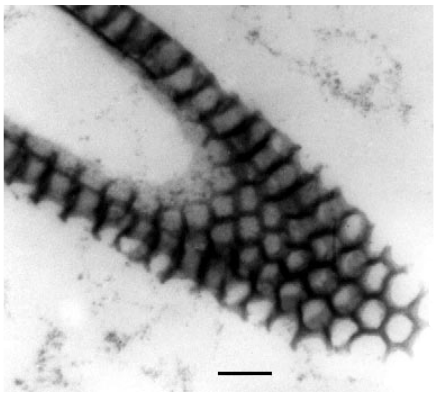

Figure 2 **Transmission electron micrograph of part of the bacterium *Leptothrix*, showing the patterned mineralized coat composed of amorphous iron hydroxide[10]. (Photograph by Z. Mason, reproduced from ref. 11; scale bar is 200 nm.)**

different crystal planes, and hence in their having different orientations. The number of crystals that nucleate at a site can also be controlled.

The next challenge is to grow the crystals in such a way as to control their shape and to merge them into a ceramic-like continuum. A step in that direction was taken by Xu *et al.*[8], who, again taking a cue from biology, grew an array of calcite crystals under a monolayer by first forming a continuous precursor phase of amorphous calcium carbonate. Another aim is to achieve nanometre-scale patterning. Douglas and Clark[9] used a biologically produced nanoscale template, namely the crystalline proteinaceous surface layer (or S-layer) of certain bacteria, for lithography. Individual protein complexes of ferritin were then selectively self-assembled onto the metal-coated template. Some bacteria, not surprisingly, can do it all by themselves with a precision of a few nanometres (Fig. 2).

The ultimate goal of many studies in this field is to produce nanometre-scale patterned crystalline materials for semiconductors, sophisticated ceramics, electro-optic materials and so on. The advances made over the past few years leave little doubt that this goal will, at least in part, be reached. Another benefit is that these studies are pointing the way to a better understanding of the biological processes that often inspired them in the first place. The experiments of Aizenberg *et al.*[1], for example, highlight the importance of directed diffusion at interfaces — a parameter that has not been sufficiently appreciated in work on the mechanisms of controlled biological crystal formation.

One day, diffusion control may even help solve health problems. Calcified crystal deposits almost inevitably form on the surfaces of artificial replacement materials implanted in the human body. By deliberately encouraging deposition of crystals on parts of these materials where they do no harm, it might be that the working surfaces could be kept crystal-free and in good operational order. □

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Neurobiology

# Slit, the midline repellent

**W. A. Harris and C. E. Holt**

In bilaterally symmetric animals, communication between the left and right halves of the body is mediated by neurons that send axons across the midline of the central nervous system (CNS). These axons move along seams, or 'commissures', that are thought to be evolutionarily ancient[1] — even very simple animals contract muscles on one side of their body to avoid a stimulus on the other side. Five reports in *Cell*[2–5] and *Neuron*[6] now describe the product of a previously known gene, *slit*, which is thought to be important not only in the formation of these commissures, but also in axon guidance and the migration of muscle cells.

Not all neurons are commissural, and there are many uncrossed projections in the CNS. Understanding what makes only some axons cross the midline has been a challenge. Several years ago, Marc Tessier-Lavigne and colleagues identified an axon-guidance molecule called netrin, which is secreted at the ventral midline of the developing vertebrate spinal cord. Axons from commissural neurons in the spinal cord are attracted to netrin[7]. At about the same time, Corey Goodman and colleagues identified two *Drosophila* mutants with midline-crossing defects. Whereas in *commissureless* (*comm*) mutants axons do not cross the midline at all, in *roundabout* (*robo*) mutants they relentlessly cross and recross it[8].

Analysis of the *robo* gene and mutant phenotype suggested that it codes for a receptor to a midline repellent. Robo protein is expressed at high levels on the tips of growing axons that do not cross the midline[9]. Growth cones that cross the midline, by contrast, express very low amounts of Robo. Comm protein, which is expressed by midline glial cells, is involved in regulating Robo[10]. Comm is transferred to commissural axons when they reach the midline, causing downregulation of Robo. With Robo low, these axons cannot sense the midline repellent, so they cross. But as they cross, they upregulate Robo, so when they reach the other side levels of Robo are high and they cannot cross again. Thus, commissural axons cross only once because of their changing sensitivity to this mysterious midline repellent.

