NEURONAL NETWORKS

Focus amidst the noise

High-resolution imaging of neuronal networks reveals that spontaneous bursts of collective activity are a consequence of an implosive concentration of noise.

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At first glance, the brain can seem random. Neuron branches look tangled, the voltage across the membrane of a single neuron follows a random walk and groups of neurons that become simultaneously active seem to be scattered with no particular pattern. One of the chief tasks in biophysics is to find regularities that could reveal order in this apparent disorder. In this respect, the work of Hodgkin and Huxley represents a major achievement from the past century: they were able to show how the seemingly noisy fluctuations in an individual neuron's membrane voltage can trigger highly repeatable voltage spikes — known as action potentials — that are the fundamental neuronal signal of the brain[1]. Now, over 60 years later, biophysics is faced with a similar problem: how does the apparently random, low-level spontaneous activity of a few-neuron system produce a structured network burst, where a large fraction of the neuronal population fires spikes nearly simultaneously? Javier Orlandi and colleagues have made an impressive step towards answering this question, as they now report in *Nature Physics*[2].

To understand their work, it is necessary to give some background about how neurons in networks interact. An individual neuron can be thought of as a threshold device: tiny currents injected through the synapses from other neurons add charge to a recipient neuron and can cause its membrane voltage to exceed a threshold for initiating a voltage spike (Fig. 1a–c). This spike travels down a cable-like fibre called an axon, in turn injecting tiny currents into many other neurons. The current injected by one neuron is rarely enough by itself to produce a spike in another neuron, and so activity in the network is driven by collective interactions among neurons. This interesting arrangement allows a host of complex emergent phenomena to exist, including waves, oscillations, synchrony, avalanches and network bursts.

Perhaps the most fundamental of these is the network burst (Fig. 1d), and intensive work has been devoted to understanding its initiation, propagation and structure[3]. Previous research has investigated burst leader neurons[4], network connectivity[5] and the time course of burst onset[6]. Although each of these has a role to play, a unified picture of burst dynamics has been missing.

To address this, Orlandi *et al.* recorded activity in thousands of individual neurons over time[2]. In contrast to more commonly used electrode-array recordings, their imaging approach enabled them to locate many more neurons, giving much-needed spatial details about how bursts developed. Interestingly, they found that although the activity preceding a burst seemed to be generated randomly, network bursts formed as waves that consistently flowed out of a few small regions they called nucleation sites. Each nucleation site was not merely a single highly active neuron, but could consist of many neurons. Because this process converted apparently random activity into structured network bursts, they called the phenomenon 'noise focusing'.

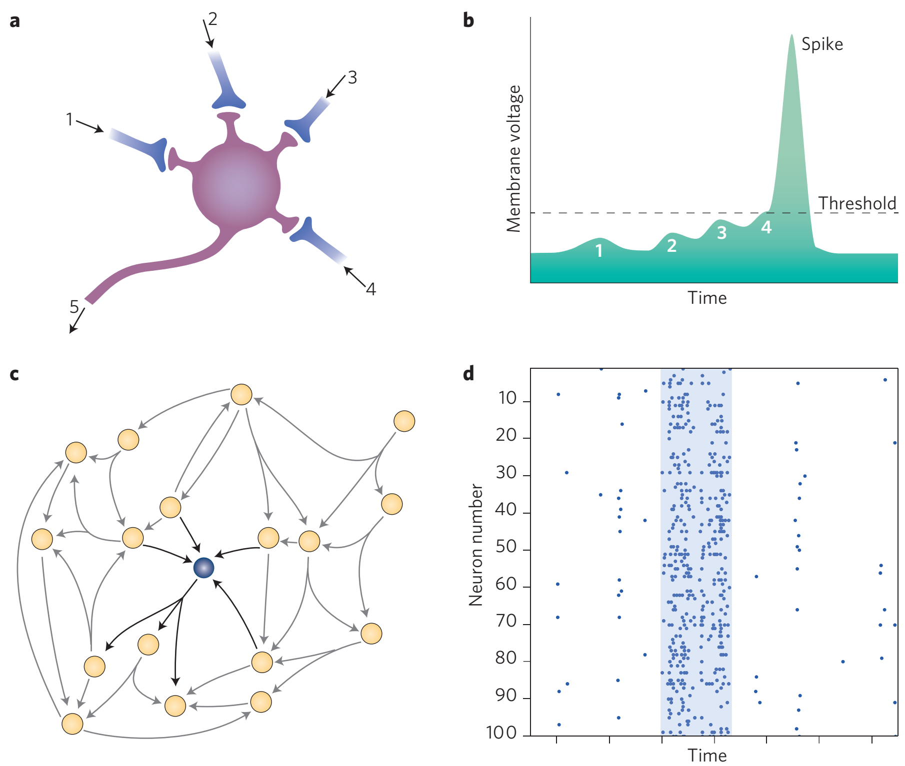

Figure 1 | Collective interactions among neurons. **a**, A single neuron can receive injected currents from other neurons (1–4) through synapses. Output travels along the axon (5). **b**, A single input (1) will not drive a neuron over threshold, but several inputs at the same time (2–4) will. Once activated, the neuron produces an action potential, also called a spike, leading to current injection at other neurons. **c**, The neuron is embedded in a network, where it receives and makes many contacts. Driving a neuron over threshold requires many simultaneous inputs. This means that network activity is typically driven by collective interactions. **d**, Network bursts are one example of such activity. Usually spontaneous activity is sparse, but occasional bursts (highlighted region) are characterized by a large fraction of the neurons spiking in a short interval.

Orlandi and colleagues provide some insight into the mechanisms underlying these nucleation sites[2]. When they cut away a peripheral part of the cultured network, the locations of the nucleation sites moved. This suggests that non-local interactions determine their placement. Detailed computer simulations also indicated that no single variable — whether firing rate of individual neurons or local clustering of connections — significantly correlated with the locations of the nucleation sites. Rather, a complex interplay of many dynamical and structural features is likely to be involved, suggesting that these sites are an emergent property of complex networks. An especially intriguing finding from the simulations is that each nucleation site establishes a basin of attraction, drawing in nearby cascades of spontaneous activity and amplifying them into bursts as they are sent out.

Although tantalizing, it is not yet clear how general this phenomenon is. The experiments used dishes of cultured networks of neurons, which may differ in their connectivity patterns from networks found in the intact brain. Thus, it will be important to see if noise focusing can indeed be found in awake animals, and if so, what functions it may serve. However, many non-neural networks are composed of units that have nonlinear activation functions similar to neural networks. Thus, the findings here in neurons might actually generalize to a wide variety of systems, like Twitter networks[7], or collections of interacting economic agents. If so, then this could be the first example of a phenomenon in the brain serving as a model system for our understanding of the external world. Usually it is the other way around. ❐

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