associated with their interaction; this absence of spin crystallization is attributed to geometrically induced frustration (*7*, *8*). Further studies identified a glass transition at lower temperatures, and the presence of spin freezing in the absence of long-range spin order was confirmed by neutron scattering (*8*). Because the initial samples did have some site disorder, the results could be ascribed to conventional random spin glass behavior. However, recent results (*10*) suggest that the observed glass transition remains in the limit of vanishing disorder. The presence of zero-spin triangular clusters as the building blocks of the frozen spin configuration is consistent with recent neutron data (*13*), thus confirming the importance of geometrically induced frustration here.

In the meantime, several other strongly frustrated materials have been identified (*9*, *11*, *14*). All have continuous spins and share the same basic building block—the triangular plaquette—for their lattices. Needless to say, each material has its strengths and weaknesses as examples of glasses (*12*).

What features are characteristic of glasses with and without disorder? How dependent are the properties of glasses on the range of their underlying interactions? At present any theoretical questions about short-range interactions can only be addressed numerically. Because the number of states in the systems scales exponentially with the number of spins, one is necessarily restricted to small cluster sizes. Furthermore, realistically one can only probe such a mini-glass on time scales roughly four orders of magnitude greater than its characteristic microscopic time. By contrast, experimentalists can access almost 12 more decades in time, and glasses exhibit interesting time-dependent behavior across this full range. Ideally, a detailed study of the effects of disorder versus geometry should be performed in a controlled environment where each effect can be tuned. Superconducting networks provide precisely such a setting (*15*, *16*). Initial results on a Kagomé network agree with the absence of ordering observed in the associated materials (*16*). An aim here is to identify characteristic features of the many ground states for possible information storage.

Thus, there is hope that a minimal model of glassiness will be found. Just as the study of disordered spin systems has had an impact well beyond its original realm (*1*–*3*, *5*, *6*), we anticipate that the study of disorder-free glasses will also lead to concepts and methods of use in many areas. For example, it appears that the characterization of ground states in several nonrandom glass models is related to problems in number theory, and the associated number sequences are important for error-correcting codes (*20*). The identification of a minimal clean-glass model could help find physical systems for quantum computation. Again, an obscure phenomenon in magnetic materials is improving our understanding of Nature's elegant complexity, yielding insights that may result in future conceptual and technological progress.

References

1. P. W. Anderson in *Ill-Condensed Matter*, R. Balian, R. Maynard, G. Toulouse, Eds. (North-Holland, Amsterdam, 1979), pp. 162–258.
2. J. Mydosh, *Spin Glasses: An Experimental Introduction* (Taylor and Francis, London, 1993).
3. S. Kirkpatrick, C. D. Gelatt Jr., M. P. Vecchi, *Science* **220**, 671 (1983).
4. N. Sourlas, *Nature* **339**, 693 (1989).
5. E. I. Shakhnovich and A. M. Guten, *ibid.* **346**, 773 (1990).
6. J. Hertz, A. Krogh, R. G. Palmer, *Introduction to the Theory of Neural Computation* (Addison-Wesley, Redwood City, CA, 1991).
7. X. Obradors *et al.*, *Solid State Commun.* **65**,1989 (1988).
8. A. P. Ramirez *et al.*, *Phys. Rev. Lett.* **64**, 2070 (1990); C. Broholm *et al.*, *ibid.* **65**, 3173 (1990).
9. B. D. Gaulin *et al.*, *ibid.* **69**, 3244 (1992).
10. B. Martinez *et al.*, *Phys. Rev. B* **50**, 15779 (1994).
11. P. Schiffer *et al.*, *Phys. Rev. Lett.* **74**, 2379 (1995).
12. A. P. Ramirez, *Annu. Rev. Mat. Sci.* **24**, 453 (1994); P. Schiffer and A. P. Ramirez, *Comm. Cond. Matt. Phys.* **18**, 21 (1996).
13. S.-H. Lee *et al.*, *Europhys. Lett.* **35**, 127 (1996).
14. A. S. Willis *et al.*, in press.
15. D. Davidovic *et al.*, *Phys. Rev. Lett.* **76**, 815 (1996).
16. M. J. Higgins *et al.*, in press.
17. G. Wannier, *Phys. Rev.* **79**, 357 (1950).
18. P. W. Anderson, *ibid.* **102**, 1008 (1956).
19. For example, P. Chandra and P. Coleman in *Strongly Interacting Fermions and High Temperature Superconductivity: Les Houches Lecture Notes (Session LVI)*, B. Doucot and J. Zinn-Justin, Eds. (North-Holland, Amsterdam, 1995), pp. 495–594.
20. M. R. Schroeder, *Number Theory in Science and Communication* (Springer-Verlag, Berlin, 1984).

