If the superconductor were, like the Ising model, self-dual, then vortices and charges would necessarily behave in exactly the same way at the critical point. We would then have $\dot{N}_v = \dot{N}_c$, and the universal resistance would simply be the quantum of resistance for charge 2e Cooper pairs: $R^* = h/(2e)^2$. It turns out, however, that realistic models are not self-dual, and R^* differs from this value by a factor of order unity (*5*).

Quantum Hall systems seem to bear no relation to superconducting condensates. In reality, however, one can view the ordered state of a QHE system as a Bose condensate of composite objects consisting of electrons that have "swallowed" the vortices (*6*). Because of the peculiarities of quantum statistics in two dimensions, there is a second view, in which the duality of the QHE system appears as particle-hole symmetry (*1*) of composite fermion objects (*7*) consisting of electrons that have swallowed some, but not all, of the vortices.

There is tantalizing evidence both from experiment and theory that the quantum Hall localization transition may exhibit self-duality. Much more work is needed, however, to explore this fully.

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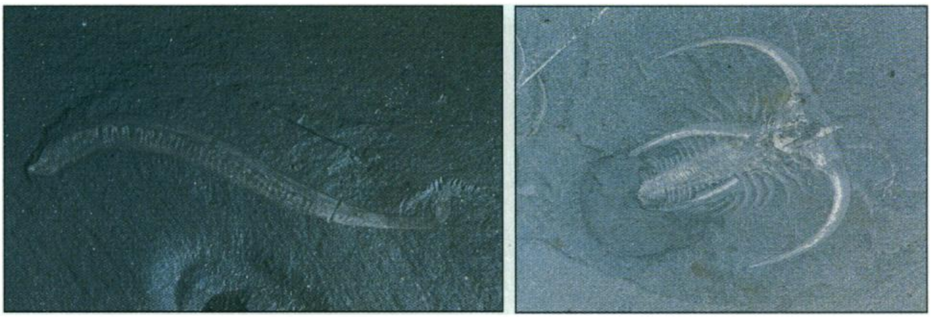
Animal Origins

Geerat J. Vermeij

When did animals first evolve and proliferate? If we could answer this question, we would know more about an extraordinary episode of evolution.

The traditional view of the origins of multicellular animals, supported by a literal reading of the fossil record, is that animals appeared about 565 million years ago (Ma) during the Vendian period of the latest Neoproterozoic era. Within 20 million years, by the beginning of the Cambrian period of the Paleozoic era, all of the major groups (phyla) had become established—the first deep burrowers, grazers, predators, and skeleton-building animals. Early comparative work on globin proteins led Runnegar (*1*) to postulate a much earlier origin of animals, between 900 and 1000 Ma. On p. 568 of this issue, Wray *et al.* now offer support for an even earlier origin and diversification of the major phyla—between 1000 and 1200 Ma—on the basis of the nucleotide sequences of seven genes in living species from 16 phyla.

Arguing that the rate of substitution of nucleotides is roughly constant, or clocklike, the authors of the new work used the post-Cambrian fossil record of vertebrates to calibrate observed differences in gene sequences among species by noting the time of occurrence of the last common ancestor of these species. Acceptance of their proposed ancient origin of animals hinges on the accuracy of the calibration and on the assumption that the rate of nucleotide substitution is constant. Wray *et al.* show that vertebrates do not differ from other animal groups in average rates of molecular evolution, and therefore that the calibration is reasonable; but the assumption of constancy is less secure. It may be, for example, that rates of molecular substitution speed up during times of diversification, when many evolutionary branches are undergoing rapid morphological change. Such acceleration could have occurred during the Vendian-Cambrian interval, before the period over which molecular rates of evolution were calibrated, as well as during later episodes of evolutionary proliferation in the Mesozoic and Cenozoic eras. Moreover, if morphological evolution generally speeded up beginning in Neoproterozoic time, as the fossil record strongly implies (*2*), then the divergence times calculated by backward extrapolation from the vertebrate record would be too early. Wray *et al.* point out that the assumption of constancy would have to be violated on a grand scale in order to wring a Vendian origin of animals out of their data, but they acknowledge that the actual time of divergence of phyla remains poorly constrained. Greater precision in this and other analyses of molecular divergence (*3*) can come only when the possibility that molecular evolution accelerates in most or all groups during certain intervals of Earth's history is closely scrutinized.



Even older than old. The major animal phyla appear in the rock record about 540 million years ago, in the form of fossils such as *Pikaia* (left), a chordate, and *Marella* (right), an arthropod. New molecular evidence suggests that these phyla actually diverged closer to a billion years ago. [Photos by C. Clark]

An origin of animals somewhere between 700 and 900 Ma, during the Early or Middle Neoproterozoic, seems likely on geochemical grounds. This was a time when oxygen levels rose in the ocean and atmosphere (*4–6*), perhaps causally linked to changes in Earth's tectonic regime and to the formation of continents (*7*). There was likely a rise in primary productivity (rate of fixation of organic matter) (*5–6*), which together with more oxygen made possible collagen synthesis (*8*) and higher levels of energy use.

