

## DEVELOPMENTAL BIOLOGY

# Asymmetry with a twist

Nipam H. Patel

In snails, manipulating the orientation of cells in the early embryo alters the left–right asymmetry of the shell and body. These findings refine the search for the symmetry-breaking event in this and other animals.

The elegant shape of seashells has long fascinated us, and their beautiful curved forms have inspired many man-made designs. The spiral shapes can be divided into two distinct groups on the basis of the direction of coiling. Hold a shell so that you look down onto the pointed end, and you will see that most shells spiral downward in a clockwise direction (Fig. 1); only a few twist in the opposite direction. This property of shell coiling is termed chirality; shells with clockwise spirals are called dextral shells, and those with anticlockwise spirals are termed sinistral shells.

These differences in chirality are a manifestation of left–right asymmetry of the organs of the animal. In the case of the shell, the gland that makes this structure is producing shell material at different rates on the left and right sides, leading to the coiling pattern as the shell grows. Through a conceptually simple, although technically challenging, study in the snail, Kuroda and colleagues<sup>1</sup> show (page 790 of this issue) that they can reverse the chirality of the shell, and the asymmetry of other organs, by mechanically altering the relative orientation of cells in the early embryo.

Kuroda *et al.*<sup>1</sup> worked with a pond snail, *Lymnaea stagnalis*. Whereas most species of snail have dextral shells, and a few have sinistral shells, *L. stagnalis* falls into a relatively rare group in which both chiralities exist within the same population. The difference between dextral and sinistral individuals can be detected during the first few cell divisions of the embryo — as the four-cell embryo undergoes cleavage to become an eight-cell embryo. For dextral snail embryos, the smaller daughter cells at the four-to-eight-cell transition twist clockwise as cell division occurs. In the case of sinistral snail embryos, the daughter cells are initially directly on top of their division partners, but then twist anticlockwise (Fig. 2, overleaf). The result is that dextral and sinistral embryos look like mirror images of each other at the eight-cell stage, just as their shells will look like mirror images of each other as adults.

Thanks to the outstanding work of ‘gentleman’ scientists of the 1920s and 1930s, we also understand the genetics of snail chirality.



**Figure 1 | Spiralling downward.** Most shells, like that of the sea snail *Architectonica perspectiva* shown here, spiral downward in a clockwise manner and are termed dextral shells. Shells with anticlockwise spirals are called sinistral shells.

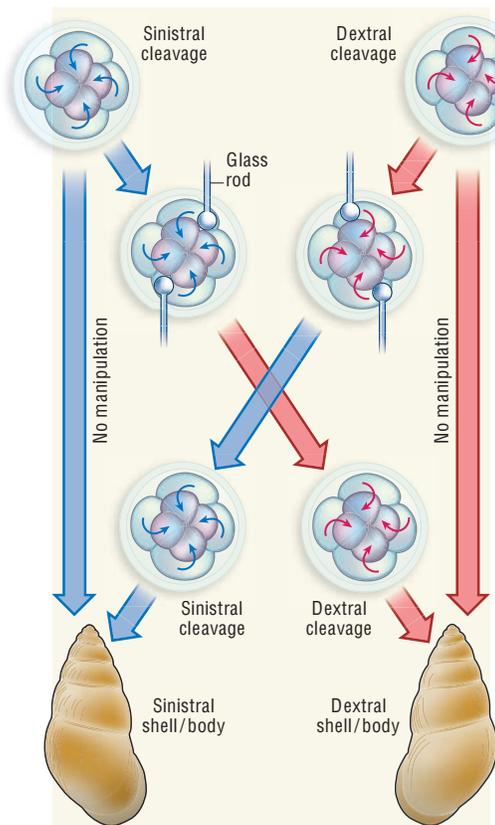
Professor Arthur Boycott of the University of London recruited a team of naturalists, most notably Captain Cyril Diver, a part-time parliamentary administrator, to examine the genetics of chirality in *Lymnaea peregra*, a close relative of *L. stagnalis*. What they described<sup>2</sup> was the founding example of the phenomenon we now call maternal-effect inheritance<sup>3</sup>. Simply put, it is not the genotype of the individual animal that determines a particular phenotype (in this case the dextral or sinistral shell); rather, it is the genotype of the mother that determines the phenotype of her progeny. In the case of both *Lymnaea* species, a single genetic locus controls chirality, with the dextral allele acting in a dominant manner. If we think of the two alleles of the chirality locus as *D* and *d*, then mothers who are *DD* or *Dd* give rise to dextral progeny, whereas *dd* mothers give rise to sinistral progeny. The genotype of the father has no bearing on the phenotype of the offspring.

