BOOKS & ARTS

Switching on evolution

How does evo–devo explain the huge diversity of life on Earth?

Endless Forms Most Beautiful: The New Science of Evo Devo
by Sean B. Carroll
W. W. Norton: 2005. 350 pp. $25.95

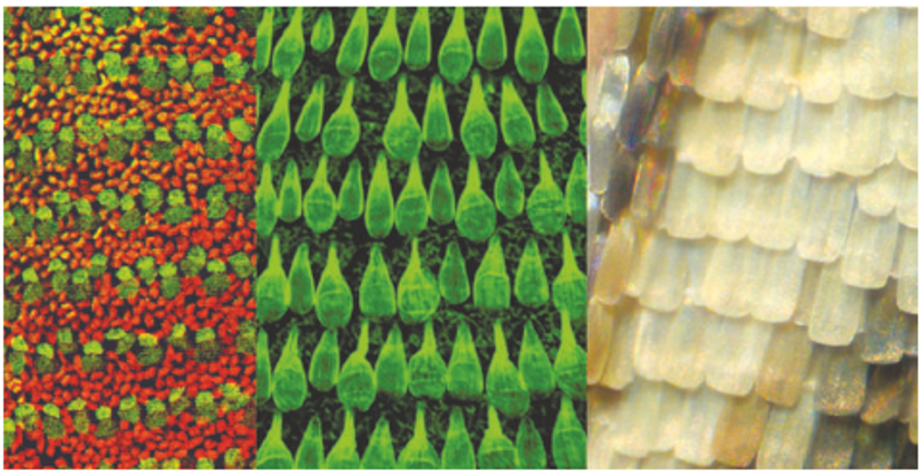
Jerry A. Coyne

Aimed at the interested lay reader, *Endless Forms Most Beautiful* (the title comes from the last paragraph of Darwin's *Origin of Species*) is a paean to recent advances in developmental genetics, and what they may tell us about the evolutionary process. The book's centrepiece is the unexpected discovery that the genes that control the body plans of all bilateral animals, including worms, insects, frogs and humans, are largely identical. These are the 'homeobox' (*Hox*) genes, whose products bind to the DNA of other genes, triggering a cascade of processes that ultimately yield eyes, limbs, hearts and other complex structures.

The evolutionary conservatism of these genes across long-diverged species is staggering. Only a jaded biologist could not be astonished at the ability of the *Pax-6 Hox* gene from mice (which triggers eye formation) to induce in the fruitfly *Drosophila* the formation of fly eyes all over the body, even on the wings. Remarkably, *Pax-6* helps to organize compound eyes in flies and camera eyes in both squid and vertebrates — structures once thought to have evolved independently. Another *Hox* gene, *tinman*, induces heart formation in both insects and vertebrates, and *Distal-less* controls the development of fly legs, fish fins and the tube feet of sea urchins.

Sean Carroll, a leader in the field of evolutionary developmental biology (evo–devo), is an adept communicator, conveying the intricacies of development in clear and lively prose. He ranges across the history of biology, linking the early concept of 'inducers' to today's more complex view of developmental networks, and explores the implications of evo–devo for the Cambrian explosion, the biology of dinosaurs, the brains of humans, and the striping of zebras.

Endless Forms Most Beautiful is a first-rate introduction to evo–devo for the scientifically curious, but its faintly self-congratulatory message — that the most important problems in understanding the evolution of development have been solved — left me feeling uncomfortable. Carroll presents his vision of the field without admitting that large parts of that vision remain controversial. I would have appreciated a caveat or two, and non-scientists may mistakenly believe that Carroll presents the scientific consensus about evolution and development.



S. PADDOCK, J. GATES, S. CARROLL/HHMI/UNIV. WISCONSIN

Differential gene expression, cellular protusions and scales combine to make butterfly wings.

Carroll emphasizes throughout that the evolution of animal form and complexity results from three factors. The first is modularity of organization: the ground plan of bilateral animals involves repeated segments that can evolve independently. The lobster, for example, is a veritable 'Swiss Army' crustacean, whose diverse appendages — antennae, mouthparts, claws, walking legs, swimming legs and tail — are all modified ancestral limbs. The second factor is that most animals share a small but similar set of 'tool-kit genes' that regulate the development of different modules. These genes, which produce regulatory proteins called transcription factors, are highly conserved in function; *Hox* genes are the canonical example.

But modularity and a shared genetic tool kit cannot by themselves account for "endless forms", because conserved genes cannot explain diversity. Carroll therefore repeatedly emphasizes his third thesis: that the main engine of evolution is not change in protein-coding genes but in the switches that control them. Changes in these switches — the promoters and enhancers in DNA that regulate the transcription of protein-coding genes — supposedly promote evolution by causing existing genes to be expressed at new times and places. This idea has been with us for a long time. Around 1970, the biologists Roy Britten, Eric Davidson and Allan Wilson were already arguing that the 'regulatory gene' is the locus of evolution, and the idea is now accepted wisdom among evo–devotees.

The evidence for this critical hypothesis, however, rests more on inference than on observation or experiment. Carroll first notes that dissimilar species can in fact be genetically similar: "Mice and humans have nearly identical sets of about 25,000 genes" and "chimps and humans are almost 99 percent identical at the DNA level. Since the sets of genes are so widely shared, how do differences arise?" His answer is the evolution of non-coding regulatory elements: whether you are a man or a mouse apparently depends solely on your promoters and enhancers. But the underlying statistics are deceptive; even a 1% difference in DNA sequence implies a substantial difference in protein sequence. We now know that humans and chimps have different amino-acid sequences in at least 55% of their proteins, a figure that rises to 95% for humans and mice. Thus we can't exclude protein-sequence evolution as an important reason why we lack whiskers and tails.

