EVOLUTION: RETURN OF THE EMBRYO

BY JULIE ANN MILLER

A chicken and egg question confronted the group of 50 biologists who recently met in Berlin. Have the forces of biological evolution determined the patterns of an organism's development? Or have the available patterns of development shaped evolution?.

The correct answer, of course, is: Both of the above. But in a week of intensive meetings, filled with argument, far-flung examples and occasional insights, the scientists could only begin to map out the interactions between evolution and development and attempt to discover how extensive those interactions might be.

Drawing parallels between development and evolution was much in vogue a century ago — as captured in the tongue-twisting slogan still memorized by students, "Ontogeny recapitulates phylogeny." But interest shifted away from development in the period following the widespread acceptance of Darwin's theory of evolution. To scientists who viewed an adult organism as a set of optimized parts comprising the best possible design, development was irrelevant, explains Stephen J. Gould of Harvard's Museum of Comparative Zoology.

Now, a rebirth of interest in embryology has occurred among biologists who think about evolution, and many of them are beginning to believe once again that important clues to the evolution of a living organism lie in its development. While scientists are not readopting the exact rule that a developing organism works its way through ancestral forms, biologists armed with new analytic methods are resurrecting the spirit underlying the ontogeny-phylogeny motto.

The philosophical shift that has renewed interest in embryology is a concern for large and relatively sudden changes that take place in evolution. Darwin and his followers occasionally admitted that major, discontinuous changes occur, but the emphasis was squarely on natural selection among small changes and thus gradual evolution. Now many scientists believe that a species spends most of its existence in a steady state; the small changes are generally fluctuations that don't build into a trend. And the major changes, which can create a new species, all crowd into a relatively short period. Then the discontinuous change creates a "hopeful monster," which can adapt to a now mode of life.

"Both modes of evolution occur in nature; there is a full continuum from gradual to punctuated," says Tony Hoffman, a paleontologist from Warsaw. While most of the scientists at the meeting agreed, each holds a strong opinion about which end of the spectrum is the most important, and that opinion influences his or her choice of research topic.

"Embryology is now mainline biology again," says Gould, who was one of the originators of the evolutionary model called "punctuated equilibrium." Focus on sudden change in evolution provokes interest in biological development for several reasons. One is that changes in an organism's development can be envisioned as a mechanism by which a small genetic change can be amplified into a major difference in the adult. A small genetic change that delays or enhances pigmentation early in development of a moth, for example, can cause large differences in the color pattern of the fully grown caterpillar. Delayed metamorphosis may be the origin of the axolotl, which reproduces in a form resembling a salamander tadpole. And prolonged brain growth may be the major difference between monkey and human brain size.

Antonio Garcia-Bellido of the Universidad Autonoma in Spain described extensive experiments on mutant fruit flies in which the alteration of a gene carries dramatic developmental effects. These flies, called homeotic mutants, have one part of the body transformed into another. One mutant has a middle leg in place of the outer part of the antenna. Another mutant has two middle thorax segments and no hind thorax segment, so it has a second pair of wings in the place of balancing organs. Although these flies are fascinating examples of a complex shape change resulting from a simple genetic change, Garcia-Bellido points out that there is no direct evidence for such a change in any organism's evolution.

Another aspect of evolution that may be influenced by development is the observed limits on characteristics. There are no six-legged vertebrates, for example. "Nature is not chaos, neither is it a boundless continuum of forms," says Pere Alberch of Harvard's Museum of Comparative Zoology. "There are discrete classes of forms that can be recognized and organized in a hierarchical manner (for example, vertebrates, mammals, rodents, house mice)."

The "empty spaces" between discrete classes can be explained in several ways. They might be structures eliminated by natural selection, or they might be body characteristics that simply cannot be produced by the available processes of development. One argument against natural selection being the sole cause of limits, for instance, involves the shells of ocean mollusks. Their color patterns are limited even though they spend their entire lives buried in the sand, and thus the shell pattern should not influence their survival.

Other things that limit the characteristics were also suggested. Mimi Koehl of the University of California at Berkeley points out that physical laws constrain the size, shape and possible forms of behavior of an organism. Biomechanics often produces an alternative explanation for trends that could generate speculation about natural selection or development.

A purely mathematical treatment of patterns of gene expression, presented by Stuart Kauffman of the University of Pennsylvania, demonstrated the capacity of a large system to settle into distinct patterns. A gene system with 10,000 genes has $10^{3,000}$ possible combinations. Given certain simple assumptions about the rules of regulatory interactions, the system spontaneously confines itself to about 100 different patterns of gene activities. Kauffman suggests that these represent the approximately 100 cell types in a complex organism. "Many properties of an organism may be trivial, such as the small number of cell types and their stability," Kauffman says. "These are powerful, deep underlying constraints that do not need natural selection."

