Repeated inefficient measurements on a single quantum system are easily described in the modern approach to quantum measurement that has its roots in the efforts to detect gravitational waves. In that setting, the idea of a quantum nondemolition measurement (QND) was developed. A sequence of QND measurements leads to a near-deterministic sequence of results. The noise added by a measurement does not dynamically feed back to the measured variable. Constants of the motion must be used as QND variables, and they need to remain constants of the motion when the measurement probe is coupled into the system. By contrast, in a non-QND experiment, any attempt to measure the position of a free particle very accurately would introduce a great deal of noise into its momentum. Changes in momentum couple back into the particle's position, so this noise contaminates future measurements of position.

The quantum control of single quantum systems requires three capabilities: state preparation, unitary control of the state, and quantum-limited measurement. In the case of NV diamond, the target quantum system is either a single electron or a nuclear spin. Usually, state preparation is achieved by passively cooling a system so that it relaxes to a ground state from which thermal excitation is improbable. Nuclear and electron spins in diamond can be polarized and remain so for sufficiently long times for these experiments, even at room temperature. Unitary control ensures that any operations on the system do not erase information about the quantum state.

A quantum-limited measurement is one that is efficient; that is, the signal-to-noise ratio is primarily determined by the quantum noise in the measured system itself and does not need many repeated trials to average out the noise added by the measurement apparatus—it yields a result in a "single shot." Until now, however, there has been no way to make efficient quantum measurements on the spins in a single NV center. Both of the experiments of (*4*, *5*) implement a QND measurement of a single spin—a nuclear spin in the case of Neumann *et al*., and an electron spin in the case of Buckley *et al*.

In the Neumann *et al*. experiment, the measured system is a single nuclear spin of nitrogen at an NV center, while the first stage of the measurement probe is the associated electron spin (see the figure, panel A). When the NV center is excited by a microwave pulse, the nuclear spin can flip the associated NV electron spin, conditional on the nuclear spin being spin-down, while remaining unchanged itself. The electron spin is read out optically by means of spin-dependent fluorescence, very much like the earliest experiments on quantum jumps in ion traps. The Neumann *et al*. experiment approaches an efficient measurement.

In the Buckley *et al*. study, the measured system is the electron spin of the NV, and the probe is the polarization of a laser field (a Faraday effect; see the figure, panel B). This experiment measures the electron spin directly and also uses spin-dependent fluorescence. Their approach has the advantage of enabling very accurate characterization of the nature of the interaction between the spin and the light. However, unwanted interactions in the diamond crystal cause this spin not to be a strict QND variable, so their measurement is not efficient and causes unwanted decoherence. The Buckley *et al*. experiment required tens of thousands of repeated samplings, and the signature of unwanted decoherence is the decay of a coherent oscillation signal created by Hahn microwave pulses. In the case of the efficient measurement of Neumann *et al*., the signature of such unwanted interactions appear as "quantum jumps" in the observed fluorescence signal in a single trial.

These two experiments bode well for future quantum computing schemes that use NV diamond, but promise a more immediate spin-off for quantum sensing applications such as magnetometry. This capability could have an impact in biology and chemistry, especially if NV centers in diamond are used as nanocrystal probes (*7*). These experiments point to a future quantum sensing technology.

References

1. T. Sauter *et al*., *Phys. Rev. Lett.* **57**, 1696 (1986).
2. M. Brune *et al*., *Phys. Rev. Lett.* **65**, 976 (1990).
3. R. McDermott *et al*., *Science* **307**, 1299 (2005).
4. P. Neumann *et al*., *Science* **329**, 542 (2010) 10.1126/science.1189075.
5. B. B. Buckley *et al*., *Science* **330**, 1212 (2010); 10.1126/science.1196436.
6. E. Schrödinger, *The Interpretation of Quantum Mechanics* (Ox Bow Press, Woodbridge, CT, 1995).
7. C. Bradac *et al*., *Nat. Nanotechnol.* **5**, 345 (2010).

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NEUROSCIENCE

Lynx for Braking Plasticity

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Knocking out the *Lynx1* gene restores plasticity in the visual cortex of adult mice.

The juvenile brain exhibits a high capacity for plasticity and repair that is severely restricted in adulthood. In young mammals, for instance, classic experiments have shown that closing one eye for several days (monocular deprivation) leads visual cortex neurons to shift their responses toward sensory inputs originating from the other, nondeprived eye (*1*). In adults, however, such plasticity in ocular dominance, while not eliminated, is strongly restricted. This knowledge gap has medical implications, because the restoration of juvenile plasticity in injured or dysfunctional adults has the potential to allow recovery of neurological performance. On page 1238 of this issue, Morishita *et al*. (*2*) identify one brake on visual cortex plasticity in adults: Lynx1, a protein that inhibits nicotinic acetylcholine receptors (nAChRs). By eliminating the gene that expresses Lynx1 in mice, the researchers were able to create adult animals that exhibited visual cortex plasticity similar to that exhibited by juveniles.

