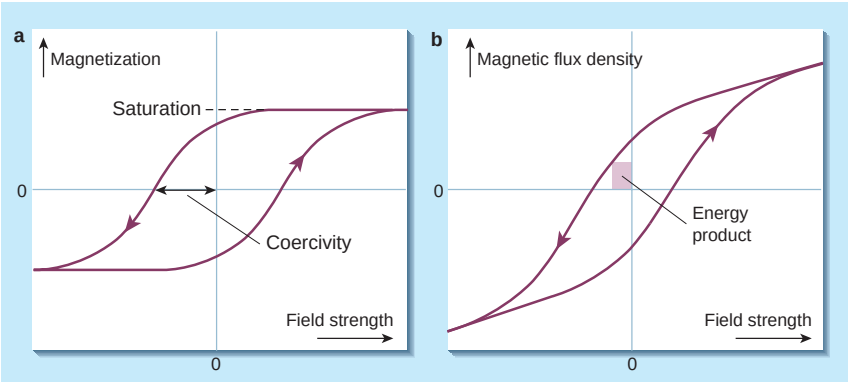

Figure 1 **Typical hysteresis loops for a permanent magnet. The response of a magnet to an applied field is shown in terms of its magnetization (**a**) and the magnetic induction or flux density (**b**). If the applied field strength is increased until the magnetization saturates, and then reduced, the variation of the magnetization and the flux density traces a hysteresis loop. The coercivity of a magnet is defined as shown in** a**, and is a factor in the figure of merit of permanent magnets, known as the energy product (shaded area in** b**).**

potential for making three-dimensional magnets with high-energy product. When FePt and Fe_3O_4 nanoparticles of similar sizes (about 4 nm) are mixed and allowed to self-organize, they form structures which, when heated and chemically reduced, form 5-nm-scale homogeneous mixtures of a hard tetragonal FePt phase and a high-magnetization soft Fe_3Pt phase. The admixture of Pt in the Fe_3Pt nanograins results from sintering at a temperature of 650 °C, which is used to induce the phase transition from disordered FePt to ordered tetragonal FePt. The energy product of the two-phase material is 20.1 MGOe — considerably higher than the value expected for isotropic FePt particles alone (13 MGOe).

There are still many practical challenges to be faced if energy products approaching the magic number of 144 MGOe are to be achieved. For instance, ways of compressing the two-phase material into a high-density compact must be explored, as well as improved alignment of the axes of the hard grains to exploit the full magnetic potential of the nanocomposite system. Nevertheless, the work of Zeng *et al.*[1] is an exciting development that shows the way to making strong magnets for practical applications. ■

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Neuroscience

How neurons compute direction

Peter Sterling

Certain retinal neurons fire specifically in response to stimuli moving in one direction. This apparently occurs when branches of an upstream nerve cell respond asymmetrically, and link asymmetrically to the firing retinal neuron.

Many of the nerve cells associated with vision respond asymmetrically to motion — they fire strongly when an object moves in one direction (the 'preferred' direction), but weakly or not at all when the object moves the other way (in the 'null' direction). This startling property is displayed by neurons in the cerebral cortex, and by certain neurons in the retina (ganglion cells) that relay visual information to lower brain centres concerned with eye movements. Because retinal neuronal circuits are simpler and more experimentally accessible than cortical circuits, almost 40 years have been devoted to learning how they compute directional selectivity. Three new papers[1–3], including one on page 411 of this issue, seem to have almost solved this maddening puzzle.

Barlow and Levick[4] were the first to identify the basic computational process (Fig. 1a, overleaf). Studying the directionally selective ganglion cell in the intact eye of a rabbit, they flashed two slits of light, either alone or separated in space and time, to simulate motion. When motion was simulated in the preferred direction, by the sequence A then B, slit B evoked more firing (the cell was more excited) than when it was presented alone. When motion was simulated in the null direction, by the sequence B then A, slit A evoked less firing than when presented alone (this is inhibition). This led to a simple suggestion: excitation evoked by motion in the preferred direction must reach the ganglion cell before inhibition can cancel it; and inhibition evoked by motion in the null direction must arrive before excitation and cancel it. But how might this occur?