Thus, Kuroda *et al.* started with *DD* or *Dd* mothers, knowing that all their progeny would exhibit a dextral cleavage pattern and normally form dextral shells, and with *dd*

mothers, whose embryos would display a sinistral cleavage pattern and form sinistral shells. By using small glass rods to push on the cells, the authors could change the cleavage pattern of the embryos. They took embryos that should have cleaved dextrally, and forced the cells at the eight-cell stage to take on the orientation normally seen for sinistral embryos, and vice versa (Fig. 2). Remarkably, this reversed the chirality of the animals as they grew into adults. So, merely changing the relative orientation of the cells at the eight-cell stage can completely override the maternal-effect specification of chirality. Before these experiments<sup>1</sup>, it was conceivable that the chirality of the cell-cleavage pattern and that of the shell and organs later on were correlated, but did not represent cause and effect. Now we know that the maternal chirality locus controls the orientation of the cells at the eight-cell stage, and that this orientation ultimately controls the adult snail's chirality.

Kuroda and colleagues' findings<sup>1</sup> suggest that it is the pattern of cell–cell interactions initiated at the eight-cell stage that dictates shell chirality, and that these interactions differ depending on the cleavage pattern. We still do not know what the maternal chirality locus encodes, but the gene product in some way regulates the cellular cytoskeleton and thus dictates the orientation of cell division and of cells at the eight-cell stage. We also do not know the nature of the subsequent cellular interactions, but we might glean some clues from studies of the nematode worm *Caenorhabditis elegans*. Similar mechanical manipulations were used to show that specific cell–cell interactions establish left–right asymmetry in *C. elegans*<sup>4</sup>, and genetic screens<sup>5</sup> have now revealed some of the molecules involved in this process.

Of course, this type of left–right asymmetry is not confined to snails and nematodes. For example, humans and other vertebrates have striking asymmetries in the placement of organs such as the heart, lungs, liver and gut. Recent work<sup>6</sup> has shown that the genes used to control left–right asymmetry in snails and vertebrates share certain features. Specifically, the genes encoding the signalling molecule Nodal



**Figure 2 | Reversing asymmetry in snails.** At the transition from the four- to eight-cell stage in the embryo of the pond snail, *Lymnaea stagnalis*, newly formed smaller daughter cells twist either clockwise or anticlockwise. This chirality (direction of twisting) correlates with the chirality of the adult shell and the left–right asymmetry of other body organs. For sinistral snail embryos, the smaller daughter cells twist anticlockwise after cell division (sinistral cleavage; blue arrows). For dextral snail embryos, the daughter cells twist clockwise as cell division occurs (dextral cleavage; red arrows). Kuroda *et al.*<sup>1</sup> used glass rods to push on the cells at the eight-cell stage, forcing them into the opposite orientation. The result was a reversal of chirality of the individual that developed from the manipulated embryo. Embryos that started with a sinistral cleavage, but were forced into a dextral orientation, grew into adults with dextral shells, whereas embryos that started with a dextral cleavage pattern, but were forced into a sinistral orientation, developed into adults with sinistral shells.

and the transcription factor Pitx, both of which have well-studied roles in vertebrate left–right asymmetry, are asymmetrically expressed (only on the right side in dextral species and only on the left side in sinistral species), and are functionally involved in determining left–right asymmetry of snails starting at about the 32–64-cell stage<sup>6</sup>. Indeed, the mechanical manipulations of Kuroda *et al.*<sup>1</sup> also reversed the left–right expression of these two genes.

