NEUROSCIENCE

Time Is Precious

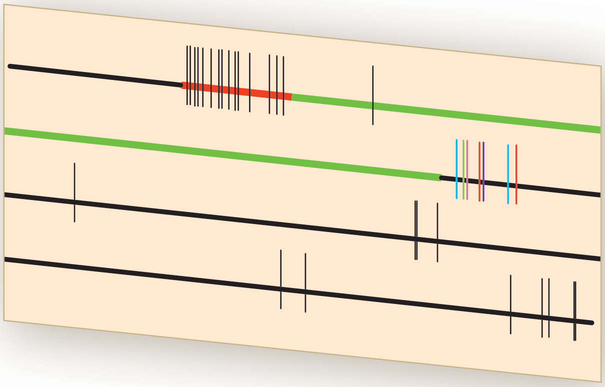
Moshe Abeles

Enhanced online at www.sciencemag.org/cgi/content/full/304/5670/523

When an activated neuron fires a series of action potentials (spikes), where is the information encoded in the spike train? Conventional wisdom dictates that the exact timing of individual spikes is random and that the sole criterion that could be used to encode information is the mean firing rate during a particular time window (typically set at 20 to 200 ms). With their report on page 559 of this issue, Ikegaya *et al.* (*1*) cast serious doubt on the conventional view.

At first glance, the complexity of the cerebral cortex seems to support the conventional view. In a cubic millimeter of cortex, there are on average 20,000 to 100,000 neurons each firing at a rate of a few spikes per second. These spikes travel unattenuated through 4 km of axons and affect other neurons through 800,000,000 synapses (*2*, *3*). A spike arriving at a synapse causes the release of a small amount of neurotransmitter, which evokes a small voltage change in the membrane of the contacted neuron. Most neurons show periods of both elevated and reduced activity (see the figure), prompting the assumption that each synapse is fairly weak. Presumably, the combined activities of all synaptic inputs onto a particular neuron result in a noisy trace that occasionally reaches the firing threshold, resulting in emission of a spike. If many synaptic inputs increase the neuron's firing rate, the chance of reaching the threshold will increase and the neuron will fire spikes at an elevated rate. Yet, the exact timing of the individual spikes remains arbitrary.

This view, although held by most neurophysiologists, is under challenge. For example, it has been shown that individual neurons reproduce exactly the same spike train when an identical "noisy" current is injected into each neuronal cell body (*4*). Indeed, Ikegaya *et al*. now show that at different times the same neuron can display regions of membrane potential changes that look "noisy" but are in fact very similar (*1*). Likewise, analysis of neuronal spike trains has revealed precise spatiotemporal firing sequences that are repeated several times (*5*). The validity of these reports, however, has been undermined by arguments that statistical analyses of the data were not adequate (*5*).



Talking in code. The figure shows the spiking activity of a single neuron in the prefrontal cortex of a monkey performing a behavioral task (in this case, free drawing). Each trace represents 3 seconds of neuronal activity (the traces are continuous from top to bottom) and the time of each spike is marked by a vertical line. Periods of elevated (red) and reduced (green) rates of activity are indicated. Many spikes fall within low rate periods. Do these isolated spikes contain information? Is it possible that the colored spikes in the second trace participate in different computational processes, such that the two blue spikes participate in one process while the red spikes participate in another? Ikegaya *et al.* have detected patterns of spontaneous neuronal activity in mouse cortical brain slices and cat visual cortex that are repeated with millisecond precision (*1*). These patterns may indicate activity in synfire chains. If so, then different spikes of the same neuron may participate in different computational processes. This may be the way that neurons encode information and pass it along to their neighbors.

Why should one care whether cortical neurons exhibit precise firing patterns? Some neural computations would be greatly facilitated if every spike had a tag identifying the subprocess that it belongs to (see the colored spikes in the figure) (*6*). For example, consider how we understand the sentence, "John gave Mary a book" (*7*). Supposing that all we had at our disposal were groups of neurons—one elevating its firing rate to signify "John," another for "Mary," another for "book," and yet another for the predicate "to give." Then, how could we tell whether it is John who gave the book to Mary, or Mary who gave the book to John, unless perhaps the book gave John to Mary? The ambiguity could be easily resolved, however, if the predicate "to give" had components such as "the giver," "the recipient," and "the given object," and if the activity of neurons representing "the giver" and those representing John were similarly tagged (for instance, by synchronous firing of the two groups of neurons). In the same way, similar tags would need to be attached to "the recipient" and Mary, and to "the given object" and book.

