Synchrony is stubborn in feedforward cortical networks

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Action potential propagation has been studied extensively in model networks. Now a new paper describes an innovative method of combining neuronal recordings with real-time neuronal modeling to create multi-layer feedforward networks. Neurons in deep layers tend to fire in synchrony, suggesting such networks may code sensory information by groups of neurons that fire together.

Layers of neurons that are sparsely connected to each other in a feedforward manner may be the most rudimentary platform for thinking about how the brain extracts important features from sensory input. Neurons in the input layer fire action potentials in response to sensory input, and then the input is progressively processed at successive, deeper, layers. Is there a 'natural' firing mode in deep layers? Are action potential rates sustained throughout the network, or do neurons start to fire in bursts[1] or in synchrony with other neurons[2,3]? An answer to these fundamental questions would shed light on how the brain codes sensory information.

Until the Reyes study[4] in this issue, exploration of this question relied on modeling studies, which yielded contradictory results[5–8]. Recordings from single neurons in large networks are not yet possible, but here—by wedding the computer to the neuron—Reyes[4] devised a clever and simple recipe for constructing a feedforward system, consisting of several thousands of neurons, from real cortical neurons.

Using layer-5 pyramidal neurons in brain slices from the somatosensory cortex of rats, and a computer, Reyes constructed networks containing ten layers each with several hundred neurons (**Fig. 1a**). The computer's task was twofold. First, it transformed each train of action potentials from the simulated input layer into a transient postsynaptic current (PSC) of a chosen size, time course and sign (simulating excitatory or inhibitory postsynaptic currents). Second, it summed all PSCs generated by many trains of action potentials (representing many presynaptic inputs in layer n converging onto a single neuron in layer

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$n + 1$) and injected the summed current intracellularly into the recorded neuron's soma. The neuron responded by producing a train of action potentials. This output train represented one neuron in layer $n + 1$. This process was then iterated (**Fig. 1a**).

With this innovative experimental design, Reyes was able to manipulate the connection probability between layers and the number of neurons in each layer (about 1,000 iterations or neurons per hour is feasible). He used dynamic clamp to simulate the transient conductance changes caused by excitatory or inhibitory synaptic input, add background noise or make the network heterogeneous by recording simultaneously from a few neurons with different firing characteristics. The general finding was that neurons in the deeper layers inherently fire in a tight, spike-to-spike synchrony with each other, even when one tries hard to manipulate the system to 'spoil' synchrony. Synchronous firing in many neurons at a given layer can be seen already after the first few layers, and this synchronous firing develops rather rapidly (within 100 ms; **Fig. 1b**).

Reyes' findings support the notion that for fast computation, feedforward cortical networks may use a 'temporal code' in which at any given time neurons that fire simultaneously form a functional group representing a specific input feature[2].
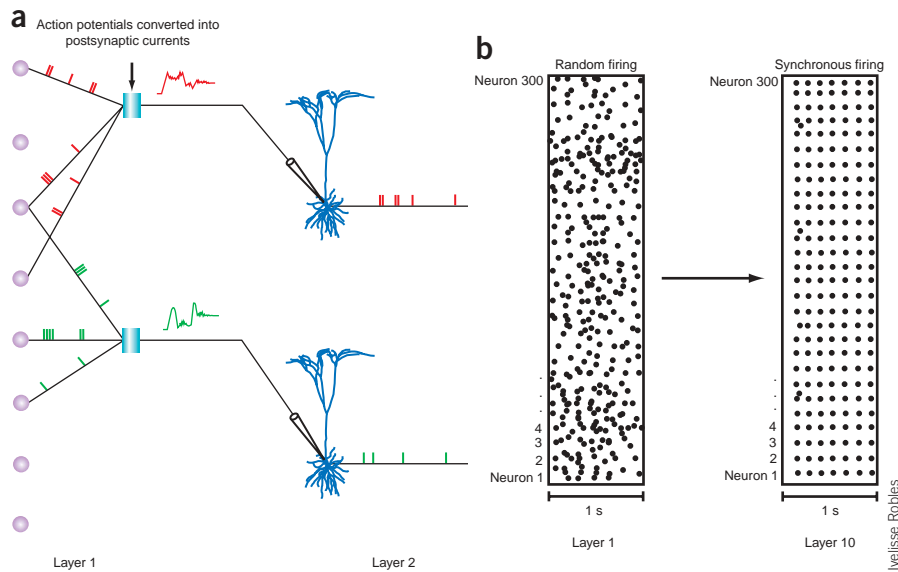
Why is synchrony is so persistent, and so stubborn, in feedforward networks? The main reason is the overpowering effect of the common inputs that impinge on different neurons belonging to a given layer. For networks of finite size, if each neuron receives multiple synaptic inputs from, say, 10% of the neurons in the previous layer, then neurons in any given layer will share about 1% of the same synaptic inputs. The larger the connection probability, the larger the probability for common inputs. When activated, this common input tends to fire action potentials in a restricted time win-