Thus, studying snail left–right asymmetry will be relevant to understanding the phenomenon in vertebrates as well. In mice, the

symmetry-breaking event seems to involve an asymmetry in extraembryonic-fluid flow set up by cilia<sup>7</sup>, whereas in chickens, it seems instead to involve early embryonic cell migration<sup>8</sup>. Snail embryos do not have cilia at the eight-cell stage, so it is difficult to predict how the maternally controlled symmetry-breaking process in snails relates to the early events in vertebrates. The final twist to this tale is yet to be told. ■

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## GAMMA-RAY BURSTS

# Magnetism in a cosmic blast

Maxim Lyutikov

**Astronomers know little about  $\gamma$ -ray bursts other than that they are the most energetic explosions in the Universe. The latest observations indicate that large-scale magnetism contributes to their power.**

Gamma-ray bursts (GRBs) are truly amazing astrophysical events. In a matter of seconds, they release more energy than the Sun will do in its lifetime of 10 billion years. These powerful stellar explosions eject material at highly relativistic velocities — differing from the velocity of light by as little as one part in a million. Because they are so bright, GRBs can be seen almost to the edge of the observable Universe, occurring, on average, about twice a day. However, their origin remains a mystery. Their outflows could be gas-dynamic phenomena, driven by gases near their central engine with a high kinetic pressure (to some extent, similar to exhaust jets in aeroplanes)<sup>1</sup>. Alternatively, and somewhat unexpectedly, magnetic fields, which on Earth have a negligible dynamic role, have been proposed as the dominant mechanism for both driving the bulk of the outflow and accelerating particles within it<sup>2,3</sup>. The coupling of magnetic fields to gravity — which occurs, for example, in the close vicinity of the event horizon (a boundary beyond which nothing can escape) of a rotating black hole through the Blandford–Znajek mechanism<sup>4</sup> — can indeed produce powerful relativistic outflows such as those seen in GRBs.

But magnetic fields in GRBs are notoriously hard to observe — just imagine the difficulties faced by an observer trying to prove the existence of Earth's magnetic field without the use of a magnetic compass. On page 767 of this issue, Steele *et al.*<sup>5</sup> report a possible detection of magnetic fields in a GRB, GRB 090102, through observations of polarization in its optical (visible-light) emission.

GRBs emit light across a broad band of frequencies, ranging from the radio to the high-energy end of the  $\gamma$ -ray part of the electromagnetic spectrum. As the name suggests, they are detected, at least initially, through their

$\gamma$ -ray radiation. Because Earth's atmosphere effectively blocks  $\gamma$ -rays, thereby protecting the planet from this highly damaging radiation, astronomers rely on space telescopes that operate at high frequencies, such as Swift, to observe them. Once a GRB is detected by a space telescope, its sky coordinates are transmitted to ground-based observatories, which then carry out follow-up observations.

In the optical waveband, GRBs tend to produce a dim flash that lasts for only a few dozen seconds. This makes ground-based follow-up observations challenging. First, the telescope must turn automatically towards a GRB, because any delay may mean that the quickly fading signal is not detected. Second, because the telescope sometimes needs to be reoriented by a large angle during this 'slewing' manoeuvre, modern, large telescopes are often too massive, and therefore too slow, to be useful.

In their study, Steele and colleagues<sup>5</sup> used the medium (2-metre) RINGO Liverpool Telescope at La Palma in the Canary Islands. The key advantage of the RINGO telescope is that it is equipped with a detector that can measure the polarization of incoming radiation. The authors were therefore able to measure a considerable degree of polarization — of the order of 10% — in the optical emission from GRB 090102. The fraction of polarization in astrophysical sources rarely exceeds several per cent.

Polarization is a property of electromagnetic waves that describes the preferred direction of their electric-field oscillations. A non-zero polarization indicates that the process that produced the waves is, in some sense, non-isotropic: it is more sensitive to one particular direction than others. The most logical — but not the only — explanation for the high degree of polarization obtained by Steele and