



100 YEARS AGO

Captain Dutton's valuable memoir on the Charleston earthquake of 1886 contains many accounts of the effects of this great earthquake on human beings. Nowhere could they be more vivid than in Charleston itself. "On every side," says one witness, "were hurrying forms of men and women, bare-headed, partially dressed, some almost nude [the earthquake occurred at 9.51 p.m.], and all nearly crazed with fear and excitement... A few steps away, under the gas-lamp, a woman lies prone and motionless on the pavement, with upturned face and outstretched limbs, and the crowd which has now gathered in the street passes her by, none pausing to see whether she is alive or dead...; many voices are speaking at once, but few heed what is said." ... Captain Dutton also gives many records of a feeling of nausea at the time of the earthquake; and, however excitable the observers may have been, these accounts are probably trustworthy, for this is not at all generally known to be a result of earthquake-motion.

From *Nature* 13 December 1900.

50 YEARS AGO

In the account in *Nature* of October 14 of machines which carry out strategic sequences of moves, it is stated: "No machine can learn from its mistakes — to improve the play the programme must be improved". It is, of course, true that a machine cannot learn unless it is provided with a programme or mechanism for learning. But it is quite possible to devise such a mechanism. Machines can be designed to make the best move at each step in a game of noughts-and-crosses or (in theory) draughts or chess. But when playing against a series of human opponents, such a machine may never do much better than draw. A good human player against the same opponents may score more wins by making unsound but more puzzling moves. Can a machine be made to imitate the human player? ... It can, by the inclusion of an empirical or statistical mechanism, in three units. One unit makes the machine experiment with different alternatives each time certain positions are reached; the second unit counts the results and relates them to the alternatives chosen; and the third steers the machine into the lines of play which have been winning most often.

From *Nature* 16 December 1950.

density and rigidity, and under tension. There is also no role for viscosity in Rayleigh's treatment, whereas Zhang *et al.*'s photographs on page 836, and indeed the whole of modern fluid dynamics, indicate the active influence of viscosity at boundaries. This is related to a further problem with Rayleigh's model: that a perturbation of any size leads to instability. That idea is roundly contradicted by Zhang *et al.*'s discovery of a stable static state.

An issue not addressed by Zhang *et al.* is the relationship between the experimental soap-film flow and a theoretical two-dimensional fluid. For a start, air is dragged along with the liquid film, and careful work has shown that this cause of energy dissipation is important for an effective two-dimensional description⁸. And the question of how thickness variations in the soap film are coupled to velocity changes has yet to be settled. Such effects are probably not very important in this experiment because, over short timescales, the thread experiences a nearly laminar flow. But even the simplest examples of vortex generation can hold some surprises^{9,10}.

The graceful undulations of the silk thread are reminiscent of the motion of slender-bodied organisms, such as eels and other types of fish^{11,12}, so it is tempting to suggest a connection. But the filament considered by Zhang *et al.* is not swimming in the conventional sense — if the support arm were removed, the thread would, of course, be carried downstream. The authors suggest that the static state is analogous to a gliding fish, but a comparison of the vortices created in similar flow conditions (Fig. 1)

provides little hope for any immediate biological insights into the mechanics of active swimmers. As von Kármán and Burgers emphasized in their 1935 review article¹³, swimming fish cast off counter-rotating vortices, which induce a jet-like flow running down the middle. The momentum carried off by this jet is in turn related to the forward thrust on the fish.

Zhang *et al.*² have shown that the one-dimensional flapping flag problem is experimentally accessible, and that it yields surprising results. It would seem that a full analysis of real flapping flags requires the development of new aspects of fluid-dynamic theory. Like any good experiment, it should provoke theoreticians, who were thinking about these questions before Edwin Abbott conjured up his two-dimensional world. ■

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Evolutionary developmental biology

Head start

John R. Finnerty

Some neat transgenic experiments show how the evolution of the vertebrate head stemmed, at least in part, from elaboration of controls on pre-existing genetic machinery.

What makes a vertebrate a vertebrate? Arguably, it is the head. All vertebrates have one, but our closest non-vertebrate relatives, the cephalochordates, do not. Clues as to how the vertebrate head came into being can be found among the genes that operate during development. The head's blueprint is somehow written in the genes, and its construction is accomplished by the process of development.

On page 854 of this issue¹, Manzanares and co-workers describe how they have investigated the genes involved, working with gene sequences from the cephalochordate amphioxus (to picture this creature, imagine a small fish that has no bony skeleton, no paired fins and, most importantly, no

head; Fig. 1). Manzanares *et al.* have assessed the head-forming potential of amphioxus gene sequences by introducing them into vertebrate embryos. Surprisingly, it seems that some of these sequences can perform developmental roles that are specific to head development in vertebrates. At first sight this is puzzling, because of course amphioxus has never evolved a head.

