

edge that arc-accretion models are also fully consistent with all the known characteristics of the Arabian–Nubian shield.

That does not obscure the main advantage of a plume-driven crustal genesis model, which is that mantle plumes are a straightforward product of the Earth's heat (from whatever depth they originate), and should have been most common in the Archaean, becoming steadily less so with time. So this is a way of making crust that predicts a closer relationship between the heat engine and continental crust growth.

The intense crustal growth in the late Archaean and early Proterozoic was followed by generally smaller-scale pulses extending to the present day. So a plausible, but by no means established picture is one where a steady trickle of arc volcanism and accretion is added to major pulses of crust growth initiated by accretion of oceanic plateaux. □

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NEUROBIOLOGY

Synapses get smarter

Terrence J. Sejnowski

THE cerebral cortex has long been known to be important for learning and memory, but because of its daunting anatomical complexity it has not been studied as well as the hippocampus, an older and simpler structure. Techniques have improved and it is now possible to pick a pair of cells in a neocortical slice, record from them with whole-cell patch recording, and induce long-term potentiation (LTP) at the synaptic contacts between those cells with Hebbian pairing of presynaptic and postsynaptic action potentials¹.

On page 807 of this issue, Markram and Tsodyks² report that LTP strengthens the response to the first stimulus in a train of stimuli, as expected from hippocampal studies, but can also reduce synaptic responses to subsequent stimuli. This shows that synaptic activity at a cortical excitatory synapse cannot be adequately described by a single number like the strength or 'weight' that is often used in models of neural networks, nor can the effect of LTP be simply described as a strengthening of the synaptic weight. This observation has important consequences for the computational power of synapses in neural networks and the biophysical basis of synaptic plasticity. Synapses may be smarter than we had imagined.

Synaptic strengths are constantly being adjusted from moment to moment. In response to a pair of closely spaced stimuli, the response to the second could get larger or smaller than the first depending on the synapse and its previous history. Short-term facilitation and short-term depression to a train of stimuli occur on time scales ranging from tens of milliseconds to many seconds^{3,4}.

A decade ago, Karl Magleby concluded a review on synaptic plasticity with the prediction that "In addition to long-term changes in synaptic efficacy, which can be assessed with single test pulses, there may be other, more dynamic, long-term changes that can only be detected with patterned stimulation"⁵. Markram and

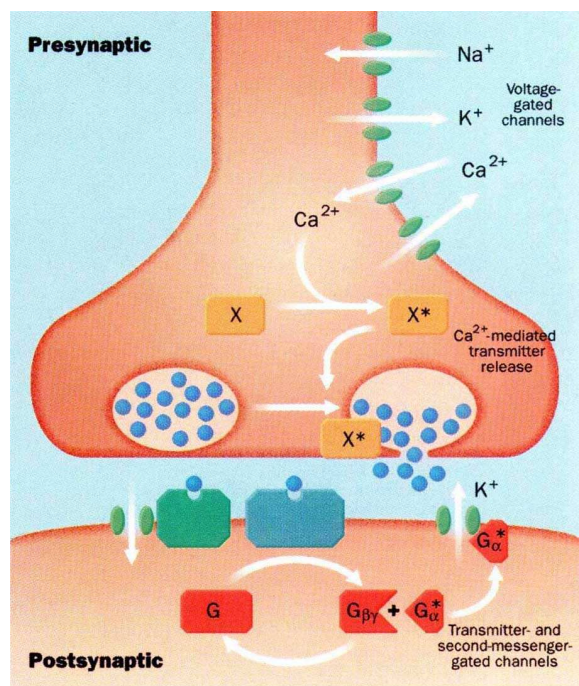
Tsodyks² have now examined long-term changes in short-term synaptic dynamics in neocortical slices and report that the rapidity of short-term depression is substantially and persistently enhanced following LTP.

Although it is possible to develop a phenomenological description of the rates at which short-term synaptic facilitation and depression occur⁵, we ultimately need to understand the subcellular mechanisms that are involved in synaptic plasticity. A cascade of intracellular events is triggered when calcium enters the presynaptic terminal following invasion by an action potential (see figure)⁶. There is a readily available pool of vesicles that can be mobilized within milliseconds⁷. Short-term depression at peripheral synapses can result from a reduced number of vesicles in the readily releasable pool. The events leading to transmitter release and vesicle recycling can be modelled by kinetic equations, and the rate constants in these equations may be subject to long-term modification⁸. The apparent change in the rate of the short-term depression could result from an increase in the probability of release and subsequent decrease in the population of readily releasable vesicles. These mechanisms make synapses dynamical systems in their own right.

