

energy is needed for a $200\text{ }\mu\text{m}^3$ volume, the same order as that achieved with larger microcavities such as the OVCSEL. The fact that the cavity can be reduced in size without increasing the threshold is an indication of the low loss experienced by the photon as it circulates many times around the zeolite waist.

Nonetheless, many challenges remain in realizing an organic laser diode. First, it is not clear how to excite these tiny microlasers electrically. Moreover, we need to identify organic materials that can withstand the high current densities required for lasing, and that are optically transparent under intense electrical excitation. Indeed, some organic systems appear to become more light absorbing (that is, they darken) as the current density increases, which may ultimately prove fatal to hopes for an organic laser diode^{12,13}. However, the self-assembly of these miniature optical devices has proven once again that our ability to manipulate materials on even the most microscopic scale

is becoming commonplace. □

Stephen R. Forrest is in the Department of Electrical Engineering, Center for Photonics and Optoelectronic Materials, Princeton University, Princeton, New Jersey 08544, USA.
e-mail: forrest@ee.princeton.edu

1. Vietze, U. *et al.* *Phys. Rev. Lett.* **81**, 4628–4631 (1998).
2. Kogelnik, H. & Shank, C. V. *Appl. Phys. Lett.* **18**, 152–154 (1971).
3. Karl, N. *Phys. Status Solidi* **13**, 651–655 (1972).
4. Soffer, B. H. & McFarland, B. B. *Appl. Phys. Lett.* **10**, 266–267 (1967).
5. Forrest, S. R., Burrows, P. E. & Thompson, M. E. *Chem. Ind.* 1022–1027 (1998).
6. Berggren, M., Dodabalapur, A., Slusher, R. E. & Bao, Z. *Nature* **389**, 466–469 (1997).
7. Kozlov, V. G., Bulovic, V., Burrows, P. E. & Forrest, S. R. *Nature* **389**, 362–364 (1997).
8. Bulovic, V., Kozlov, V. G., Khalfin, V. B. & Forrest, S. R. *Science* **279**, 553–555 (1998).
9. Frolov, S. V., Vardeny, Z. V. & Yoshino, K. *Appl. Phys. Lett.* **72**, 1802–1804 (1998).
10. Kuwata-Gokokami, M. *et al.* *Opt. Lett.* **20**, 2093–2095 (1995).
11. Meier, M. *et al.* *Appl. Phys. Lett.* **74**, 7–9 (1999).
12. Kozlov, V. G., Burrows, P. E., Parthasarathy, G. & Forrest, S. R. *Appl. Phys. Lett.* (in the press).
13. Tessler, N., Harrison, N. T. & Friend, R. H. *Adv. Mater.* **10**, 64–68 (1998).

Developmental biology

A new spin on handed asymmetry

Kyle J. Vogan and Clifford J. Tabin

In vertebrates, most internal organs develop asymmetrically with respect to the body's midline, with the liver on the right and the stomach on the left, for example. This phenomenon, known as left–right (L–R) asymmetry, raises an intriguing question — how is the early bilateral symmetry of the embryo first broken such that the L–R axis is always orientated the same way? A report by Nonaka *et al.*¹ in *Cell* now provides a remarkable insight into this problem. They show that the mouse node, a cup-shaped cavity in the embryo's midline, uses anticlockwise rotation of cilia to create a directional flow of extraembryonic fluid.

The authors propose that this 'nodal flow' concentrates critical L–R determinants to one side of the node, activating distinct downstream signalling pathways on the left and right sides of the embryo.

People with defective cilia in their airways and immotile sperm cells often have mirror-image reversals of the L–R axis (Kartagener's syndrome)². Moreover, the *inversus viscerum* (*iv*) mouse has L–R patterning defects that have been linked to a mutation in an axonemal dynein protein (dyneins are critical force-generating components of ciliary motors)³. Such findings have led to the suggestion that cilia are