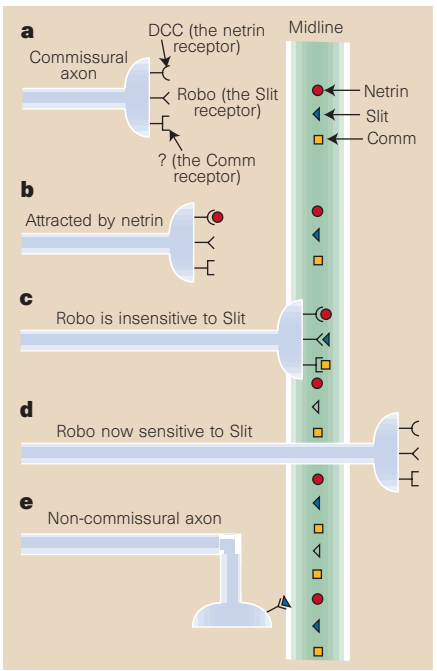


Figure 1 **The function of Slit in axon guidance.** a, **Commissural axons express receptors for netrin, Slit and Comm.** b, **The commissural axon is attracted to the midline by netrin.** c, **Comm downregulates the Slit receptor, Robo, so the axon is insensitive to Slit and can cross the midline.** d, **Having crossed the midline the axon re-expresses Robo, making it sensitive to Slit and preventing it from recrossing the midline.** e, **Non-commissural axons are repelled by Slit, so cannot cross the midline.**

The five papers[2–6] now identify the repellent as the product of the *slit* gene. First described in 1984 as an embryonic mutant by Nüsslein-Vollhard and Wieschaus[11], *slit* is one of many genes that affect the larval cuticle pattern in *Drosophila*. In 1988, Rothberg *et al.*[12] identified Slit as a secreted molecule expressed in midline glial cells, and showed that *slit* mutants have a collapsed axonal scaffold at the midline. Just as commissural axons bind Comm as they cross the midline, they also bind Slit[13]. So Slit is a good candidate for a Robo ligand (Fig. 1).

Kidd *et al.*[3] show genetic interactions between *slit* and *robo* mutants, suggesting that these two molecules act in the same pathway. Brose *et al.*[4] and Li *et al.*[5] show that Slit binds to Robo on cell surfaces and in solution. There are at least three forms of Slit in mammals[14], and at least two of Robo, all of which bind to each other across species boundaries. Moreover, human Slit repels rat motor axons. This is all excellent evidence that Slit is an evolutionarily conserved repulsive ligand for Robo. Interestingly, Slit also binds netrin and laminin *in vitro*, although we don't yet know why.

It is not uncommon for axon-guidance molecules to be used at more than one place in the brain. For example, as well as acting at the midline, netrin is expressed in the vertebrate visual system and in the body-wall muscles of flies. So, the finding of Ba-Charvet *et al.*[6] and Li *et al.*[5] — that the Robo–Slit system is used at other places in the CNS — is not surprising. The first clear case of axons being repelled by a diffusible ligand was in 1993. Adrian Pini[15] showed that cultured axons from the olfactory tract are repelled from a region of the forebrain called the septum. Olfactory-bulb axons, it turns out, express high levels of Robo-2, whereas Slit-2 is highly expressed in the septum. Then there is the hippocampus. Hippocampal axons, which express Robo, do not invade the adjacent entorhinal cortex, which expresses Slit-2. Cell lines expressing Slit-2 can repel both olfactory-tract and hippocampal axons *in vitro*.

Although the new papers show that Slit should join the growing family of evolutionarily conserved, repulsive guidance factors in the CNS, Wang *et al.*[2] report the identification of Slit through a different approach — one that suggests a distinct function for Slit. During development, the axons of pain and temperature receptors enter the spinal cord and travel up and down on the same side for a short distance. They then produce branches along these axon shafts. The branches make synapses with the commissural interneurons that take the message of pain or temperature to the brain. By culturing these pain- and temperature-sensitive neurons in isolation, while exposing them to different CNS fractions, Wang *et al.* discovered that the fraction containing Slit dramatically promoted axonal branching and growth. So, although it has just been identified as a repellent, Slit can also serve as a positive growth- and branch-promoting substance.