Nicotinic receptors are present throughout the nervous system. They form "channels" that enable small ions to pass through neuronal membranes, and have "gates" that are opened by acetylcholine, a common neurotransmitter. Lynx1 is similar to snake venom proteins that inhibit nicotinic receptors, and deleting the *Lynx1* gene is known to increase cholinergic neurotransmission (the activity of acetylcholine) (*3*). Morishita *et al*. noted that, in juvenile mice, Lynx1 expression increases as the critical period for visual cortex plasticity closes. To better understand the role of Lynx1, they created knockout mice that lacked the *Lynx1* gene. Then, they used electrophysiological methods to measure the effect of monocular deprivation on neocortical ocular dominance (the eye preference of single cortical neurons) in both the knockout mice and wild-type mice that still expressed Lynx1. After 4 days of monocular deprivation, 60-day-old adult knockout mice exhibited plasticity that matched that of 30-day-old juvenile wild-type mice; in contrast, adult wild-type mice did not show such plasticity. Subsequent experiments with drugs that blocked nicotinic receptors produced results

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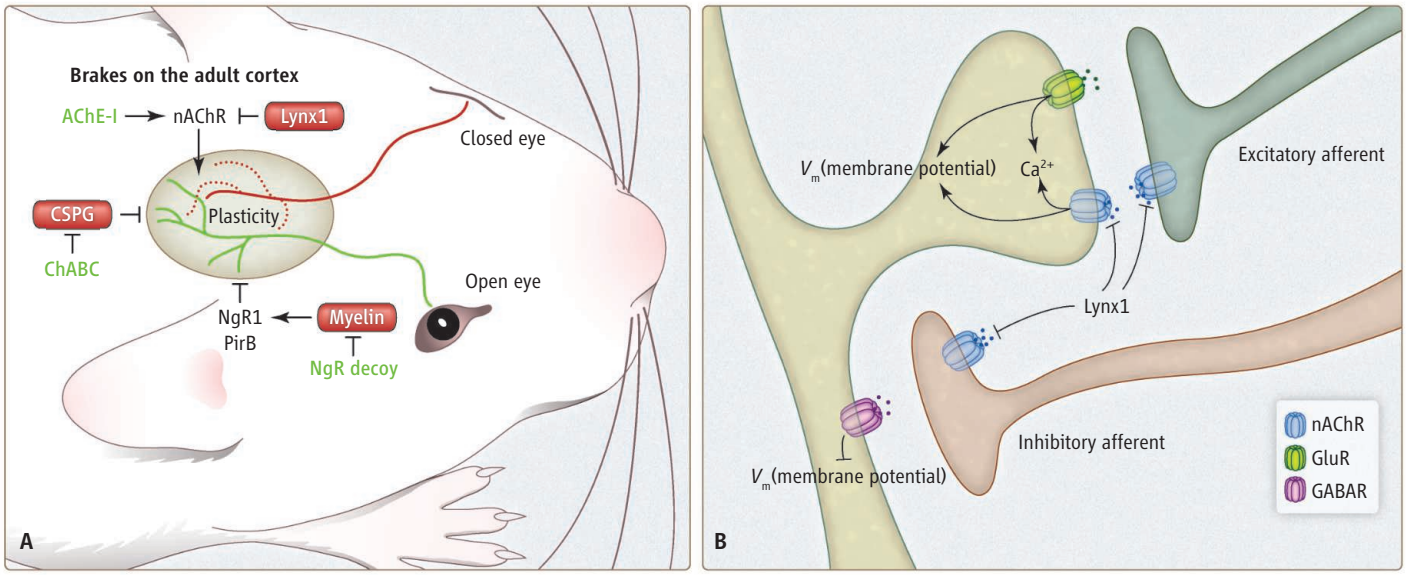

Easing the brakes on plasticity. (**A**) In juvenile wild-type mice, closing one eye for several days causes the loss of projections on the inactive pathway from the retina to the visual cortex (red lines for this polysynaptic pathway) and gains on the active pathway (green). In the adult, several pathways function as brakes on this plasticity in ocular dominance. Lynx1 inhibits nAChRs. Myelin inhibitors or CSPG-rich perineuronal nets also prevent rearrangement (*11*, *12*). Specific interventions can remove each of these brakes, including acetylcholinesterase inhibitors (AChE-I), NgR decoy protein, and chondroitinase (ChABC). (**B**) Nicotinic receptors are found on both pre- and postsynaptic elements of excitatory and inhibitory cortical neurons. Regulation of nAChRs by Lynx1 likely influences the balance of synaptic excitation and inhibition, and calcium influx through nAChRs may contribute to biochemical signaling pathways.

that were consistent with the hypothesis that Lynx1 acts by inhibiting nAChRs.

