

The adaptable synapse

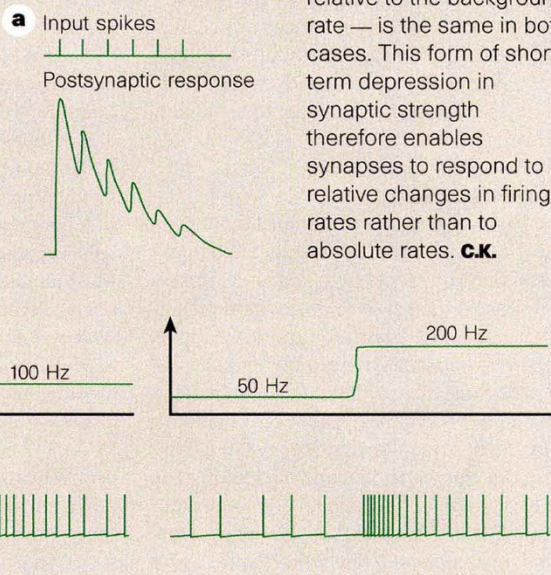
In short-term synaptic depression, the postsynaptic response to a regular train of presynaptic spikes firing at a fixed frequency f gradually lessens. The response to the first spike might be large, but subsequent responses will be diminished until they reach a steady state (expressed in terms of A , the fractional reduction in postsynaptic effect). This is shown here (part a) for presynaptic spikes at 40 Hz frequency (data from ref. 26).

This depression generally recovers within 0.1 to 0.5 s. For firing rates above 10 Hz, A is roughly inversely proportional to the firing frequency. In other words, within a few hundred milliseconds the synapse will have adapted to the

presynaptic firing with a response roughly independent of the firing rate (due to the inverse relationship between A and f). If the synaptic input now abruptly increases by δf , the adapted cell will initially increase its response by $\delta f A$ which is proportional to $\delta f/f$. As a consequence, the transient change in the postsynaptic response will be proportional to the relative change in firing frequency. This is demonstrated in

computer simulations in which the presynaptic firing rate to a couple of hundred such synapses converging onto a model neuron is increased fourfold (part b — the increases are from 25 to 100 Hz on the left and from 50 to 200 Hz on the right; data from ref. 27).

Even though the final input rate is twice as high on the right side as on the left, the firing rate of the neuron is roughly the same. This is because the fractional increase — relative to the background rate — is the same in both cases. This form of short-term depression in synaptic strength therefore enables synapses to respond to relative changes in firing rates rather than to absolute rates. **C.K.**



process²⁸. Like biological synapses, they can change their effective weight in a continuous manner while they carry out computations. Floating-gate synapses will greatly aid attempts to replicate the functionality of nervous systems by the appropriate design of neuromorphic silicon neurons using analog very-large-scale-integrated (VLSI) circuit-fabrication technology²⁹.

Hybrid computer

Overall, then, current thinking about computation in the nervous system has the brain as a hybrid computer. Individual nerve cells convert the incoming streams of digital pulses into spatially distributed variables, the postsynaptic membrane potential and calcium redistribution. This transformation involves highly dynamic synapses that adapt to their input.

Information is then processed in the analog domain, using a number of linear and nonlinear operations (multiplication,

saturation, amplification, thresholding) implemented in the dendritic cable structure and augmented by voltage-dependent membrane and synaptic conductances. The resulting signal is then converted back into digital pulses and conveyed to the following neurons. The functional resolution of these pulses is in the millisecond range, with temporal synchrony across neurons likely to contribute to coding. Reliability could be achieved by pooling the responses of a small number (20–200) of neurons.

And what of memory? It is everywhere (but can't be randomly accessed). It resides in the concentration of free calcium in dendrites and the cell body; in the presynaptic terminal; in the density and exact voltage-dependency of the various ionic conductances; and in the density and configuration of specific proteins in the postsynaptic terminals.

Only very little of this complexity is reflected in today's neural-network literature. Indeed, we sorely require theoretical tools that

deal with signal and information processing in cascades of such hybrid, analog–digital computational elements. We also need an experimental basis, coupled with novel unsupervised learning algorithms, to understand how the conductances of a neuron's cell body and dendritic membrane develop in time. Can some optimization principle be found to explain their spatial distribution?