Carroll also claims that proteins are resistant to evolutionary change: they are often involved in many pathways, and therefore a change in protein sequence, while enhancing one aspect of the protein's many functions, could damage several others. In contrast, changing an enhancer or promoter can affect the expression of a single protein without altering its

structure, so such changes are more likely to be adaptive. He deduces that "the evolution of 'new genes' is not the explanation for the origin of diversity of most animal groups". Rather, "it is the switches that encode instructions unique to individual species and that enable different animals to be made using essentially the same tool kit," he says. "Evolution of form is very much a matter of teaching very old genes new tricks!"

But recent data cast doubt on this argument. Humans have about 32,000 protein-coding genes, fruitflies only 13,000. Clearly, the difference between these species involves the origin of new proteins: in fact, between 40% and 50% of our protein-coding genes have no known homologues in flies. So one could argue that the evolution of form is very much a matter of teaching old genes to make new genes. And, given the data, this cannot be difficult.

There are several ways that protein structure can evolve without injurious side effects. One of the most common is gene duplication. Extra copies of a gene can arise by unequal crossing over or by reverse transcription, allowing one copy to retain its function while the other assumes a new function. This process has been a major force in evolution. A large fraction of genes (at least 39% in humans) are members of families derived from repeated duplications and diversification of ancestral genes, a process that has yielded many evolutionary novelties. These families include the globins (such as myoglobin and the various haemoglobins); immunoglobulins; opsins (which led to colour vision in Old World primates); and olfactory receptors (almost certainly involved in the evolution of a keen sense of smell in land animals). Lactalbumin, which helps to produce milk in mammals, resulted from a duplication of lysozyme, and the crystallins of our eye lenses are ultimately derived from heat-shock genes.

This 'multiply and diversify' model of molecular evolution does not depend solely on the duplication of individual genes; the evolution of tetrapods apparently involved at least two bouts of whole-genome duplication. Many evolutionists agree with the geneticist Wen-Hsiung Li's conclusion that "there is now ample evidence that gene duplication is the most important mechanism for generating new genes and new biochemical processes that have facilitated the evolution of complex organisms from primitive ones". Carroll, however, seems too enamoured of his 'regulation is all' thesis to consider this alternative view.

There are other ways beside gene duplication that proteins have evolved adaptively. These include gene conversion, recruitment of genes to new functions (responsible for creating the antifreeze glycoproteins that allow fish to live in frigid waters), exon shuffling (involved in the evolution of blood clotting factors) and the addition of transposable elements to coding sequences. Finally, and simplest of all, we have many examples of adaptive changes of protein sequence between closely related species, including differences in the coat colour of mice, the digestive enzymes of herbivores, and the haemoglobins of high-altitude birds and mammals.

In contrast, the evidence for the adaptive divergence of gene switches is still thin. The best case involves the loss of protective armour and spines in sticklebacks, both due to changes in regulatory elements. But these examples represent the loss of traits, rather than the origin of evolutionary novelties. Carroll also gives many cases of different expression patterns of *Hox* genes associated with the acquisition of new structures (such as limbs, insect wings and butterfly eyespots), but these observations are only correlations. One could even argue that they are trivial. Given the centrality of *Hox* genes in development, it is almost inevitable that such genes are involved in the evolution of a new trait. Carroll's correlations, however, do not compel us to believe that changes in these genes are the key factor in the evolution of such traits. We now know that *Hox* genes and other transcription factors have many roles besides inducing body pattern, and their overall function in development — let alone in evolution — remains murky.

In the end, we simply don't know the relative importance of protein and non-protein changes in creating biological diversity. In many cases, both must have evolved in tandem, as different members of gene families are often expressed in different tissues or at different times. For example, the protein sequence of fetal γ-haemoglobin evolved adaptively to wrest oxygen from the mother's blood, but its gene is turned off after birth, probably by new regulators. Carroll's emphasis on gene switches may prove correct, but this awaits the labours of the next generation of biologists.

Although *Endless Forms Most Beautiful* is a lucid and valuable summary of evo–devo, it does proclaim a clever but still unproved hypothesis as central to the evolutionary process. As Carroll himself notes: "Simplification may indeed be necessary for news articles, but it can distort the more complex and subtle realities of evolutionary patterns and mechanisms." ■

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EXHIBITION

Fresh flowers

A New Flowering: 1000 Years of Botanical Art
At the Ashmolean Museum in Oxford, UK, until 11 September 2005.
www.ashmol.ox.ac.uk/ash/exhibitions/exh075.html

Colin Martin

Botanical artists face the dual challenge of capturing the essence of each plant species artistically, yet representing the plants and their stages of growth with absolute scientific accuracy. The veracity of great botanical art derives from artists' skill at producing work that both records plant species in technical detail and heightens viewers' perception of the natural world.

The exhibition *A New Flowering* is a clever juxtaposition of examples of contemporary botanical art, selected from a private collection assembled since 1990, with rarely exhibited works from the past millennium, chosen from the collections of the Ashmolean Museum and several Oxford colleges. It highlights both the novelty of current practice in botanical art and its continuity with the past.

SHIRLEY SHERWOOD COLLECTION

Setting the scene: the Scottish island of Ailsa Craig is the backdrop to Rory McEwen's painting of monk's hood.

Historic works on show include eleventh-century herbals, which name and describe plants and list their properties and uses; fifteenth-century illuminated manuscripts, whose borders are decorated with flowers; sixteenth-century printed books, illustrated with woodcuts; seventeenth-century books that are illustrated with engravings; and eighteenth- and nineteenth-century works, notably some particularly sumptuous volumes that depict freshly discovered plant species. Throughout, contemporary botanical images are displayed alongside related earlier works.