Previous studies have shown that blocking cholinergic signaling in the juvenile visual cortex during the critical period inhibits ocular dominance plasticity (*4*). In adults, enhanced cholinergic activity can promote activity-dependent plasticity in both auditory (*5*) and motor (*6*) regions of the brain. Morishita *et al*., however, provide the first demonstration that acetylcholine signaling serves as a brake on adult visual cortex plasticity.

Other pathways have been implicated in preventing adult plasticity. Myelin proteins can act via the receptors NgR1 and/or PirB to inhibit the growth of neurites (*7*–*9*). Both NgR1 and PirB limit adult visual cortex plasticity to an extent similar to that shown for Lynx1 (*10*, *11*). In addition, the perineuronal nets that surround inhibitory interneurons are rich in chondroitin sulfate proteoglycans (CSPGs). The development of these nets parallels both Lynx1 expression and the development of intracortical myelin sheaths, and CSPGs function as an additional brake on plasticity (*12*). Specifically, digesting CSPGs reestablishes ocular dominance plasticity in the adult brain (*12*). However, Lynx1 appears to be unique in its regulation of neurotransmission, in contrast to the anatomical role proposed for myelin and CSPGs.

Although inhibition of nicotinic signaling appears to be the primary mechanism by which Lynx1 regulates cortical plasticity, the specific cellular targets are not yet defined. Nicotinic receptors are expressed on axonal terminals and postsynaptic membranes of both excitatory and inhibitory cells. Their activation likely alters the balance of synaptic excitation and inhibition, thereby changing the complex patterns of neuronal activity evoked by sensory inputs. Many nAChRs exhibit permeability to calcium ions, enabling them to contribute to calcium-dependent signaling pathways that may regulate synaptic plasticity. Lynx1 expression is also observed in subsets of inhibitory neurons (*2*), although it is not clear if this site is relevant for control of plasticity.

The mechanism of ocular dominance plasticity also is unclear. Given the persistent nature of cortical plasticity and the anatomical actions of NgR1, PirB, and CSPGs, Lynx1 and nAChR activation might modulate some aspect of intracerebral synaptic connectivity. Future studies will be required to elucidate whether this modulation involves changes in axonal branching, the formation or elimination of synaptic contacts, or simple changes in the efficacy of existing synapses. It also remains unclear whether nAChR function, myelin, and CSPGs act independently or cooperatively in influencing plasticity.

There is strong reason to believe that increasing adult brain plasticity can support neurologic recovery in a range of conditions (*13*). Morishita *et al*. examined how mice that experienced 2 weeks of juvenile monocular deprivation recovered from amblyopia (loss of visual acuity due to disuse). In adult mice lacking Lynx1, simply reopening the closed eye caused electrophysiological signals to return to patterns indicating normal acuity. They obtained a similar degree of recovery from amblyopia in wild-type mice by administering an acetylcholinesterase inhibitor that increased acetylcholine transmission. Similar recovery through plasticity may underlie the beneficial effects of digesting CSPG or blocking NgR after spinal cord injury or stroke (*14*–*16*), and it will be of great interest to assess whether Lynx1 deletion or facilitation of nAChR activity enhances recovery from such neurological damage.

References and Notes

1. T. K. Hensch, *Annu. Rev. Neurosci.* **27**, 549 (2004).
2. H. Morishita *et al*., *Science* **330**, 1238 (2010); 10.1126/science.1195320.
3. J. M. Miwa *et al*., *Neuron* **23**, 105 (1999).
4. M. F. Bear, W. Singer, *Nature* **320**, 172 (1986).
5. R. C. Froemke *et al*., *Nature* **450**, 425 (2007).
6. D. Ramanathan *et al*., *J. Neurosci.* **29**, 5992 (2009).
7. J. K. Atwal *et al*., *Science* **322**, 967 (2008).
8. A. E. Fournier *et al*., *Nature* **409**, 341 (2001).
9. W. B. Cafferty, S. M. Strittmatter, *J. Neurosci.* **26**, 12242 (2006).
10. J. Syken *et al*., *Science* **313**, 1795 (2006).
11. A. W. McGee *et al*., *Science* **309**, 2222 (2005).
12. T. Pizzorusso *et al*., *Science* **298**, 1248 (2002).
13. W. B. Cafferty *et al*., *Trends Neurosci.* **31**, 215 (2008).
14. E. J. Bradbury *et al*., *Nature* **416**, 636 (2002).
15. X. Wang *et al*., *Ann. Neurol.* **60**, 540 (2006).
16. J. K. Lee, J. E. Kim, M. Sivula, S. M. Strittmatter, *J. Neurosci.* **24**, 6209 (2004).

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