The answer to the puzzle lies in the patchwork nature of evolution. Evolutionary innovations blend novelty and antiquity — a relatively small number of serendipitous modifications are superimposed on a larger genetic legacy inherited from ancestors. According to this operating principle, the evolutionary origin of the head cannot

have been based exclusively on new gene sequences, but also on numerous pre-existing sequences. Indeed, the results of Manzanares *et al.* reveal that the invention of the head involved a combination of conservation and elaboration in the gene sequences that regulate development.

Two properties of a gene determine its function in development²: its spatiotemporal expression (where and when the protein encoded by the gene is actually produced), and its interactions with other genes. The spatiotemporal expression of a gene depends in part on *cis*-regulatory sequences. These are sequences of DNA which are not themselves transcribed or copied into messenger RNA, but which regulate the transcription of adjacent genes. Transcription is a necessary precursor to protein synthesis, so regulation of the process is a common mechanism for controlling spatiotemporal gene expression. Modifications to *cis*-regulatory sequences may be the most important proximate cause of morphological innovation during animal evolution³, and such changes do seem to underlie the invention of the vertebrate head.

During development, much of the vertebrate head is derived from two cell populations that do not occur in cephalochordates: neural crest and neurogenic placodes⁴. The neural crest contributes to many of the bones, muscles and nerves of the head and face. The neurogenic placodes contribute to most of the sensory organs, such as the nose and ears, and the associated nerves. Different populations of crest and placode cells contribute to different cranial structures depending on their location along the anterior–posterior axis. For example, the eyes must develop in front of the ears.

But how does a population of cells know its location? Its position along the anterior–posterior axis is specified by the expression of a particular class of developmental genes, the *Hox* genes⁵. Different *Hox* genes are expressed in different places along the anterior–posterior axis, a given *Hox* gene directing the cells in which it is expressed to adopt a certain fate appropriate to their location. Inappropriate expression of *Hox* genes, which can result from mutations in their *cis*-regulatory sequences, can cause an inappropriate structure to develop in a particular location. So the *cis*-regulatory sequences are critical to the spatially appropriate development of cranial structures.

Manzanares *et al.*¹ introduced *cis*-regulatory sequences from amphioxus into the cells of mouse or chick embryos. These transgenic regulatory sequences were fused to a gene encoding a reporter protein, which produced a visible stain in the embryo if the *cis*-regulatory sequences induced transcription. This method allows evaluation of the ability of amphioxus sequences to induce transcription in various vertebrate tissues.

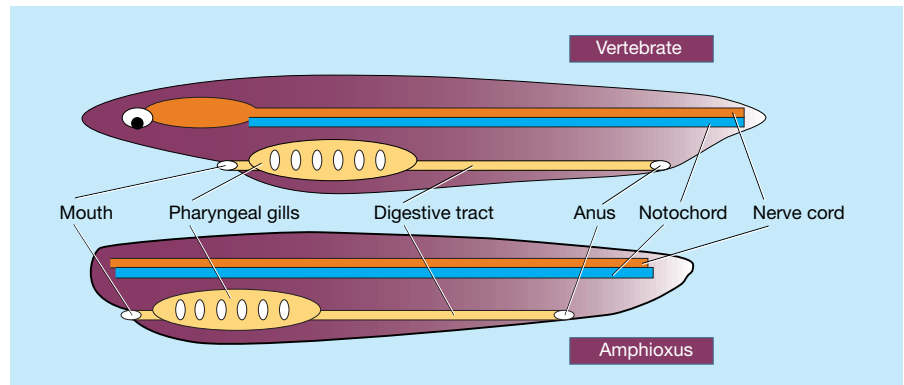


Figure 1 The cephalochordate amphioxus compared to a primitive vertebrate (similar to a modern-day lamprey). The overall construction of the organisms is very similar, with a dorsal nerve cord, a more ventral axial skeleton known as the notochord, and a ventral digestive tract. Both creatures have gills in the pharyngeal region, structures that are designed to capture food or remove oxygen from the water. The notochord extends right to the front of amphioxus, but the vertebrate has a prominent head at the anterior end, extending beyond the notochord. Early in development, human embryos have a notochord that subsequently becomes greatly reduced, giving rise to the discs between the adult vertebrae.

