

Figure 1 | Converting wavefronts. Grillo *et al.*⁶ have designed a blazed phase hologram that has a sawtooth-thickness structure. The device converts an electron beam in which the wavefronts form planes into a beam with a wave crest that rotates about its axis of propagation, tracing out a helical wavefront.

But there are caveats to this approach. Obtaining bright electron vortex beams by this method is challenging because it requires the thickness profile of the blazed phase hologram to be controlled with nanometre-level accuracy. Also, part of the electron beam passing through the hologram will inevitably lose energy through a process called inelastic scattering, which leads to a non-vortex background signal. For beam diagnostics, this inelastic component of the beam can be removed using energy-filtering methods. However, the use of purely phase-shifting devices, such as those that exploit an effect known as optical aberration⁸, instead of a blazed phase hologram, might be preferable for applications such as spectroscopy based on the chirality (handedness) of the vortex beams.

The helical form of an electron vortex beam's wavefront means that the exact phase of the beam is ill-defined at its centre, resulting in a doughnut-shaped beam-intensity structure that can be less than 1 nanometre in diameter⁹. This length scale is about 1,000 times smaller than that of existing optical vortex beams, which are used to trap and move micrometre-sized particles. Bright electron vortex beams produced using Grillo and colleagues' method may therefore allow nanoparticles and even individual atoms to be easily manipulated. In fact, existing, rather 'dim' electron vortex beams have already been used to transfer orbital angular momentum from the beams to nanoparticles^{3,10,11}.

The authors' method will also allow the production of bright electron vortex beams of very high orbital angular momentum, which will enable the investigation of subtle quantum effects associated with the giant magnetic moments of such beams. Finally, owing to the beams' intrinsic chirality, intense electron vortex beams could be used for the spectroscopic study of chiral materials^{3,12},

such as magnetic materials, certain polymers and biological macromolecules. The future of electron vortex beams is undoubtedly getting brighter. ■

Jun Yuan is in the Department of Physics, University of York, York YO10 5DD, UK. e-mail: jun.yuan@york.ac.uk

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NEUROSCIENCE

Feedback throttled down for smooth moves

A group of regulatory neurons in the spinal cord has been found to reduce sensory feedback to muscles in mice. Removal of these neurons leads to repetitive limb oscillations during reaching. [SEE ARTICLE P.43](#)

STEPHEN H. SCOTT & FRÉDÉRIC CREVECOEUR

Sensory signals from our limbs allow us to interpret a wealth of information, from perceiving the objects we touch to correcting errors during movement. But despite their importance, the signals are turned down (throttled down) when we move¹. How does this happen, and why? On page 43 of this issue, Fink *et al.*² report that, in mice, the signals are throttled down by a set of neurons in the spinal cord, and that removal of these neurons causes the animals' limbs to oscillate

dramatically whenever they reach for food.

Although motor control involves many pathways and circuits in the spinal cord and brain, Fink and colleagues' study focused on the simplest: the feedback between muscle sensory afferent neurons (which carry impulses from the muscle towards the spinal cord) and efferent motor neurons (which carry signals from the spinal cord to the muscles; Fig. 1a). Your doctor examines this pathway when she or he taps your tendon: contact between the hammer and the tendon excites sensory afferents in the stretched muscle, and the impulses are then transferred from the axon terminal

at the end of the afferent to the motor neuron, across the sensory–motor synapse — the junction between the two neurons. The feedback leads to muscle activity and a flinching movement at the joint.

Most neural feedback pathways involve intermediary neurons, called interneurons, which form connections with the motor neurons after the synapse, and permit substantial processing of signals. But the direct projection from sensory afferents to motor neurons precludes such processing. Instead, the activity of these synapses (and other afferent synapses in the spinal cord) is regulated before the synapse. In these cases, the axon terminal of the sensory afferent is contacted by the terminal of another axon, from a subgroup of GABAergic interneurons — named for the γ -aminobutyric acid (GABA) neurotransmitter they release. The ‘axo-axonic’ synapse at this junction can inhibit the afferent axon terminal, diminishing the amount of neurotransmitter released across the sensory–motor synapse (Fig. 1b). This reduces the feedback gain: the ratio between sensory-afferent input and motor-neuron output.

Presynaptic inhibition of sensory signals has been shown to correlate with voluntary motor actions, such as reaching for objects^{1,3}. The mechanism is thought to filter incoming sensory information and help the brain to extract relevant information¹⁴. However, why sensory feedback to control movement should also be reduced at this time remains unclear.

Unravelling this mystery required several steps. First, Fink *et al.* used a strain of mice designed to enable labelling of a subgroup of GABAergic interneurons in the spinal cord to make the interneurons express the proteins Channelrhodopsin-2 and yellow fluorescent protein. Examination of how yellow fluorescent protein was distributed in the spinal cord showed that these neurons almost exclusively create axo-axonic synapses on afferent axon terminals. Next, the researchers took advantage of the fact that Channelrhodopsin-2 causes the interneurons to fire when exposed to light. Light activation reduced transmission across the sensory–motor synapse, demonstrating that this specific group of GABAergic neurons generates presynaptic inhibition.