As always, we are left with a feeling of awe for the amazing complexity found in nature. Loops within loops across many temporal and spatial scales. And one has the distinct feeling that we have not yet revealed every layer of the onion. Computation can also be implemented biochemically — raising the fascinating possibility that the elaborate regulatory network of proteins, second messengers and other signalling molecules in the neuron carry out specific computations not only at the cellular but also at the molecular level.

Christof Koch is in the Computation and Neural Systems Program, California Institute of Technology, Pasadena, California 91125, USA (e-mail: koch@klab.caltech.edu).

1. Hebb, D. O. *The Organization of Behavior: A Neuropsychological Theory* (Wiley, New York, 1949).
2. Arbib, M. (ed.) *The Handbook of Brain Theory and Neural Networks* (MIT Press, Cambridge, MA, 1995).
3. Hertz, J., Krogh, A. & Palmer, R. G. *Introduction to the Theory of Neural Computation* (Addison-Wesley, Redwood City, CA, 1991).
4. Nicoll, R. A. & Malenka, R. C. *Nature* **377**, 115–118 (1995).
5. Stevens, C. F. *Nature* **381**, 471–472 (1996).
6. Newsome, W. T., Britten, K. H. & Movshon, J. A. *Nature* **341**, 52–54 (1989).
7. Segev, I., Rinzel, J. & Shepherd, G. *The Theoretical Foundation of Dendritic Function: Selected Papers of Wilfrid Rall with Commentaries* (MIT Press, Cambridge, MA, 1995).
8. Johnston, D., Magee, J., Colbert, C. & Christie, B. *Annu. Rev. Neurosci.* **19**, 165–186 (1996).
9. Cauter, L. J. & Connors, B. W. *J. Neurosci.* **2**, 751–762 (1994).
10. Bernander, O., Douglas, R. J. & Koch, C. *J. Neurophysiol.* **72**, 2743–2753 (1994).
11. Mel, B. W. *Neural Computation* **6**, 1031–1085 (1994).
12. Koch, C. & Poggio, T. in *Single Neuron Computation* (eds McKenna, T., Davis, J. & Zornetzer, S. F.) 315–345 (Academic, Boston, 1992).
13. Stuart, G. J. & Sakmann, B. *Nature* **367**, 69–72 (1994).
14. Sofky, W. R. *Curr. Opin. Neurobiol.* **5**, 239–247 (1995).
15. Svoboda, K., Denk, W., Kleinfeld, D. & Tank, D. W. *Nature* **385**, 161–165 (1997).
16. Bair, W. & Koch, C. *Neural Computation* **8**, 1185–1202 (1996).
17. Rieke, E., Warland, D., van Steveninck, R. R. D. & Bialek, W. *Spikes: Exploring the Neural Code* (MIT Press, Cambridge, MA, 1996).
18. Alonso, J. M., Usrey, W. M. & Reid, R. C. *Nature* **383**, 815–819 (1996).
19. Abeles, M. *Corticones: Neural Circuits of the Cerebral Cortex* (Cambridge Univ. Press, 1990).
20. Hopfield, J. J. *Nature* **376**, 33–36 (1995).
21. Singer, W. & Gray, C. M. *Annu. Rev. Neurosci.* **18**, 555–586 (1995).
22. DeCharms, R. C. & Merzenich, M. M. *Nature* **381**, 610–613 (1996).
23. Sofky, W. R. & Koch, C. *J. Neurosci.* **13**, 334–350 (1993).
24. Markram, H., Lübke, J., Frotscher, M. & Sakmann, B. *Science* **275**, 213–215 (1997).
25. Montague, P. R., Dayan, P., Person, C. & Sejnowski, T. J. *Nature* **377**, 725–728 (1995).
26. Markram, H. & Tsodyks, M. *Nature* **382**, 807–810 (1996).
27. Abbott, L. F., Varela, J. A., Sen, K. & Nelson, S. B. *Science* **275**, 220–224 (1997).
28. Diorio, C., Hasler, P., Minch, B. A. & Mead, C. *IEEE Trans. Electron. Devices* **43**, 1972–1980 (1996).
29. Douglas, R. J., Mahowald, M. & Mead, C. *Annu. Rev. Neurosci.* **18**, 255–281 (1995).
30. Braitenberg, V. & Schüz, A. *Anatomy of the Cortex* (Springer, Berlin, 1991).