Such tags could be provided by phase-locked oscillations of groups of neurons that belong together through precise synchrony of their spike trains or through precise intervals between the spikes. All such combinations have been recorded in the brains of mammals using electrodes, yet the debate rages on. In their study, Ikegaya *et al.* (*1*) used intracellular recordings from cat visual cortex and mouse cortical brain slices to search for repeat patterns of spontaneous synaptic currents. They show conclusively that repeat patterns of synaptic currents and of precise spatiotemporal firing sequences are abundant in the cat and mouse brain tissue.

How can precise spatiotemporal firing patterns be generated in the noisy cortical environment? More than 20 years ago, it was suggested that if neurons were organized in a feed-forward network—one group providing multiple connections to neurons in another group, which in turn provide multiple connections to neurons in a third group, and so forth—activity would be organized as a synchronous volley of spikes traversing from group to group with an almost constant time delay (*8*). Multiple theoretical studies, simulations, and some direct testing in brain slices (*9*) have revealed that this is indeed the case (*10*). A feed-forward network with random connections between

---

The author is at Gonda Brain Research Center, Bar Ilan University, Ramat-Gan, Israel, and Center for Neural Computation, the Hebrew University, Jerusalem, Israel. E-mail: moshe.abeles@mail.biu.ac.il

groups of neurons showing synchronous firing is termed a "synfire" chain.

It has been suggested that synfire chains could be the building blocks that enable neurons to encode simple signals and then combine them dynamically into more complex patterns (*11*). Thus, if neuronal activity within an individual synfire chain is like a "motif," then combining a series of synfire chains could create what has been called a cortical "song." The Ikegaya *et al*. study provides direct evidence that cortical neurons are able to combine such motifs into cortical songs.

Can such precise spatiotemporal firing sequences (motifs) serve as a code that can be recognized by other neurons? Probably not. According to the synfire chain hypothesis, what can be recognized is a wave of synchronous firing that travels through the synfire chain. These sparse firing sequences are only a signature of synfire activity, which may be used by the experimenter to detect when a given synfire chain is active and to analyze how it is related to other active synfire chains. Although the synfire chain hypothesis is very appealing, it still remains to be shown that synfire chains exist in the intact brain and that they are relevant to the behavior of animals and humans.

References and Notes

1. Y. Ikegaya *et al.*, *Science* **304**, 559 (2004).
2. M. Abeles, *Corticonics: Neural Circuits of the Cerebral Cortex* (Cambridge Univ. Press, New York, 1991).
3. V. Braitenberg, A. Shuez, *Cortex: Statistics and Geometry of Neuronal Connectivity* (Springer, Berlin, ed. 2, 1998).
4. Z. F. Mainen T. J. Sejnowski, *Science* **268**, 1503 (1995).
5. M. Abeles, I. Gat, *J. Neurosci. Methods* **107**, 141 (2001).
6. C. von der Malsburg, *The Correlation Theory of Brain Function. Internal Report 81-2* (Max Planck Institute for Biophysical Chemistry, Goettingen, Germany, 1981).
7. L. Shastri, V. Ajjanagadde, *Behav. Brain Sci.* **16**, 417 (1993).
8. M. Abeles, *Local Cortical Circuits: An Electrophysiological Study* (Springer, Berlin, 1982).
9. A. Reyes, *Nature Neurosci.* **6**, 593 (2003).
10. M. Diesmann *et al.*, *Nature* **402**, 529 (1999).
11. E. Bienenstock, in *Brain Theory: Biological Basis and Computational Principles*, A. Aertsen, V. Braitenberg, Eds. (Elsevier, Amsterdam, 1996), pp. 269–300.
12. Supported in part by grants from ISF, GIF, and DIP.