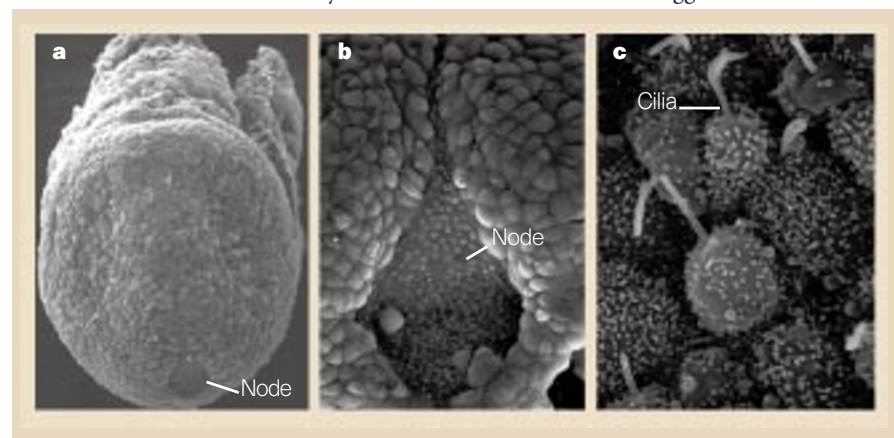


Figure 1 Monociliated cells on the ventral surface of the mouse node. a, The node is at the apex of the egg cylinder, and the head process, which will give rise to the notochord, extends anteriorly. b, Close-up showing the cup-like shape of the node. The anterior is orientated towards the top. c, Higher magnification showing the monocilia on each cell in the head process and on the ventral surface of the node. (Micrographs courtesy of K. Sulik and T. Poe, Univ. North Carolina.)



100 YEARS AGO

During my visit to South Australia, I wished to obtain some specimens of insects of the country, for my naturalist friends at home. At first I experienced considerable difficulty in catching those whose movements were rapid, without injuring their bodies. Recently I have been able to secure nearly every specimen seen, by the following method. A small antitoxin syringe was charged with benzol, and a small jet of liquid was directed towards the beast sought for (a large tarantula, for example); the result of this form of attack was to render the beast almost instantly inert, so that it was easily secured. I am not at all sure that benzol is the best liquid for the purpose; but I used it, as it happened to be the only substance I could obtain; at a distance from a township, which appeared likely to produce the desired effect.

From *Nature* 26 January 1899.

50 YEARS AGO

Driven by his deafness to read his way through the Detroit Public Library, Edison wrote long afterwards that he found that almost any book would supply entertainment or instruction. This book, which contains selected excerpts from his writings, supplies the first in good measure and, for those who reflect on reading, more than a modicum of the second. The pages from the diary which form the opening section of the book are full of whimsical humour which one would not have expected from a prodding experimenter who died with more than a thousand inventions to his credit. There is little reference in the book to Edison's experimental work, except for a short account of his early struggles to make a motion picture machine, carried out in a studio irreverently called the "Black Maria". But the background is there, revealed in the words that experiments in a laboratory consist mostly in finding out that something will not work. ... Edison's observations on the possibilities of atomic energy, his somewhat casual remarks on the influences that make for peace or war and his comments on disarranged economic systems — all these make reading which is the more interesting because of all that has happened since the last of these lines was written.

From *Nature* 29 January 1949.