Why are animals missing from the pre-Vendian fossil record? The answer may reside in their minute size. Although Neoproterozoic oceans supported bottom-dwelling seaweeds and single-celled planktonic algae (*2, 5, 9*), there is no indication that these primary producers were being consumed by grazing or suspension-feeding animals (*10*), and the only known potential animal traces are tiny horizontal tracks on, or 1 mm beneath, the surface of the seafloor (*11*). Pre-Vendian animals may therefore have been minute creatures crawling and sliding between grains of mud or sand on the seabed (*12*). Unmineralized animals prominent in

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such interstitial environments today are not known as fossils. Small animals of this type are consistent with the microscopic phase in pre-Vendian animal evolution predicted on embryological grounds by Davidson *et al.* It was in such minute forms that the great diversity of body plans characteristic of living animal phyla evolved (*13*).

The new work in no way diminishes the significance of the Vendian-Cambrian revolution, but it does separate the ecological innovations of that episode from the earlier evolution of the basic animal body plans. Contrary to some perceptions of the Early Cambrian (*14*), a large array of developmental patterns was already available when the momentous evolutionary spurt of the latest Neoproterozoic and earliest Paleozoic eras ensued. Much of this evolution, which may have been associated with a rise in primary productivity (*15*), is marked by the appearance of animals with a higher per capita energy use. Proterozoic animals relied on passive gas exchange and food intake, which took place over the whole body surface. They were therefore very small, flat, or tubular (*11, 16*). The elaboration of circulatory systems and active respiration and feeding enabled some Vendian and many Cambrian animals to become larger (*16*), to create water currents for feeding, to use sophisticated musculature for feeding and locomotion (swimming, walking, and burrowing), and to cover the body with a protective skeleton.

These innovations marked a significant ecological expansion of animals as well as an overall diversification of life, which continued episodically into the first half of the succeeding Ordovician period (*17*). As we learn more about the anatomy and environment of the earliest animals, the initial Proterozoic diversification of multicellular animals may prove to be an early episode in the stepwise economic expansion and proliferation that has characterized the history of life.

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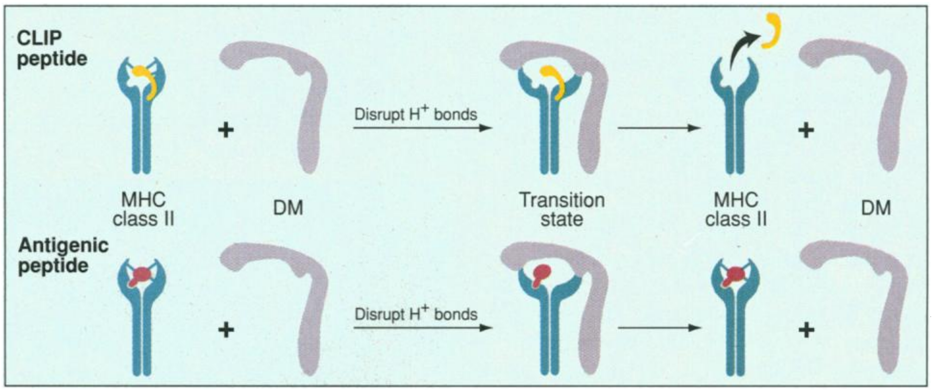
Out, Damned CLIP! Out, I Say!

Paul A. Roche

Major histocompatibility complex (MHC) class II molecules are the billboards of the immune system. Peptides derived from foreign proteins are inserted into MHC's binding groove and displayed on the surface of antigen-presenting cells (APCs). These peptides are then recognized by T lymphocytes so that the immune system is alerted to the presence of foreign material. One of the most hotly investigated topics in immunology is the mechanism by which these antigenic peptides are generated and bind to class II molecules within APCs. In this issue, a major advance in our understanding of this process has been achieved: Weber *et al.* (*1*) describe how the antigen-processing protein human leukocyte antigen (HLA)–DM (DM) facilitates the insertion of foreign peptides into the groove.

Antigenic peptides are generated by proteolysis of foreign protein within pre-lysosomal antigen-processing compartments in APCs. Newly synthesized class II molecules gain access to these antigenic peptide–containing compartments by binding to a protein known as the invariant chain (Ii). Ii directs and escorts class II molecules into these antigenic peptide–containing compartments. In addition, Ii also prevents peptides from binding to nascent class II molecules in the endoplasmic reticulum and Golgi apparatus, effectively blocking premature access of endogenous peptides to the peptide-binding groove of class II.



Removing a placeholder. CLIP is bound to class II molecules predominantly by hydrogen bonds, whereas most antigenic peptides are bound by both hydrogen bonds and other stabilizing forces (such as the interaction with a deep pocket shown here). DM binds and induces a conformational change that destabilizes the hydrogen bonds. CLIP then readily dissociates from the class II molecule, but the antigenic peptide is held in place by the additional binding interactions.

In the later stages of class II assembly, it is only a portion of Ii that blocks access of antigenic peptides to the groove. Ii is proteolyzed, but not all of the Ii protein is released from the class II molecule; a small class II–associated Ii peptide (called CLIP) remains bound to the class II molecule to act as a sort of placeholder. In fact, the crystal structure of the class II–CLIP complex is almost indistinguishable from a "normal" class II–antigenic peptide complex (*2*). Yet somehow CLIP, at one time bound to every class II molecule, is selectively removed from the class II peptide-binding groove and replaced with a foreign peptide. Indeed, the repertoire

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