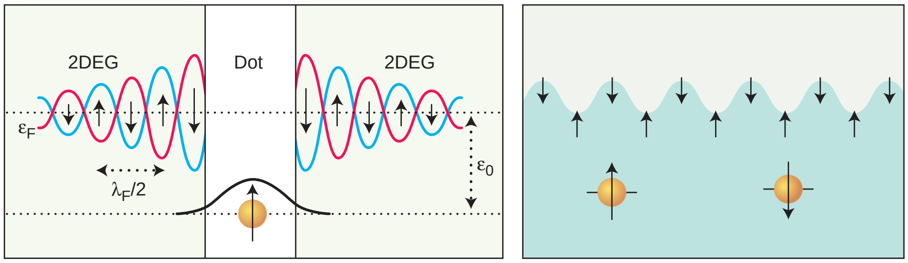
PHYSICS

Coupling Qubits by Waves on the Electron Sea

L. I. Glazman and R. C. Ashoori

Exploiting quantum mechanics as a tool for computation may allow entirely new ways of performing a number of difficult computing tasks, such as drastically cutting the time necessary for factoring a number by its primes, the cornerstone of modern cryptography. At the heart of quantum computing is the concept of a qubit (quantum bit), which requires a whole new set of physical devices to replace the "classical" devices implementing the conventional bit operations. A conventional bit may reside in one of two states at a time. In contrast with binary logic, the qubit must be capable of residing in a superposition of two states. The element of a computation consists of a quantum-mechanical evolution of such a superposition. As with the bits in the conventional computer, the qubits must act together, requiring controllable interactions between them. On page 565 of this issue, Craig *et al.* (*1*) report an important step toward this goal.

Building devices to store and process qubits is a challenging problem. In a typical field-effect transistor in a computer chip, 10,000 to 100,000 electrons participate in a single switching event. It is impossible to isolate, out of such a complex system, two quantum mechanical states that would evolve coherently to play the role of a qubit. Just over a decade ago, physicists first learned to measure the movements of single electrons in semiconductor structures that isolate electrons into small "quantum dots." In such "single-electron transistors," the electrical conductance depends strongly on the position of a single electron. However, the same factors that make single-electron detection simple also complicate construction of a quantum computer based on sensing an electron's position. Charged electrons are easily jostled by stray electric fields, and electrons placed in delicate entangled quantum states rapidly lose quantum coherence.



Connecting the dots. (Left) The activation energy $\varepsilon_0 > 0$ localizes electrons in the dot but still allows the wave function to penetrate beyond it. Because of the Pauli principle, some itinerant electrons of the same polarization are forced to shift away from the dot, resulting in anti-phased Friedel oscillations in the density of two spin species forming the sea of electrons (blue and red lines). The period of oscillation is half of the Fermi wavelength λ_F. **(Right)** Two localized spins interact via the Friedel oscillation. The sign of this RKKY interaction depends on the interspin distance. 2DEG, two-dimensional electron gas.

Aside from its charge, an electron carries with it an elementary magnetic moment, characterized by its spin. There are two quantized states for the spin, and an electron may exist in a superposition of the two. The electron's spin is much less perturbed than its position, allowing for long coherence times (*2*) and raising hopes of building an electron-spin–based quantum computer. Although it is much harder to measure the state of a single electron's spin, progress in this direction has been reported recently (*2*).

Qubit connections pose another central problem in moving toward spin-based quantum computing. Computation requires the means to control the interaction between the spins of distant electrons, each working as qubits. In their experiment, Craig *et al.* (*1*) demonstrate a controllable interaction between spins localized in two quantum dots that need not be adjacent to each other. Understanding their measurement involves several key notions, in particular the use of quantum dots as "artificial atoms" and how these "atoms" interact.

L. I. Glazman is in the Department of Physics, University of Minnesota, Minneapolis, MN 55455, USA. E-mail: glazman@physics.spa.umn.edu R. C. Ashoori is in the Department of Physics, Massachusetts Institute of Technology, Cambridge, MA 02139, USA. E-mail: ashoori@mit.edu