The new studies raise further questions. For instance, is the branch-promoting activity of Slit on sensory neurons mediated through Robo? And why does Slit, the repellent, bind netrin, the attractant? Whatever the answers, by uncovering the repellent that keeps some axons from crossing the midline and others from recrossing, these studies shed considerable light on the ancient mysteries of commissure formation. □

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**Motor proteins**

# Another step ahead for myosin

**Malcolm Irving and Yale E. Goldman**

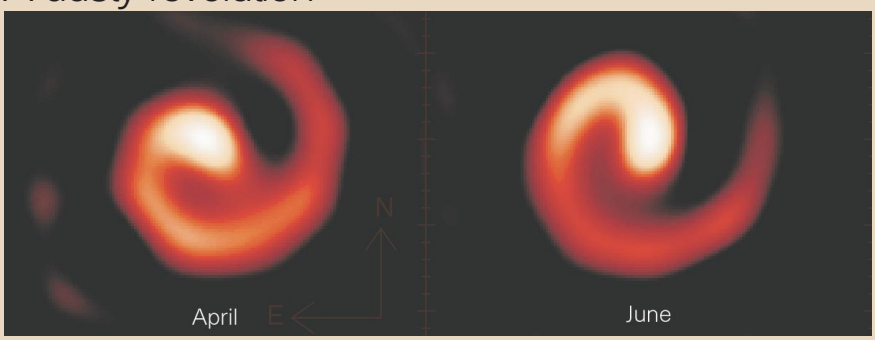
Eukaryotic cells contain many different protein motors, which use metabolic energy to transport cell components along polymer tracks such as actin filaments, microtubules or DNA. A single motor molecule moves along an isolated track in nanometre-scale steps corresponding to hydrolysis of single ATP molecules[1–4]. But two studies on myosin — the motor protein in muscle — by Veigel *et al.*[5] (page 530 of this issue) and Kitamura *et al.*[6], show that each interaction with actin can include two or more sub-steps per ATP hydrolysed.

The head region of myosin, which embodies its motor function, contains a catalytic domain that binds actin and ATP, and an elongated carboxy-terminal domain containing a variable number of calmodulin-like light chains. The light-chain domain is thought to act as a lever arm in the motor mechanism[7,8]. It is often connected to its cargo (which may be a vesicle or filament) through a coiled-coil tail.

Veigel *et al.*[5] exploited the slow kinetics of two single-headed myosins, myr-1 from rat liver and brush-border myosin-I (BBM-I)

**Astronomy**

## A dusty revolution




**Collectors of unusual astronomical objects have another to add to their list: the first spiral star ever observed. Elsewhere in this issue (*Nature* 398, 487–489; 1999) Peter Tuthill and colleagues report high-resolution infrared images of a spiral structure in the hot dust around a Wolf–Rayet star (WR104). They use a powerful aperture-masking technique at the 10-m Keck telescope in Hawaii to produce images much better even than those taken by the Hubble Space Telescope.**

**Wolf–Rayet stars are a phase in the life of exceptionally hot, massive stars, just before they are thought to become supernovae. Some Wolf–Rayet stars are surrounded by shells of dust, but it has been a mystery as to how dust survives the harsh ultraviolet radiation they emit.**

**Now, not only have Tuthill *et al.* detected a spiral pinwheel in the dust around WR104, but they also watched it rotate every 220 days. The image above shows the dusty spiral as seen in April and June 1998. The authors say the spiral and its rotation are the consequence of a companion star. In their hypothesis, dust is created around the binary star where the stellar winds collide, and is then carried along with the orbital motion.**

**Whether every dusty star has a binary remains open for debate. But in this case, the images of the spiral are so good that the orbital period, distance and separation of the binary system can be inferred from its effect on the stellar dust, without ever detecting the two central stars.** **Sarah Tomlin**