The effects of short-term synaptic dynamics can be counterintuitive. For instance, the steady-state response of a postsynaptic cell to a train of stimuli is independent of firing rate above around 20 Hz (refs 2,

4). This occurs because short-term depression is inversely related to the firing rate, which cancels the term that is proportional to the firing rate. One consequence is that the postsynaptic neuron becomes more sensitive to changes in the firing rate especially when the baseline firing rate is high (L. F. Abbott, personal communication). The changes in short-term dynamics reported by Markram and Tsodyks following LTP would tend to make the cortical network even more sensitive to changes in inputs, because potentiating the response to the first stimulus and more rapidly depressing responses to subsequent stimuli shifts the impact of a train towards the onset of the response (H. Markram, personal communication). The actual impact of LTP *in vivo*, though, could be more complex because the inputs to cortical neurons are highly irregular⁹; when the same irregular train of stimuli is delivered before and after LTP, the responses to some spikes are potentiated, but others can be depressed².

During visual recognition of complex objects, changes in the event-related potential correlated with the category of the object can be registered 150 ms after presentation of a stimulus¹⁰. This is within the range of short-term dynamical changes in strengths of cortical synapses, so synaptic dynamics could be an essential compo-



Synapses are dynamical systems. Presynaptic mechanisms triggered by the entry of calcium into the presynaptic terminal release neurotransmitter molecules into the synaptic cleft, which bind to postsynaptic receptors, and change the conductance of the postsynaptic membrane. In the paper discussed here, Markram and Tsodyks² show that long-term changes in the short-term kinetic parameters governing these steps may lead to changes in the dynamics of synaptic efficacy. Further experiments will be needed to distinguish presynaptic mechanisms from dynamical changes that might also occur at the postsynaptic cell. (Modified from ref. 8.)

ment of object recognition¹¹. The long-term changes now observed in short-term depression, which are synapse specific, may be crucial to understanding the dynamics of memory¹². In neural networks with excitatory recurrent collaterals like those in the cerebral cortex, the positive feedback tends to amplify transient inputs (ref. 13 and C. van Vreeswijk, personal communication). But not all transients will be amplified equally, so only those that match the stored patterns will be filtered and their associations passed onto further stages of processing.

The results reported by Markram and Tsodyks raise various questions which should spur many new studies. What are the effects of LTP on the short-term dynamics at other cortical synapses, particularly those between excitatory and inhibitory cells? How do neuromodulators, which can also change short-term dynamics at synapses, interact with these long-term changes⁹? How does long-term depression affect short-term depression¹⁴? At synapses with low probabilities of release, short-term facilitation can be more prominent than short-term depression¹⁵. How does LTP affect short-term facilitation?

The answers will provide the foundation for approaching many issues in cortical processing, such as how cortical neurons in visual cortex are able to compute the direction of movement of visual stimuli¹⁶, and how novel temporal patterns of inputs are handled¹⁷ — issues that are at the heart of how the cerebral cortex allows us to react intelligently to the changing world. □

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1. Markram, H. & Sakmann, B. *Soc. Neurosci. Abstr.* **21**, 2007 (1995).
2. Markram, H. & Tsodyks, M. *Nature* **382**, 807–810 (1996).
3. Deuchars, J., West, D. C. & Thomson, A. M. *J. Physiol. (Lond.)* **478**, 423–435 (1994).
4. Nelson, S. B., Varela, J. A., Sen, K. & Abbott, L. F. *Soc. Neurosci. Abstr.* **22** (1996). <http://www.faseb.org/sfn96/>
5. Magleby, K. L. in *Synaptic Function* (eds Edelman, G. M. et al.) 21–56 (Wiley, New York, 1987).
6. Sudhof, T. C. *Nature* **375**, 645–653 (1995).
7. Rosenmund, C. & Stevens, C. F. *Neuron* **16**, 1197–1207 (1996).
8. Destexhe, A., Mainen, Z. F. & Sejnowski, T. J. *J. Comput. Neurosci.* **1**, 195–230 (1994).
9. Softky, W. R. & Koch, C. *J. Neurosci.* **13**, 334–350 (1993).
10. Thorpe, S., Fize, D. & Marlot, C. *Nature* **381**, 520–522 (1996).
11. von der Malsburg, C. in *Models of Neural Networks II* (eds Domany, E., van Hemmen, J. L. & Schulten, K.) 95–119 (Springer, Berlin, 1994).
12. Lisberger, S. G. & Sejnowski, T. J. *Nature* **360**, 159–161 (1992).
13. Tsodyks, M. V. & Sejnowski, T. J. *Network* **6**, 111–124 (1995).
14. Bear, M. F. & Malenka, R. C. *Curr. Opin. Neurobiol.* **4**, 389–399 (1994).
15. Stevens, C. F. & Wang, Y. *Neuron* **14**, 795–802 (1995).
16. Abbott, L. F., Sen, K., Varela, J. A. & Nelson, S. B. *Soc. Neurosci. Abstr.* **22** (1996). <http://www.faseb.org/sfn96/>
17. Buonomano, D. V. & Merzenich, M. M. *Science* **267**, 1028–1030 (1995).

