzed within the framework of standard circle percolation problem. Let $n$ be the cells density defined e.g. as the number of circles' centers in a unit area. According to ( Quintanilla & Ziff, 2007; Shante & Kirkpatrick, 1971), emergence of large groups of interconnected cells, the percolation transition, in a set of randomly distributed circles can be characterised by the mean number of centers that fall within a circle of radius $R$:

$$B = \pi R^2 n. \tag{1}$$

In particular, there exists a critical concentration $B = B_c$ at which two arbitrary circles become connected with high probability. Thus percolation occurs and a large cluster of connected circles appears. In contrast with typical thermal phase transitions where a transition between two phases occurs at a critical temperature, percolation transition relates to distribution and topology of clusters corresponding to the values of $B$ in a neighborhood of $B_c$. At low values of $B$ only small clusters of overlapping circles exist. When the concentration $B$ increases the average size of the clusters increases too. At the critical concentration value, $B = B_c$, a large cluster appears; it includes groups of cells that are close to the opposing boundaries of the original square. This cluster is called *spanning cluster* or percolating cluster. In the thermodynamic limit, i.e. in the infinite size system limit the spanning cluster is called *infinite cluster*. For scalar problem the value of $B_c \approx 1.1$.

*Case 2*. Cells have axons, $H > 0$, and axons are allowed to transmit signals in both directions. Each neuron can be represented as an undirected pair of head- and tail-circles both having radius $R$. When the head-circle or the tail-circle of an neuron overlaps with the head- or the tail-circles of another neuron we consider these neurons connected. Despite obvious difference of this setting from the previously considered one in that we are to operate with dipoles here rather than with just circles as in Case 1, the problem remains within a class of scalar percolation, albeit for dipoles of circles not just a single circle.

*Case 3*. Cells have axons, $H > 0$, and these axon can only transmit signals along a straight line that determines direction of connectivity for a given cell. The coupling direction from soma to synaptic terminal has isotropic distribution, and hence each neuron could be represented as a directed pair of head- and tail-circles both having radius $R$. Vectors linking centers of the head- and tail-circles are allowed to have arbitrary direction. Their lengths, $H$, however, are fixed. When the tail-circle of a neuron overlaps with a head-circle of another neuron the pair is considered as connected. In contrast with two other ways of establishing neuronal connectivity considered above this is the most realistic scenario. It is no longer within the scope of simple scalar circle percolation framework but is a vector percolation problem.

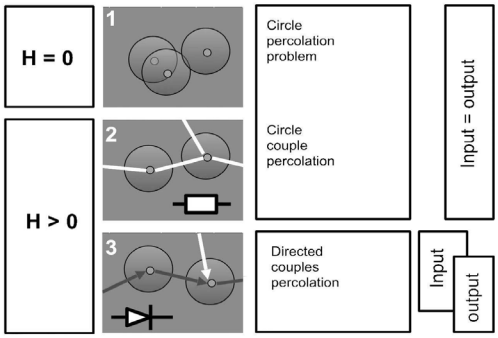


Fig. 1. Schematic representation of three different percolation settings for the geometrical model.

The three cases are illustrated with Figure 1. Figure 2 shows dependence of the percolation threshold parameter, $B_c$, on the ratio $H/R$. In accordance with he definition of $B$ in (1) the cell's concentration variable $B$ can be related