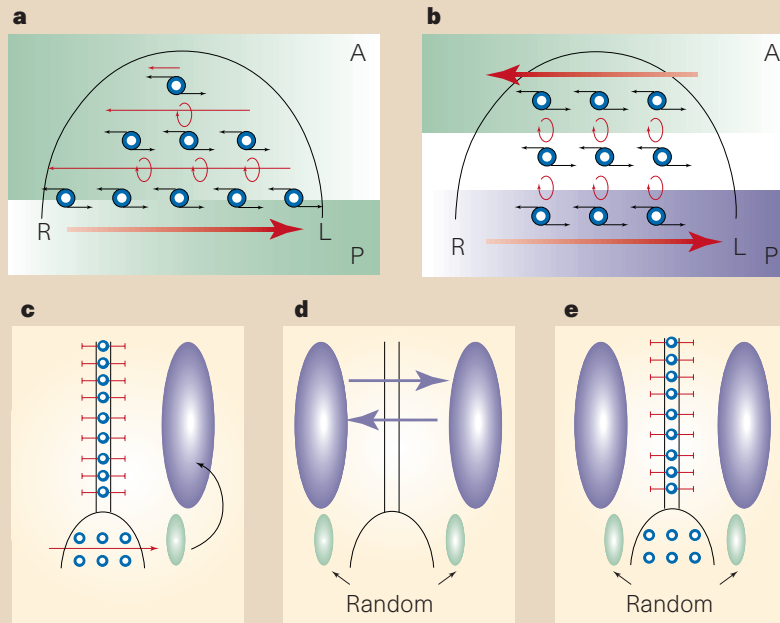


Figure 2 Proposed roles of cilia during left–right (L–R) patterning. **a**, On the ventral surface of the node, cilia (blue circles) rotate anticlockwise. Because of the shape of the node, there are more cilia towards the posterior (P). Nonaka *et al.*¹ propose that interference (red circles) between the currents set up by successive rows of cilia limits flow to a weak rightward current across the anterior (A) and central regions of the node, but leaves a strong leftward flow in the posterior (bold red arrow), which concentrates a uniformly produced factor on the left side (green shading). **b**, Alternatively, the currents generated by individual cilia could result in interference throughout much of the node, leaving a net rightward flow at the anterior and a net leftward flow at the posterior. **c**, Wild-type cilia may both initiate L–R asymmetry at the node (red arrow), and act as a barrier (red lines) to prevent the diffusion of L–R factors (green and purple) across the midline. **d**, In *kif3b* mutants there are no cilia, so L–R initiation is random and signals can cross the midline. **e**, In *iv* mutants the cilia are thought to be immotile, so L–R initiation is random but the midline barrier is still intact.

critical for establishing L–R pattern, and two embryonic structures have become particularly attractive candidates for the site at which they might act. The first is the node, which is an important source of patterning signals in the early embryo, and is also the site of the earliest known molecular asymmetries^{4,5}. The second is the notochord, a structure at the midline that has been proposed to act as a barrier to prevent asymmetric signals from crossing over to the opposite side^{6,7}. Both the ventral side of the node and the notochord consist of monociliated cells^{8,9} (Fig. 1), and the *iv* gene product itself is highly expressed at the node during early development³.

Despite these suggestive findings, the function of nodal cilia remained unclear. For one, nodal cilia do not share the ‘9+2’ organization of microtubule doublets typical of most motile cilia^{8,9}. Moreover, attempts to assess the motion of these cilia directly yielded equivocal results^{8,9}. Although one group⁸ reported motility, they saw no directionality to suggest that these cilia could bias L–R pattern.

To address these issues, Nonaka *et al.*¹ generated a mouse lacking the kinesin

superfamily member KIF3B, a force-generating motor protein that was suspected to be critical for the assembly of cilia. Strikingly, mutant embryos showed randomized L–R asymmetry and were completely devoid of cilia. Inspired by this result, the authors examined the motility of nodal cilia in normal embryos, and made a dramatic discovery — nodal cilia rotate anticlockwise, a type of motion that is never seen with conventional cilia. Furthermore, by tracking the motion of fluorescently labelled beads, Nonaka *et al.* found a net leftward flow of extraembryonic fluid in the node region. This flow, the authors note, can arise without any input of L–R positional information, so could provide the initial bias that is needed to generate the L–R axis.

This work offers an elegant solution to a vexing problem — namely, how does the embryo orientate the L–R axis relative to the other axes of the body? It was proposed that morphological L–R asymmetry might be linked to the chirality of a hypothetical ‘F’ molecule, which is aligned in cells with respect to the anteroposterior and dorsoventral axes¹⁰. But this leaves unan-

swered the question of how the F molecules might be orientated in this way. The ciliary model circumvents this problem because the cilia themselves carry information about the dorsoventral axis (they all project ventrally) and, unlike the hypothetical F molecule, there is no need to align them further. The orthogonal flow of extraembryonic fluid at the node is derived from anticlockwise rotation of the cilia, which is presumably determined by the chirality of the molecules that drive their motion.

How, then, is information about the anteroposterior axis integrated in the system? Anticlockwise motion of the cilia should produce flow with equal and opposite left and right vector components. Paradoxically, however, Nonaka *et al.* find no evidence for rightward flow. To explain this, they propose that differences in the width of the node along the anteroposterior axis lead to more cilia towards the posterior end, which synergistically intensify the leftward flow at the posterior edge (Fig. 2a). They propose that this strong, narrow, leftward flow is balanced by a much broader and weaker rightward flow, the effects of which could be negated by passive diffusion. Alternatively, if equal and opposite leftward and rightward flows do exist (Fig. 2b), anteroposterior information could be imparted to the system by localizing L–R determinants either anterior or posterior to the node itself. In this model, molecules that diffused into the node from its anterior side would meet a rightward current and be concentrated to the right, whereas factors that originated posterior to the node would experience a leftward flow and be concentrated to the left.