Has the fat lady sung?

David Bishop

THIS year is the tenth anniversary of the discovery of high-temperature superconductors. To those of us who have worked on the problem for the past decade, it has been an object lesson in humility. I am reminded of the old joke that you should be careful about what you wish for, as it might come true. If asked ten years ago, most solid-state physicists, including me, might have wished for a liquid-nitrogen-temperature superconductor, believing that it would revolutionize modern electronic technology and society along with it. Just such a class of materials was indeed discovered ten years ago by Bednorz and Müller¹, with superconducting transition temperatures now twice the boiling point of liquid nitrogen. But to the best of my knowledge, a revolution has not yet occurred. Where did we go wrong?

The answer lies partially in the pathological behaviour of the magnetic vortices that penetrate these compounds. How these vortices can misbehave is clearly demonstrated in an experiment described

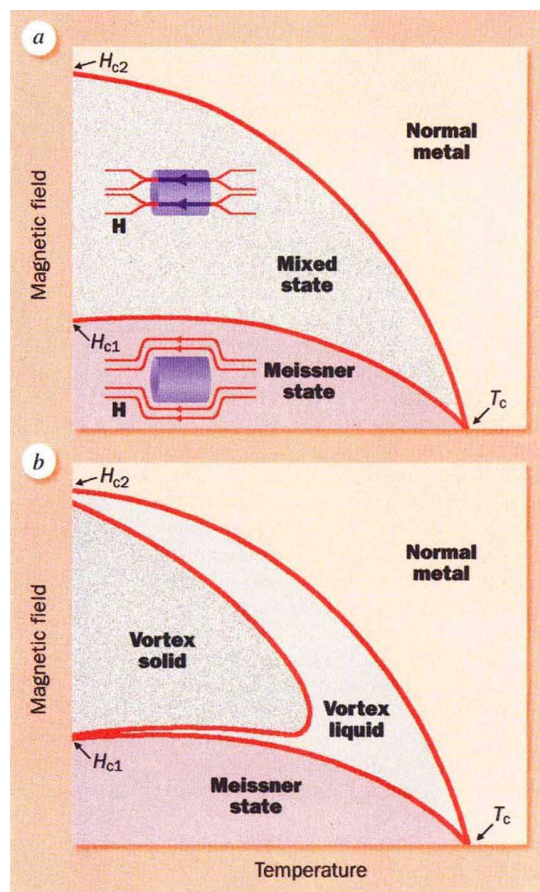
on page 791 of this issue² by Schilling and colleagues. They have confirmed that the magnetic vortex lattice is able to melt into a new state of matter called a vortex liquid. The presence of this liquid means that even modest magnetic fields can cause these materials to be more resistive to the flow of electrical currents than an ordinary piece of copper wire. Therefore, no revolution, or at least one that is going to take a little longer to roll out.

To understand why this happens, one needs to think about how superconductors respond to an applied magnetic field, and about the two classes of superconductor. In general, the superconducting state is inimical to magnetic fields and develops a number of responses to minimize the amount of magnetic flux in its interior. At low fields, below a critical field called H_{c1} , all the flux can be excluded from the interior of a sample — this is the Meissner state. Above a second critical field, H_{c2} , the superconducting state is destroyed and the normal metal is regained.

The first class of superconducting materials, called type I, has $H_{c1}=H_{c2}$. In equilibrium, the field is either totally expelled or superconductivity is completely destroyed. In general, type-I materials are low-field superconductors and are not useful.

All of the technologically important superconductors, including the high- T_c materials, belong to the second class, type II. In these materials $H_{c2}>H_{c1}$, and at intermediate values of the applied field, between H_{c1} and H_{c2} , the field can penetrate but not completely or uniformly (a in the figure). Instead it enters the sample in the form of quantized bundles of magnetic flux called flux lines. The amount of field in each flux line is exactly the same, so the density of lines changes with the applied field. These lines of magnetic flux arrange themselves into a triangular lattice. In the absence of defects this lattice will be a perfectly arranged solid — a solid in the same sense that the chair you are sitting on is a solid: it has a finite shear modulus, whereas liquids and gases have zero shear modulus.

Soon after the high- T_c



a, Phase diagram of a low-temperature type-II superconductor, showing penetration by magnetic vortices in the 'mixed' state. b, High-temperature type-II superconductors have another state, the vortex liquid, which gives them a finite resistance, destroying their usefulness in this region.