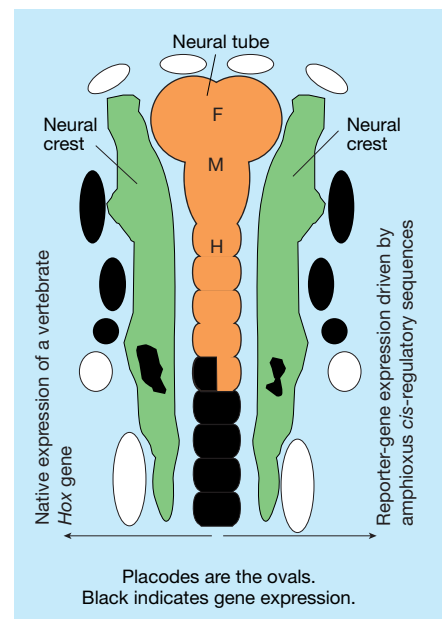
In both mouse and chick cells, the *cis*-regulatory sequences from specific amphioxus *Hox* genes were able to reproduce portions of the native expression of corresponding vertebrate *Hox* genes (Fig. 2). The amphioxus reporter was expressed in the developing hindbrain, the neural crest and the neurogenic placodes, even though amphioxus lacks both crest and placodes. As the authors say, this conserved pattern of expression most likely represents an ancient aspect of *Hox* expression that was present in the ancestral cell type from which neural crest and neurogenic placodes evolved. Where the amphioxus reporter expression differed from the native vertebrate expression, the difference could sometimes be

attributed to specific sequence differences in the *cis*-regulatory region. Unfortunately, it is not yet feasible to study gene expression directly in amphioxus, so the native expression of amphioxus *Hox* genes is not known.

This work¹ illuminates the two forces of greatest interest to the evolutionary biologist: stasis and change. Clearly, much change was involved in the evolution of the vertebrate head. For example, distinct expression patterns, attributable to changes in *cis*-regulatory sequences, are seen in the hindbrain. But there is also evidence of much stasis, including the preservation of ancestral patterns of gene expression, even as new cell types have evolved.

Insights such as these are possible only

Figure 2 Manzanares *et al.*¹ show that gene sequences from amphioxus can perform developmental roles specific to head development in vertebrate embryos. Three tissues are shown in this dorsal view of the head region of a vertebrate embryo: the neural tube, precursor to the nerve cord; the neural crest, which emerges from the dorsal neural tube; and the neurogenic placodes, which are formed from the epidermis overlying the neural tube. On the left is the native *Hox* gene expression driven by the vertebrate's own *cis*-regulatory DNA. On the right is the expression of a reporter gene driven by the *cis*-regulatory sequences of the corresponding amphioxus *Hox* gene. The amphioxus sequences duplicate much of the native vertebrate expression, including that evident in the neural crest and neurogenic placodes. The differences in the neural-tube expression can be attributed directly to differences in the DNA sequence of the *cis*-regulatory regions of amphioxus and vertebrates. The diagram shows the general pattern of cranial *Hox* expression, not of any particular *Hox* gene. Vertebrate *Hox* genes are normally expressed in specific segments of the hindbrain (termed rhombomeres), and in a subset of neural crest and neurogenic placode from the same axial level. F, forebrain; M, midbrain; H, hindbrain.



through the study of evolutionary diversity. An abundance of similar comparative studies will be required to reconstruct the causal connections between genome evolution, developmental evolution and morphological evolution. In the coming years, comparative studies may reveal the genomic and developmental bases for many of the most intriguing evolutionary innovations. For example, comparisons between lampreys and more advanced fishes may elucidate the origins of jaws and complex feeding habits. Comparisons between reptiles and mammals may reveal the origins of the middle ear and sophisticated hearing mechanisms. And comparisons between

reptiles and birds may tell us more about the origins of wings and flight. Clearly, there is no shortage of stimulating questions for the practitioners of evolutionary developmental biology.

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Condensed-matter science

Five-fold symmetry in liquids

Frans Spaepen

A complete description of the structure of simple liquids is missing from our understanding of matter. But new observations show that liquids contain many configurations with five-fold symmetry.

Understanding the structure of simple liquids is a fundamental, unsolved problem in the mathematical and physical sciences. Attempts to describe liquids as disordered crystals have all failed, and their description as dense gases (fluids) remains too complex. The best approach so far, though far from complete, is to describe liquids as dense packings of tetrahedral (four-sided) building blocks. On page 839 of this issue, Reichert *et al.*¹ report the first direct evidence for such polytetrahedral structures in a monatomic liquid trapped at a solid interface.

