DEVELOPMENTAL BIOLOGY

Left, right, left... turn

Rosa Beddington

THE body of every vertebrate has three distinct axes: anterior–posterior, dorsal–ventral and left–right. Of the three, the origin of left–right asymmetry has been the least studied, possibly because it is the last to be determined during embryogenesis, and left–right only acquires meaning once the other two axes are in place.

But we are getting somewhere. Last year the first evidence for left–right asymmetrical gene expression preceding any gross morphological manifestation of the left–right axis was discovered in chick embryos[1]. This is now followed by three reports in this issue[2–4] that dramatically demonstrate left-handed gene expression in mammalian and amphibian embryos. What is more, disturbance in the handedness of this gene expression is seen in two mouse mutants in which the left–right axis is partially or completely reversed (a condition known as *situs inversus*); and an unexpected genetic interaction affecting placement of the organs has been uncovered in embryos doubly heterozygous for targeted mutations in a transcription factor and a secreted protein.

For all that it is the last to be determined, left–right is by no means the least important of the three axes. Left–right asymmetry is essential for normal development and the correct functional juxtapositioning of the organs: heart on the left, liver on the right and so on. Although left and right are not in themselves significant, asymmetry is. *Situs inversus* does not have particularly dire consequences, but ambiguity of the axis does because it affects the interconnection of organs and the partitioning and plumbing of the heart.

What of the new work? On page 151 Meno *et al.*[2] describe a new divergent member of the transforming growth factor-β (TGF-β) superfamily of secreted molecules, which they call *lefty* because it is expressed exclusively in the mesoderm of the left lateral plate. This one-sided expression precedes the characteristic right-handed looping of the heart tube and the subsequent axial rotation of the embryo, which normally is towards the right. Remarkably, at a similar stage *lefty* transcripts are also found only in the left half of the floorplate in the developing mid- and hindbrain indicating some hitherto unrecognized asymmetry in this region where axons will cross the midline.

On pages 155 and 158 Collignon *et al.*[3] and Lowe *et al.*[4] show that the murine *nodal* gene, another member of the TGF-β superfamily and one required for mesoderm formation at the onset of gastrulation[5,6], is expressed asymmetrically around the node by the early somite stage and its transcripts are only ever found in left-lateral-plate mesoderm, presumably coincidentally expressed with *lefty*. Likewise, a *Xenopus* homologue of *nodal*, *Xnr-1*, is expressed only in left-lateral-plate mesoderm although no comparable asymmetry is apparent around the blastopore.

Although these patterns are intriguing, both the lateness of their one-sided expression and, more importantly, genetic

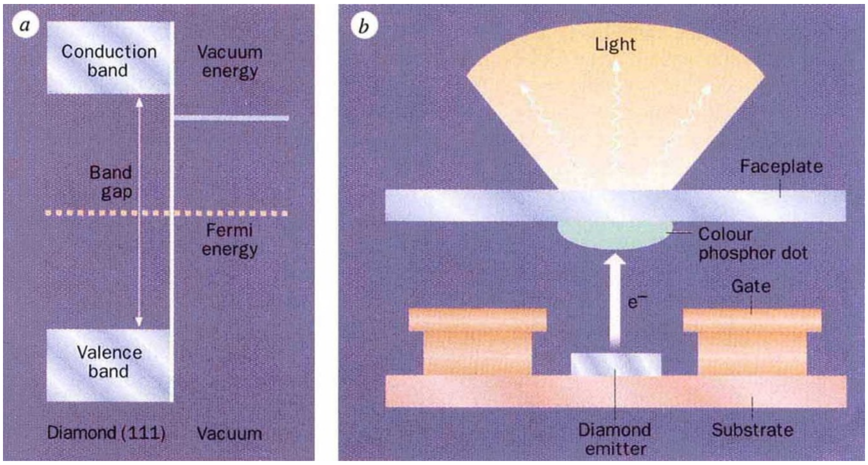
MICROELECTRONICS

Diamond films put on display

VACUUM-TUBE technology is making a comeback, and the report by Ken Okano *et al.* on page 140 will help it on its way. They report efficient electron emission from nitrogen-doped diamond films grown by chemical vapour deposition (CVD), an attribute that augurs well for the use of diamond as a cathode material in diode and field-emission display devices.

Why diamond? It is one of the few materials that possesses a negative electron affinity (NEA), meaning that the bottom of the electronic conduction band lies above the 'vacuum level', the energy of a free electron in a vacuum (part *a* in the figure). So electrons in the conduction band can escape spontaneously from the surface (in fact the electron affinity is surface-dependent: diamond's (111) surface has an NEA, whereas the affinity of the (100) surface is positive). This property gives diamond the potential to act as a 'cold' cathode in vacuum diode devices — conventional vacuum diodes (the old-style 'valves' or 'tubes') relied on thermal activation to achieve electron emission from heated metal filaments.

Cold cathodes can in principle be fabricated on a microelectronic scale, so they could be incorporated into integrated circuits. Here they would offer the potential advantages over solid-state devices of high speed, energy efficiency and resistance to radiation damage — all a consequence of the



fact that the carriers do not move through the solid state but through a vacuum. In addition, cold cathodes could provide electron emitters for phosphorescent display devices (part *b* in the figure), whose fabrication requires only simple lithographic procedures. Several devices of this kind have now been demonstrated.

In pure diamond, the conduction band is empty — the material is an insulator. So it must be doped (either p-type or n-type) to provide mobile charge carriers. To a first approximation, the greater the degree of doping, the lower the threshold voltage needed to attain efficient emission and high current densities. Doping with boron gives only a small emission enhancement, phosphorus doping does better, and nitrogen doping appears best of all (M. W. Geis *et al.*, *Appl. Phys. Lett.* 67, 1328; 1995). But Murphy's law applies: getting nitrogen into CVD diamond films in high concentrations is hard.

This is where Okano *et al.* have taken the crucial step. They find that using urea as the nitrogen source in the CVD synthesis gives films with a high nitrogen content — around 0.2 per cent. The diamond cathodes so fabricated have threshold voltages low enough that adequate emission currents for display and microelectronic applications should be possible in vacuum devices powered by a single commercial 1.5-volt battery.

Philip Ball