The turn of the screw

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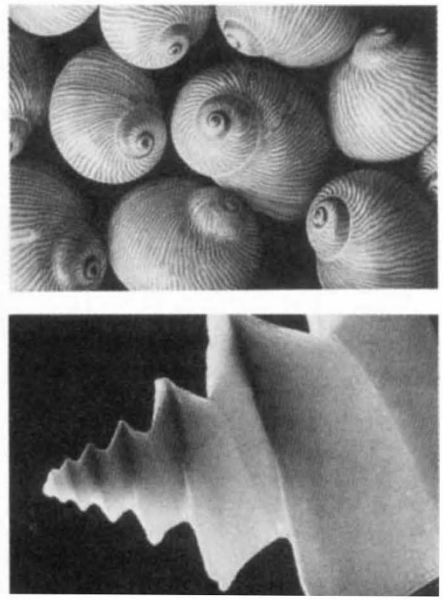
Biological Asymmetry and Handedness, Ciba Foundation Symposium 162. Edited by Gregory R. Bock and Joan Marsh. Chairman: L. Wolpert. *Wiley: 1991. Pp. 327. £39.50, $69.50.*

LEWIS Wolpert is left-handed, but we know that he is not made of antimatter, neither are his proteins composed of D-amino acids. He does not even have *situs inversus viscerum*, the rare condition in which the internal organs are arranged as a mirror-image of the normal. So at what level is his own bilateral symmetry broken, and how does it happen? Wolpert has long been concerned with the general issue of why there are left–right asymmetries in organisms such as vertebrates, which seem to a good approximation to be bilaterally symmetrical. This book, the proceedings of a Ciba Foundation Symposium held last year, investigates the problem in detail and considers every level of asymmetry from nonconservation of parity in the weak nuclear interaction to laterality of human motor functions.

The story starts with life on Earth and why all proteins are composed of L-amino acids. According to the principle of CP conservation, the true mirror-image of a chiral molecule must be made of antimatter. The terrestrial enantiomers, the D-amino acids, are slightly less stable in the protein alpha-helix or beta-sheet than are the L-forms. Although this difference is not measurable, it is sufficient to lead to the extinction of the D-forms in the primaeval soup of the early Earth if we assume that there was an autocatalytic stereospecific synthesis of the amino acids from achiral precursors. Of course we cannot exclude the possible additional effects of asymmetrical environmental influences such as circularly polarized sunlight.

Having got L-amino acids (and D-sugars, which are also CP-favoured), do all higher asymmetries flow inexorably from them? Probably not. It does seem that the main themes of protein secondary structure would be reversed if the handedness of the monomers were reversed. This might carry us up as far as large helical structures such as viruses, but the arrow of causality becomes lost in the more complex three-dimensional patterns that are required for packing and recognition of globular proteins. At this level, the same structure can be made in many different ways. For instance, if we make an antibody to a biologically active molecule and then make an antibody to the first antibody, the second antibody (an 'anti-idiotype') sometimes shares the biological activity of the original antigen. But the primary sequence of the anti-idiotype will be different from that of the original antigen. So it is true that three-dimensional structure is determined by primary structure, and asymmetries in this structure will be determined by the asymmetry of the monomers, but there are so many ways of making any required structure that higher asymmetries could be created from any kind of basic monomer. At the meeting, this became known as the 'Chothia gap', but it is also the familiar epistemological gap that exists in embryology between understanding structures that arise from molecular self-assembly and understanding those that require higher levels of causation.



Mollusc shells of the right-handed persuasion. From the third edition of *The New Ambidextrous Universe: Symmetry and Asymmetry from Mirror Reflections to Superstrings* by Martin Gardner. Published by Freeman, £10.95 (pbk), £15.95 (hbk).

The next theme of the book concerns the symmetry of embryos. Some embryos develop without bilateral symmetry from the outset. It is well known that the left-handed adults of the snail *Lymnaea* begin their lives with a laevotropic rather than the normal dexiotropic spiral cleavage. But it is less well known that the veligar larvae of gastropods are at least roughly bilaterally symmetrical, and the connection between the sense of early cleavages and the sense of the shell gland torsion is not understood. Some embryos acquire an early bilateral symmetry, probably because this is an automatic consequence of having two signalling centres in a cell mass such as the vegetal pole and the dorsal lip of an amphibian blastula. There is much evolutionary speculation about which axes or planes of symmetry in vertebrates are homologous to those in protosome invertebrates, and whether bilateral symmetry or asymmetry is primitive, a discussion that seems to me to be blissfully unencumbered by data.

In vertebrate embryos, there are ways of reversing the left–right asymmetry of the viscera. Fifty per cent of *Xenopus* embryos have *situs inversus* if they are treated during gastrulation with agents that interfere with cell contacts and adhesion, such as RGD peptides, heparinase or inhibitors of glycosylation. The same proportion of mice homozygous for the mutant *iv* gene have *situs inversus*. Also, about half of those humans homozygous for a related disorder, Kartagener's syndrome, associated with a defect in the dynein arms of cilia, may have *situs inversus*. The molecular causes of these changes are probably diverse, and may not necessarily be closely related to the normal breaking of bilateral symmetry in development. But these examples do show that inhibition of the normal mechanism does not reverse the normal asymmetry; instead it causes a loss of preference for the sense of asymmetry. Various models for normal development are discussed. All seem to depend on an asymmetrical molecule that can be aligned with the body axes and hence allow different processes to occur on right and left sides. Whether this really represents a bridge from molecular to organismic asymmetry depends on how big the asymmetrical molecule is, or, to put it another way, on which side of the Chothia gap it lies.

Yet another epistemological gap may separate the asymmetries of vertebrate embryos from asymmetries of cortical function in postnatal life. Anatomical asymmetries in the human brain are apparently more pronounced than those of other mammals. The prevalence of left-handedness is about 8 per cent in the overall human population, rising to 26 per cent in offspring of left–left matings — as usual in human biology there seems to be some genetic input, but it is not clear-cut. Despite inherited or acquired preferences for the use of a particular organ, these can later be overridden, as in people who have lost the use of their hands but have learned to draw using their mouth or toes.

I still suspect that the small perturbations likely to be responsible for the breaking of left–right symmetry are not very specific or easy to investigate. But fortunately, no book that jumps from spiral staircases to flatfish to dynein arms in a few pages can fail to be stimulating.

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