dow, yielding partial synchrony between the corresponding postsynaptic neurons. In the next layer downstream, neurons will tend to 'pick up' synchronous firing in their common inputs and, consequently, they will tend to fire even more synchronously. Synchrony is therefore expected to become more precise (and with more neurons recruited to this so-called 'syn-fire' chain) in progressively deeper layers. Indeed, Reyes showed that, under a variety of conditions, the firing of neurons was asynchronous for the first 2–3 layers, but became gradually more synchronous in successive layers, even with strong uncorrelated background noise.

An important issue that has yet to be studied is how the specific biophysical properties of cortical neurons, in particular their voltage- and time-dependent membrane conductances, contribute to the emergence of synchrony. It seems that synchrony *in vitro* is considerably more resistant to uncorrelated background noise than is synchrony in models of feedforward networks, which typically uses leaky 'integrate-and-fire' (LIF) neuron models that do not incorporate the full-range of membrane dynamics. Modeling studies show that, due to the difference in voltage buildup toward threshold for action potential firing, the synchronization properties in networks composed of conductance-based neurons compared to LIF networks are fundamentally different. The development of synchrony is more robust to noise in networks with conductance-based neurons[9]. Yet it is not clear exactly which of the nonlinear currents embedded in the membrane of cortical neurons is responsible for the robustness of synchrony or what biophysical mechanism underlies this robustness.

Another issue yet to be explored is the effect of dendritic, rather than somatic, inputs on network synchrony. By injecting current into the neuron soma, the consequence of signal delay in dendrites[10] and nonlinear dendritic dynamics (which strongly affect the pattern firing in the

a Action potentials converted into postsynaptic currents

Layer 1

Layer 2

b

Neuron 300

Random firing

Neuron 1

1 s

Layer 1

Neuron 300

Synchronous firing

Neuron 1

1 s

Layer 10

Ivelisse Robles

Figure 1 Making a sparsely connected multi-layer feedforward network using a single cortical neuron and a computer. (**a**) Each action potential (AP) from the red trains in the simulated 'input' layer 1 is transformed, by the computer, to a transient postsynaptic current (PSC). The summed PSCs are injected intracellularly to a real neuron. The resultant AP train represents the firing of one neuron in layer 2. Another set of trains is randomly chosen from layer 1 (green traces); the new output train represents a second neuron in layer 2. The set of AP trains representing layer 2 are, in turn, used to construct the activities of layer-3 neurons, and so forth. (**b**) Fast and robust synchrony develops in deep layers.

axon[11,12]) are ignored. This could be partially circumvented by impaling the cortical neuron with two or even three electrodes in soma and dendrites[13,14]. Two dendritic electrodes could be used to mimic multiple inputs into the neuron while the somatic electrode could be used to monitor the resultant firing as above. How would these multiple dendritic inputs be represented through the feedforward network?