NEUROSCIENCE

The Year of the Dendrite

Terrence J. Sejnowski

The dendrites of neurons appeared to the neuroanatomist Ramon y Cajal to be elaborate receiving antennae, studded with thousands of synapses—contacts from other neurons. Now we know that the dendrites of pyramidal neurons in the neocortex and hippocampus of the brain possess fast sodium and high-threshold calcium currents that make synaptic integration in their dendritic trees a highly nonlinear affair (*1*, *2*). What computational function could these currents have? Active dendritic currents can affect the propagation of electrical current down the dendrites, consistent with Cajal's view that information in dendrites flows from the synapse to the soma. Or active currents could carry information about the timing of spikes generated near the soma backward toward the synapses. Two reports in this issue (pages 209 and 213) provide evidence that such backpropagating action potentials do indeed influence the strengths of dendritic synapses in the hippocampus (*3*) and the neocortex (*4*).

The synapses between the Schaffer collaterals and the pyramidal neurons in the CA1 region of the hippocampus are plastic and exhibit a form of long-term potentiation (LTP) that depends on the entry of calcium into the dendritic spine on which the synapse is located. Depolarization of the dendrite by injection of current into the cell body, coupled with glutamate activation of *N*-methyl-D-aspartate (NMDA) receptors, is sufficient to induce LTP at these synapses. Magee and Johnston (*3*) show that action potentials in the soma paired with weak excitatory inputs at the dendrites can induce LTP far from the soma. Furthermore, the amount of calcium entering the dendrites, measured by optical imaging, is significantly enhanced by pairing of the synaptic input and the backpropagating action potential above that expected by linear summation (*5*). In addition to regulating LTP, the backpropagating action potentials also regulate long-term depression (LTD) (*6*) and the

Dendrite of a pyramidal neuron in vivo. Fluorescence image acquired with two-photon excitation laser scanning microscopy of a basal dendrite from a calcium green–filled layer 2/3 neocortical pyramidal cell from the rat somatosensory cortex. The field of view is 40 μm on each side. [Courtesy of K. Svoboda, W. Denk, D. Kleinfeld, and D. W. Tank]

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coupling between synapses and the spike-initiating zone in the region near the cell body (7). Hebb, who postulated such a coincidence-based learning mechanism to explain associative learning, would have been pleased by these discoveries, although perhaps not surprised (8).

In the second report, a technical tour de force, Markram *et al.* (4) recorded from neighboring pyramidal neurons in layer 5 of neocortical slices and varied the timing of the spikes in the presynaptic and postsynaptic cells. When the presynaptic action potential preceded the postsynaptic action potential, the synaptic response increased, but if the order was reversed, the synaptic response decreased. The window for synaptic plasticity was around 100 ms wide, and a difference in spike timing of 10 ms near coincidence switched the plasticity from LTP to LTD. The discovery that dendrites can transmit information about spike timing and that differences in spike timing of a few milliseconds are crucial for synaptic plasticity raises the stakes in the debate as to whether the precise timing of action potentials is important in cortical processing (9).

These remarkable results must now be put into the context of normal information processing in the cortex, which is characterized by a constant chatter of ongoing spike activity. Every spike in a pyramidal cell could potentially affect every excitatory synapse of that cell that was active within 100 ms. Even if the mean synaptic strength were not changed by a particular spike, the random walk would wash away any information stored at the synapse. There are, however, reasons to believe that synaptic plasticity is strictly regulated in vivo. First, backpropagation of an action potential in the dendrite can be throttled by input from inhibitory neurons (*10*, *11*), suggesting that there may be local control of the invasion of backpropagating action potentials into dendritic branches. Second, the delivery of neuromodulators such as acetylcholine and dopamine, which depends on the behavioral and cognitive state of an animal, could affect the induction of synaptic plasticity (*12*, *13*).

The most direct evidence for the regulation of backpropagating dendritic action potentials comes from a new technique that promises to revolutionize cortical physiology. Svoboda *et al.* (*14*) have recently shown that cortical neurons can be visualized in vivo by means of two-photon laser-scanning microscopy, which allows the full three-dimensional dendritic tree of a neuron to be scanned and reconstructed. Spines on the dendrites of cortical pyramidal neurons can be visualized (see figure). After injection of a calcium indicator dye, these authors observed dendritic calcium entry during sodium spikes recorded from the cell body. Under the conditions that they studied, however, these responses declined steeply and disappeared in the distal apical dendrite, suggesting failure of the back-propagating spikes. In addition, widespread calcium influx expected for dendritic calcium action potentials was not observed in response to sensory stimulation. This result suggests that calcium influx triggering synaptic plasticity may only occur in vivo under special conditions that have yet to be determined.