Various clues were gradually pieced together. First, the directionally selective ganglion cell proved to be identifiable by its characteristic branching pattern[5]. Second, these branches were found to closely intertwine with those of a special type of neighbouring neuron, named the starburst cell[6] (for obvious reasons; see Fig. 1c). And third, the starburst cell was discovered to release the inhibitory neurotransmitter GABA[7], which is essential for directional selectivity[8] — all of which suggested some role for the starburst cell in computing direction.

Yet these findings provided little clue to directional selectivity, because both starburst and ganglion cells branch out symmetrically from their centres, and a stimulus swept across a starburst neuron evokes the same response in all directions[9]. Furthermore, the heroic laser-induced ablation of most starburst neurons on the ganglion cell's null side (the side first stimulated by motion in the null direction) failed to affect directional selectivity[10]. Thus, evidence seemed to be accumulating against a specific role for starburst cells in computing direction. But when Yoshida *et al.*[11] used an immunotoxin to ablate all starburst cells, directional selectivity was abolished. This revived the idea that starburst cells are essential.

Attention then turned to a fine-scale asymmetry of the starburst cell. This neuron receives excitatory inputs all along its branches. But its outputs occur only near the tips[6] (Fig. 1). This led Borg-Graham and Grzywacz[12] to predict an asymmetry of neurotransmitter release from starburst cells — more transmitter should be released after a stimulus moving outward along a branch than after one moving inward. This would imply that individual branches can serve as distinct computational units. Also, Vaney *et al.*[13] predicted that starburst branches pointing in opposite directions might connect to ganglion cells with opposite preferred directions. If both predictions were true, directional selectivity could be explained.

To test whether starburst branches

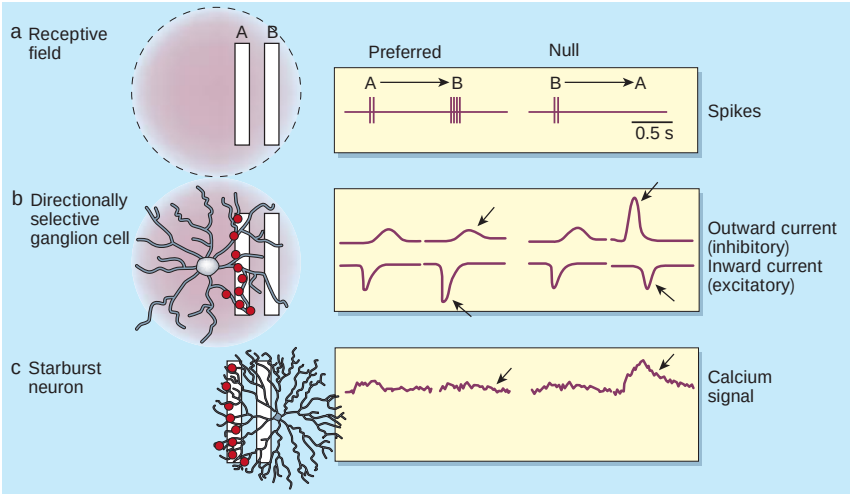

Figure 1 **Directional selectivity in the visual system.** a, **Barlow and Levick[4], recording spikes from a retinal ganglion cell, simulated motion by flashing slits successively. The preferred sequence (A then B) evoked greater firing in response to B. The null sequence (B then A) evoked few or no spikes to A.** b, **Fried *et al.*[3] show that, with the preferred sequence, an excitatory input to the ganglion cell starts earlier and rises higher than an inhibitory input. With the null sequence, the inhibitory input starts earlier and rises higher than the excitatory input. The excitatory input is probably suppressed upstream of the ganglion cell.** c, **Euler *et al.*[1] suggest the cause of enhanced inhibition and reduced excitation in response to the null sequence. They show that the preferred sequence, stimulating a starburst cell, evokes no calcium influx at the sites where this cell releases neurotransmitter (red dots). But the null sequence evokes a large calcium influx, which leads to release of inhibitory transmitter (GABA) at these sites. The sites contact branches of the ganglion neuron (red dots in** b**) and thus deliver GABA to that neuron asymmetrically.**