Finally, Fink and colleagues removed the GABAergic interneurons from the motor circuits of the mice, and analysed motor function in the mutants. This required another genetic trick — the authors forced the neurons to express a toxin-receptor protein, which killed the neurons when the toxin was injected into the spinal cord. The mice could still walk after this treatment, even across a ladder, and they could also maintain stationary body postures. However, whenever they reached towards food, their forelimbs oscillated dramatically. This suggests that presynaptic inhibition has a key role in maintaining smooth voluntary movements.

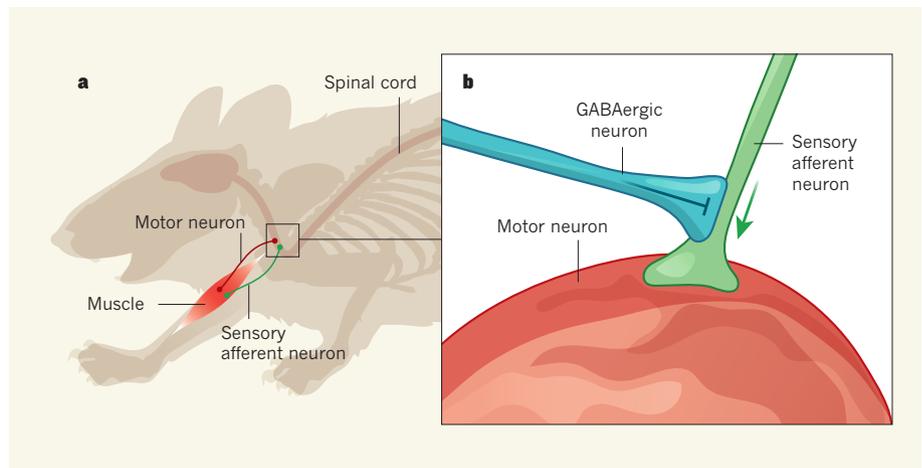


Figure 1 | Controlling reaching movements in mice. **a**, When muscle is stretched, sensory afferent neurons are stimulated, and impulses travel towards the spinal cord. A sensory–motor feedback pathway causes motor neurons to transmit impulses back to the muscles, generating muscle activity and movement at the joint. **b**, A close-up of the sensory–motor synapse, where the end of the afferent neuron (the axon terminal) contacts the motor neuron. Fink *et al.*² report that a subtype of regulatory GABAergic interneuron in the spinal cord contacts the afferent axon terminal and, when active, diminishes the amount of neurotransmitter molecules released across the sensory–motor synapse, thereby inhibiting feedback to motor neurons.

Why does the forelimb oscillate when presynaptic inhibition is removed? Oscillations occurred during reaching, but not when animals were maintaining a fixed posture or walking, suggesting that there is something special about voluntary movement that suddenly makes feedback to motor neurons too high. Fink and co-workers suggest a simple interpretation, based on a pair of opposing muscles pulling at a joint: when feedback is too strong they become reciprocally active, oscillating the limb.

There are, however, other interpretations of this result that deserve attention. For instance, when muscles are forced to lengthen, they initially generate a large resistive force (high stiffness), which quickly recedes as lengthening proceeds, leaving a smaller resistive force (low stiffness)^{5,6}. The same is true for muscle shortening during movement⁷. These muscle properties influence feedback control, so the feedback gains that provide smooth corrections when animals are maintaining a fixed posture could potentially generate oscillations during voluntary movement. Alternatively, oscillations may arise during voluntary movement because of an imbalance between spinal and brain feedback. In any case, presynaptic inhibition seems to throttle down spinal feedback to ensure smooth movement — a clever biological trick!

The need to reduce sensory feedback during movement seems to be at odds with a growing body of evidence⁸ showing its powerful contribution to the control of voluntary movement. This apparent paradox is reconciled by evidence^{9,10} suggesting that the brain supports more-complex sensorimotor processing than the spinal cord, so high-gain control is processed through brain pathways. Faster,

direct spinal feedback may be used in some behaviours, but in others it must be reduced through presynaptic inhibition.

The past few years have seen an explosion of molecular and genetic techniques that have allowed us to identify different types of neuron, artificially modify their activity and remove them from neural circuits. For example, removal of the V2a spinal neuron, which projects to motor neurons and indirectly to the cerebellum, impairs reaching, but does not generate large oscillations¹¹. Together, these techniques provide a powerful set of tools to tease apart spinal (and brain) circuits, leading to a more-complete understanding of how these distributed networks support smooth and highly flexible motor actions. ■

Stephen H. Scott and Frédéric Crevecoeur are in the Department of Biomedical and Molecular Sciences, Centre for Neuroscience Studies, Queen's University, Kingston, Ontario K7L 3N6, Canada.
e-mail: steve.scott@queensu.ca

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