Somewhat unexpectedly, the *kif3b* and *iv* mutations have distinct effects on the expression of downstream L–R patterning genes. These differences can be explained if the cilia at the midline also act as a barrier during L–R signalling (Fig. 2c). In the *kif3b* mutant, where the cilia fail to form, both initiator and barrier functions would be lost (Fig. 2d). By contrast, the *iv* mutation is predicted to cripple the motor that drives the cilia, rendering them immotile. These cilia could, nevertheless, still act as a midline barrier (Fig. 2e).

How general is this mechanism of L–R determination? Because rotating the chick node by 180° at an early stage of development does not affect L–R patterning, it had been suggested that the initial L–R decision is made outside the node¹¹. However, rotating the node through 180° should not perturb the uniform, anticlockwise motion of the cilia so, if the same biasing mechanism operates in the chick, normal L–R patterning should still occur. Assuming that rotation of nodal cilia is indeed a universal mechanism for determining L–R asymmetry in vertebrates, we now have a broad

conceptual outline that describes the key steps in L–R patterning — from the initial breaking of symmetry at the node, through a cascade of signals that culminates in the direct induction of asymmetrically biased morphogenetic events¹². As we continue to fill in the details of this outline, we will discover further how spatial orientation is controlled during the assembly of an embryo and, judging by the extraordinary pace at which this story has unfolded over the past few years, we should not have long to wait. □

Kyle J. Vogan and Clifford J. Tabin are in the Department of Genetics, Harvard Medical School, 200 Longwood Avenue, Boston, Massachusetts

02115, USA.

e-mails: vogan@rascal.med.harvard.edu

tabin@rascal.med.harvard.edu

1. Nonaka, S. *et al. Cell* **95**, 829–837 (1998).
2. Afzelius, B. A. *Science* **193**, 317–319 (1976).
3. Supp, D. M., Witte, D. P., Potter, S. S. & Brueckner, M. *Nature* **389**, 963–966 (1997).
4. Levin, M., Johnson, R. L., Stern, C. D., Kuehn, M. & Tabin, C. *Cell* **82**, 803–814 (1995).
5. Levin, M. *et al. Dev. Biol.* **189**, 57–67 (1997).
6. Danos, M. C. & Yost, H. J. *Development* **121**, 1467–1474 (1995).
7. Levin, M., Roberts, D. J., Holmes, L. B. & Tabin, C. *Nature* **384**, 321 (1996).
8. Sulik, K. *et al. Dev. Dyn.* **201**, 260–278 (1994).
9. Bellomo, D., Lander, A., Harragan, I. & Brown, N. A. *Dev. Dyn.* **205**, 471–485 (1996).
10. Brown, N. A. & Wolpert, L. *Development* **109**, 1–9 (1990).
11. Pagán-Westphal, S. M. & Tabin, C. J. *Cell* **93**, 25–35 (1998).
12. Harvey, R. P. *Cell* **94**, 273–276 (1998).

Astrophysics

Stress drives gas into a black hole

Kartik Sheth and Peter J. Teuben

On page 324 of this issue, Beck *et al.*¹ present new measurements of interstellar magnetic fields in the bar region of the galaxy NGC1097 (Fig. 1). From this, they infer the direction of gas flow in the galaxy and the location of regions of gas compression, where the gas traces visible dust lanes. It is suspected that gas flows inward along these lanes to fuel bursts of star formation in a ring of dense molecular gas known as the circumnuclear ring. Or, the gas may reach the very centre of the galaxy and provide fuel for an ‘active galactic nucleus’ — the extremely bright core where enormous amounts of energy are generated by the accretion disk around a supermassive black hole. This is the first time that the relationship between magnetic fields and gas flow in barred spiral galaxies has been investigated. The features of the magnetic field in the nuclear region lead Beck *et al.* to suggest that

magnetic stress might be an efficient mechanism for fuelling the central black holes of active galactic nuclei.