A complete picture of the short-range order in a liquid (between nearest neighbours) requires knowledge not only of the number and length of the bonds, but also of their directions. Consider, for example, the two 13-atom clusters shown in Fig. 1a and b. Both consist of 12 atoms surrounding a central one at an equal distance, but the two forms are quite distinct. The cuboctahedral configuration (Fig. 1a), in which the bonds form eight tetrahedra and six half-octahedra (composed of four triangles on a square base), makes up the face-centred cubic packing found in simple crystalline structures. The icosahedral configuration (Fig. 1b) consists of 20 tetrahedra, and is an important building block of the polytetrahedral model for monatomic liquids.

The atomic structure of a liquid changes over space and time, so conventional scattering experiments using X-rays or electrons or neutrons provide only directionally averaged information — specifically the distribution of interatomic distances. Such data already favoured the polytetrahedral

model, but Reichert *et al.*¹ provide valuable direct evidence for it. They captured some of the polytetrahedral configurations in liquid lead by aligning them against a crystalline silicon wall. They observed the characteristic five-fold symmetry of the bonds from the scattering of totally internally reflected X-rays, which are sensitive only to the structure of the interface.

Finding a simple structural description of liquids, such as ‘periodicity’ for crystals or ‘sparsity’ for gases, is a persistent challenge in condensed-matter science. It is now accepted that a liquid is not a heavily defective crystal or a random assembly of microcrystals, but a well-defined phase in its own right. This was demonstrated most dramatically in the late 1940s by Turnbull² when he showed that many simple liquids could be supercooled far below their freezing points

without crystallization occurring. This is possible only if the liquid structure is fundamentally different from that of a crystal. That crystals can be substantially superheated later reinforced the idea of a fundamental structural discontinuity between the crystal and liquid states.

Turnbull’s observation led Frank³ to suggest that the structural difference between crystals and liquids arises from liquids having polytetrahedral short-range order. Specifically, he pointed out that, if the interatomic forces act between the centres of the atoms, an icosahedral cluster of 12 atoms surrounding a central one (Fig. 1b) is more stable than a cuboctahedral cluster (Fig. 1a).

The face-centred cubic structure of many crystalline solids (Fig. 1a) maximizes the long-range density of closely packed spheres. Polytetrahedral packing can be viewed as an attempt to maximize the short-range density of a structure. The densest local configuration that can be created with hard spheres is a tetrahedron. Five tetrahedra can be packed around a common edge (shown in red in Fig. 1c), but they leave a gap of about 7°. Twenty tetrahedra can also be packed around a common point, or vertex, to form an icosahedron, which can also be thought of as 12 interpenetrating five-fold rings.

Five-fold symmetry is incompatible with long-range periodicity, so the polytetrahedral short-range order favours disordered or amorphous structures. The model that has been most successful at explaining scattering data from liquids is Bernal’s dense random packing of hard spheres^{4,5} and its computational successors⁶. Analysis of the short-range order in these models reveals ubiquitous polytetrahedral packing, in particular five-fold rings.

Moving the gap between the tetrahedra in a five-fold ring (Fig. 1c) requires very little energy. The thermal disorder of a liquid, the ease by which it flows, and the rapidity by which its atoms diffuse can be qualitatively understood by the redistribution of these gaps. The gaps are there because it is impos-

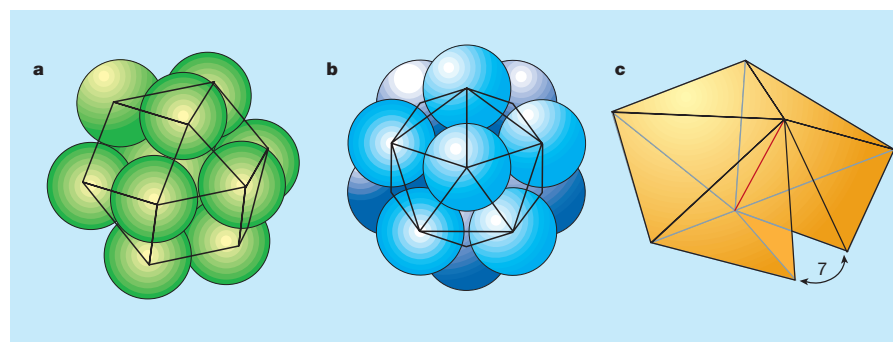


Figure 1 Structural building blocks. Twelve atoms surrounding a central one can form: a, a cuboctahedral arrangement, as in a face-centred cubic crystal; or b, an icosahedral arrangement, as found in a liquid. c, A ring formed by five tetrahedra sharing an edge, leaving a gap with an angle of 7°. The work of Reichert *et al.*¹ suggests that five-fold symmetry is ubiquitous in the structure of liquids.