Clearly, the most demanding assignment for the novel method presented here is to mimic real cortical networks that are dominated by recurrent connections. In this case, the firing of the neuron should be updated in real time in response to the activity arising from the feedback connections. One may push the method to start doing this by simultaneously recording from several synaptically connected neurons (preferably from different cortical layers) and/or by using the dynamic-clamp method to effectively connect the neurons to each other (electrically, via the respective intracellular electrodes). A small recurrent network created in this way can then serve as a building block for larger networks using the iterative method described above. Theoretical studies[15] of the behavior of such networks—with balanced excitatory and inhibitory activity—predict chaotic dynamics and linear responses to input rates; this could then be examined directly.

So we should celebrate this innovative marriage between real neurons and the computer. It enables one to construct semi-realistic cortical networks of different size and architecture. The computer traces down how action potentials are transmitted and processed through cortical networks with thousands of neurons; the neurons, in turn, help us to understand how signal processing in cortical networks depends on the synaptic and membrane properties of single neurons. This fruitful collaboration between the neuron and the computer will shed light on how cortical circuits encode (rate-wise, temporal-wise or otherwise) the world around us.

1. Izhikevich, E.M., Desai, N.S., Walcott, E.C. & Hoppensteadt, F.C. *Trends Neurosci.* **26**, 161–167 (2003).
2. Abeles, M. *Corticonics: Neural Circuits of the Cerebral Cortex* (Cambridge Univ. Press, Cambridge, UK, 1991).
3. Singer, W. *Neuron* **24**, 49–65 (1999).
4. Reyes, A. *Nat. Neurosci.* **6**, 595–601 (2003).
5. Shadlen, M.N. & Newsome, W.T. *J. Neurosci.* **18**, 3870–3896 (1998).
6. van Rossum, M.C.W., Turrigiano, G.G. & Nelson, S.B. *J. Neurosci.* **22**, 1956–1966 (2002).
7. Litvak, V., Sompolinsky, H., Segev, I. & Abeles, M. *J. Neurosci.* **23**, 3006–3015 (2003).
8. Diesmann, M., Gewaltig, M.O. & Aertsen, A. *Nature* **402**, 529–533 (1999).
9. Golomb, D. & Hansel, D. *Neural Comput.* **12**, 1095–1139 (2000).
10. Agmon-Snir, H. & Segev, I. *J. Neurophysiol.* **70**, 2066–2085 (1993).
11. Mainen, Z.F. & Sejnowski, T.J. *Nature* **25**, 363–366 (1996).
12. Reyes, A. *Annu. Rev. Neurosci.* **24**, 653–675 (2001).
13. Larkum, M.E., Zhu, J.J., Sakmann, B. *Nature* **398**, 338–341 (1999).
14. Williams, S.R. & Stuart, G.J. *Science* **295**, 1907–1910 (2002).
15. van Vreeswijk, C. & Sompolinsky, H. *Science* **274**, 1724–1726 (1996).

A signature of salience in the *Drosophila* brain

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Electrophysiological recordings coupled with genetic manipulations in fruit flies reveal activity patterns in the brain associated with the conspicuousness of visual objects, providing an elusive physiological link between gene products and behavior.

Some of the most complex animal behavior is so commonplace that it escapes our attention. For example, seeking, detecting,

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approaching and landing on a piece of fallen fruit is a seemingly simple task for a fruit fly, yet it requires that the animal track a fragmented odor plume through a changing and varied landscape. Eventually, the fly must orient toward some conspicuous visual feature that might represent the source of the attractive odor. Does this behavior reflect a confluence of sensori-motor reflexes, or do higher centers of the brain decide that a smelly blob is sufficiently conspicuous to warrant further investigation? More generally, how do brains distinguish environmental features worthy of selective attention?

In this issue, van Swinderen and Greenspan[1] identify neural activity that may be associated with perception in the