Perhaps as many as two-thirds of spiral galaxies have a bright, central bar of stars. Indeed, our own Milky Way appears to have a bar². These bars can extend over most of the optical disk and contain a large fraction of the stellar mass, as in NGC1097; or they may be confined to the nuclear region or form slight oval distortions to the disk, which are only evident at infrared wavelengths. A bar can have a dramatic influence on the evolution of the galaxy. Its gravitational pull induces large-scale non-circular motions in the stars and the interstellar gas. Although the resulting stellar orbits intersect, stars do not collide because of their small collision cross-sections. In the interstellar gas, on the other hand, there are many collisions between particles and considerable dissipa-

tion of energy; as a consequence, the gas can lose angular momentum and fall inwards.

The infall of gas can produce major changes in a galaxy. It can trigger a nuclear starburst (a relatively short period of intense star-forming activity in the nucleus), or the inflow may lead to formation of a new bulge of young stars at the centre of the galactic disk³. The mechanisms and timescales for bulge (and disk) formation are crucial for understanding the evolution of galaxies. If the gas falls deep enough into the centre of the galaxy, it may fuel the supermassive black hole thought to exist in the active nucleus of many galaxies⁴. The large-scale mixing of the gas due to the bar can also change the overall chemical abundance in a galaxy⁵, which bears upon our understanding of the history of star formation and predictions of its future activity. Finally, one of the most dramatic effects of the gas infall is the destruction of the bar itself when sufficient mass accumulates in the centre³. The bar can be its own worst enemy.

So gas inflow in barred galaxies has many effects, but there is disagreement about its exact nature. Although all models of the process predict inflow, they differ in how the gas reaches the centre. In one set of models, which simulate the interstellar dust as a collection of distinct clouds, the gas experiences occasional collisions and slowly spirals inwards⁶. In another set of simulations^{7,8} in which the gas is modelled as an ideal fluid, experiencing hydrodynamic forces, the gas undergoes a compression, or shock, at the leading edge of the bar and flows directly into the centre. Some of these latter models show gas flowing close to the nucleus, but the bars required for this type of behaviour are not usually observed. The hydrodynamic models of gas inflow that best imitate observations show the gas stalling in a ring around the centre of the galaxy and not reaching the nucleus. These models successfully predict the dust lane morphology⁸ and gas velocities⁹ observed in bars.

Beck *et al.*¹ measure polarized radio synchrotron emission in the bar region of the galaxy NGC1097. From the intensity and direction of the radio emission, they determine the direction of the magnetic field in the bar and conclude that the field vectors are consistent with the gas flow vectors predicted by hydrodynamic models (as long as one makes the usual assumption that the magnetic field is frozen into the fluid). They observe a strip of zero polarization, which appears to be offset from the bar dust lane, about 800 parsecs (2,600 light years) in the upstream direction. Beck *et al.* interpret this strip to be the location of the hydrodynamic shock, in contrast with previous observations and models which concluded that the shock loci are in the dust lane itself. The strip may be an artefact produced by a varying field strength or gradually changing gas flow

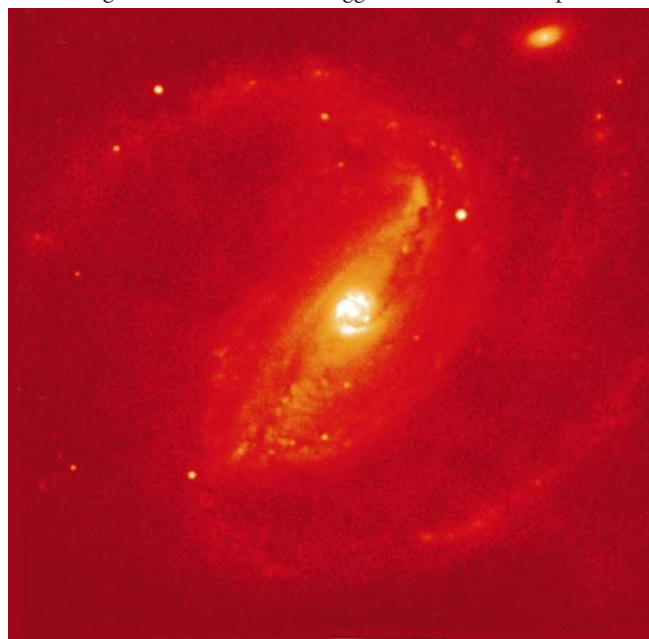


Figure 1 Optical image¹¹ of spiral galaxy NGC1097 studied by Beck *et al.*¹. The bar region is the elongated feature in the centre of the galaxy with two prominent straight dust lanes along the leading edge. Trailing spiral arms can be seen emerging from the ends of the bar.