Dendrites have additional levels of complexity that we are just beginning to understand (*1*, *15*). Many types of voltage-dependent ion channels are distributed nonuniformly throughout neurons, with a wide range of time courses for activation and inactivation (*2*, *16*). A cortical neuron is, therefore, like a city with diverse neighborhoods, each with a different character, with constant traffic between them. Compartmental models of reconstructed neurons that incorporate detailed biophysical properties of ion channels provide a way to explore the dynamic properties that emerge from the nonlinear interactions between different parts of the neuron (*17*).

More has been learned about the secret lives of dendrites in the last year than in all previous years. At the recent Annual Meeting of the Society for Neuroscience, there was a collective sense that new techniques for studying cortical neurons are ushering in an exciting era that will lead to many more surprises.

An enhanced version of this Perspective, with live links, can be seen in *Science* Online on the Web at http://www.sciencemag.org/

References

1. R. Yuste and D. Tank, *Neuron* **16**, 701 (1996).
2. D. Johnston, J. Magee, C. Colbert, B. Christie, *Annu. Rev. Neurosci.* **19**, 165 (1996).
3. J. Magee and D. Johnston, *Science* **275**, 209 (1997).
4. H. Markram, J. Lubke, M. Frotscher, B. Sakmann, *ibid.*, p. 213.
5. R. Yuste and W. Denk, *Nature* **375**, 682 (1995).
6. B. Christie, J. Magee, D. Johnston, *Learn. Mem.* **3**, 160 (1996).
7. J. Jester, L. Campbell, T. Sejnowski, *J. Physiol.* **484**, 689 (1995).
8. L. Nadel, personal communication.
9. F. Rieke, D. Warland, R. van Steveninck, W. Bialek, *Spikes: Exploring the Neural Code* (MIT Press, Cambridge, MA, 1997).
10. H. Tsubokawa and W. Ross, *J. Neurophysiol.* **76**, 2896 (1996).
11. H. Gaudreau, E. Lang, A. Destexhe, D. Pare, *Soc. Neurosci. Abstr.* **22**, 790 (1996).
12. P. R. Montague and T. J. Sejnowski, *Learn. Mem.* **1**, 1 (1994).
13. P. Huerta and J. Lisman, *Neuron* **15**, 1053 (1995).
14. K. Svoboda, W. Denk, D. Kleinfeld, D. Tank, *Soc. Neurosci. Abstr.* **22**, 1058 (1996).
15. I. Segev, J. Rinzel, G. Shepherd, *The Theoretical Foundation of Dendritic Function: Selected Papers of Wilfrid Rall with Commentaries* (MIT Press, Cambridge, MA, 1995).
16. R. R. Llinás, *Science* **242**, 1654 (1988).
17. Z. Mainen and T. Sejnowski, *Nature* **382**, 363 (1996).

NEUROSCIENCE

More Than Just Frequency Detectors?

Alex M. Thomson

Synapses, the junctions through which neurons communicate with each other, can display frequency and pattern-dependent behavior—no surprise to those familiar with the work of Katz *et al.* (*1*) in the 1950s and 1960s on the neuromuscular junction. Now two recent studies (*2*, *3*), one on page 221 of this issue, present a simplified mathematical model of the frequency-dependent behavior of one class of synapse to predict the outcome of changes in the activity of many similar inputs impinging on a single target neuron. This is a welcome refinement of more traditional models, in which inputs were simply assigned a static efficacy, regardless of their pattern of activity.

The experimental observation underlying these studies is that the connection from one cortical pyramidal cell to another exhibits frequency-dependent depression (*4*); that is, a second action potential elicits a smaller response than the first, the third a smaller response than the second, and so on until a plateau or steady-state output is reached (*5*) (see figure, P3→P2 and P1→P2). The faster the rate at which the presynaptic neuron fires, the more rapidly and powerfully does the connection depress, so that over a large range of rates, the summed potential elicited at steady state is the same (P3→P2). These properties determine that the connections transfer little information about steady-state frequency. Whether a hundred inputs fire steadily at a low or high average rate makes little difference to the response. Connections like these would be sensitive, however, to significant proportional changes in frequency of individual inputs (as in P1→P2) or to simultaneous changes in many inputs. Such depressing synapses, therefore, en-

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