operate independently was a difficult task. Electrical currents are normally recorded through a microelectrode attached by suction to the plump cell body, but this integrates currents from all the branches. Yet it is impossible to attach an electrode to just one gossamer-fine branch. Euler and colleagues[1] circumvented this problem by recording responses of single branches optically. Viewing the retina on the stage of a two-photon microscope, they injected a starburst cell body with an indicator dye that diffused throughout the cell. This dye can be excited by coincident, infrared photons to fluoresce in the presence of calcium; thus, whenever calcium levels fluctuate, either spontaneously or after a stimulus, changes in fluorescence can be localized to specific branches.

Euler *et al.* found that spontaneous calcium fluctuations occur in each branch independently of its neighbours. Furthermore, a 'pie-wedge' light stimulus over one sector of the branches evoked a calcium rise strictly in that sector, especially at the output sites. Finally, a stimulus moving outward along a branch did evoke a larger response (in terms of calcium rise) than a stimulus moving inward (Fig. 1c). Because calcium enters via voltage-gated ion channels, its rise in one branch probably reflects depolarization spreading outward along that branch, and the calcium induces neurotransmitter release. Euler *et al.* conclude that this could be the source of directional selectivity — if indeed starburst branches connect asymmetrically to ganglion cells.

Fried *et al.*[3] advance both points with new, technically difficult electrical recordings. The technology of the 1960s prevented Barlow and Levick[4] from observing patterns of excitation and inhibition directly. They could only infer these patterns retrospectively — after excitatory and inhibitory events had been integrated at the ganglion cell's output. But Fried *et al.*[3] and Taylor and Vaney[2] could 'clamp' a cell's voltage at specific levels, and so directly record excitatory and inhibitory currents. They found that the excitatory current is greater in the preferred direction than in the null, and vice versa for the inhibitory current (Fig. 1b). In short, both inputs were themselves directionally selective.

Next, Fried *et al.* showed that slits flashed in the null sequence (B then A) on the null side of the ganglion cell, but well beyond its branches (Fig. 1b), evoke a strong inhibitory current. This would strongly depolarize the tips of starburst branches that reach out towards the ganglion cell, implying that it is their depolarization that causes the inhibitory current. This same sequence and location also reduced the excitatory current evoked by stimuli from the preferred direction, presumably by suppressing release of an excitatory neurotransmitter (presynaptic inhibition). Finally, in a very difficult experiment, Fried *et al.* recorded from a ganglion cell while electrically stimulating a starburst cell whose branches overlapped it. When the starburst cell was on the ganglion cell's null side, an inhibitory current was observed in the ganglion cell, and the two cells' branches were seen by confocal microscopy to closely entwine. But when the starburst cell was on the ganglion cell's preferred side, electrical stimulation did not affect the ganglion cell, and their branches intersected but did not entwine.

If this last point holds up (only three pairs of each type were studied), the basic mechanisms for directional selectivity would be explained. A stimulus on the ganglion cell's null side and moving in its null direction depolarizes starburst branches that point in that direction. These release GABA onto the ganglion cell and also onto its excitatory inputs. So, as Barlow and Levick[4] predicted, inhibition would be evoked before excitation reached the ganglion cell branches; and the inhibition would also reduce excitation from the null direction. Similarly, a stimulus on the ganglion cell's preferred side and moving in its preferred direction also depolarizes starburst branches that point in that direction. These starburst branches would also release GABA; however, they do not connect to the ganglion cell in question, but to one with the opposite preferred direction.

All in all, these three papers[1–3] represent a major intellectual and technical triumph. Yet it would be premature to dismantle the cottage industry that this problem has spawned, because some fascinating questions remain. For example, precisely what biophysical mechanism causes asymmetrical neurotransmitter release by starburst branches? Why is excitation by acetylcholine, another starburst-cell neurotransmitter[7], not observed in response to the stimuli that trigger GABA release? Finally, by what developmental trick do ganglion and starburst neurons manage to connect asymmetrically? ■

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