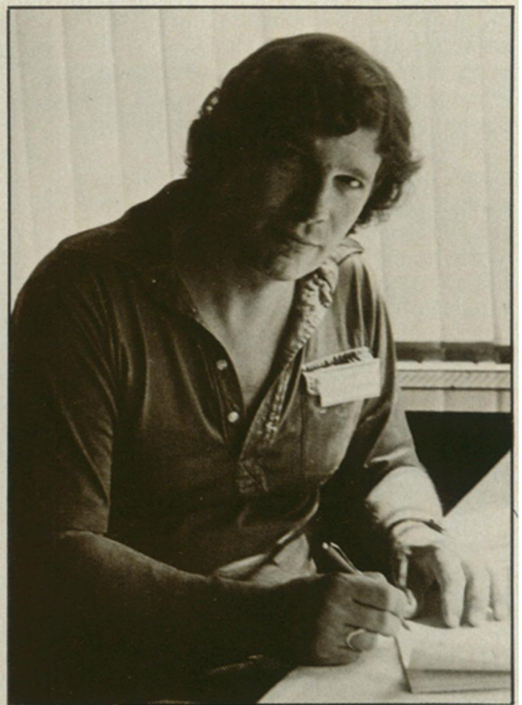
Gould summarizes eloquently: "The common lesson in all this states that organisms are not pieces of putty, infinitely moldable by infinitessimal degrees in any direction, but are, rather, complex and resilient structures endowed with innumerable constraints and opportunities based upon inheritance and architecture."

Convincing examples of constraints and opportunities were difficult to come by. In part, the scientists were frustrated by the limited understanding of how an organism develops. Something determines symmetry early in development; something instructs cells where to move, how often to divide, what characteristics to express and when to die. But the details have not been spelled out.

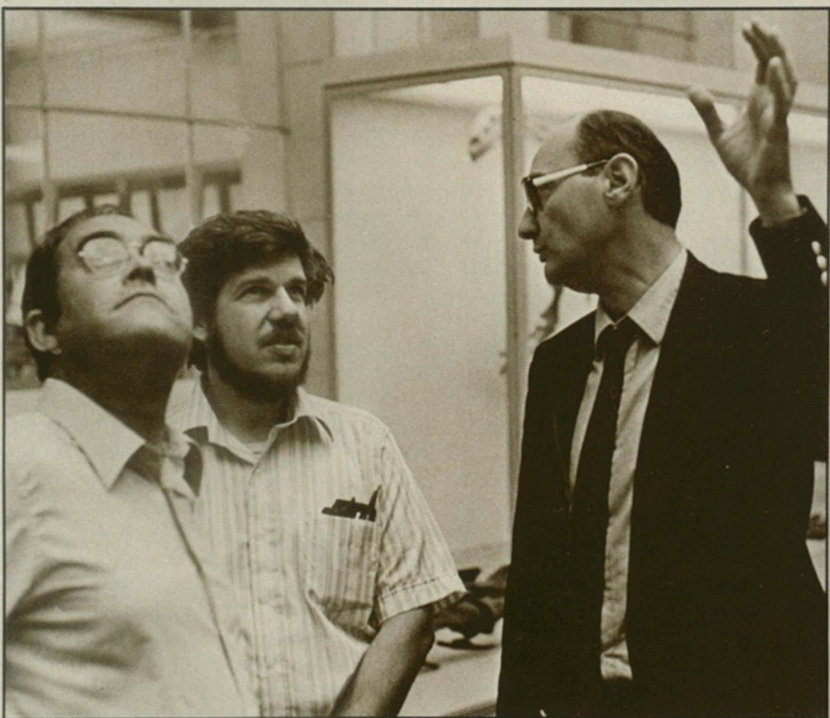
One evolutionary opportunity now being analyzed was described by Michael Katz of Brown University. There have been few "quantal jumps" in the evolution of the nervous system, he says, but there is one on which neuroanatomists agree. The corpus collosum, the bundle of nerve fibers that connects the two halves of the brain, is found only in placental mammals. "The corpus collosum is really something new," Katz says.

Exactly what is new about the corpus collosum is not the number of nerve cells or the number of nerve fibers, called

Current interest in the 'quantum jumps' of evolution has moved developmental biology into the spotlight. A select group of paleontologists and biologists in West Berlin recently discussed the interactions of evolution and development.



Incessant discussion of biological changes, big and small, fast and slow, filled the week of meetings. Mimi Koehl and George Oster (top left) continue conversation begun in workshop sessions. Stuart Kauffman (above) and Gabriel Dover and Michael Katz (below) review rapidly written workshop reports before the final general discussion.



Photos by Julie Ann Miller and Jeffrey L. Fox

Busman's holiday: On their free afternoon, many of the scientists visited the Museum of Natural History in East Berlin. Antonio Garcia-Bellido, Steven Gould and Armand de Ricqles (above) look up at the three-story-high Brachiosaurus skeleton. De Ricqles (right) describes to colleagues the dinosaur's lifestyle.

axons. It is that there is a new tract, a bundle of axons that travel together to a new destination. Based on studies of development, such as those by Jerry Silver at Case Western Reserve University in Cleveland, Ohio, Katz suggests an evolutionary scenario. During development glial cells, the support cells of the nervous system, form "slings" across the midline of the brain. Then the nerve cell axons cross this bridge. In some mutant mice the glial cells don't migrate across the brain midline, and no corpus collosum forms.

Katz hypothesizes that during evolution a small genetic change allowed the glial cell to migrate from one brain hemisphere to the other. The axons, already present, simply followed the new path. Norman Wessels of Stanford University points out that a developmental sequence is not necessarily the same as the evolutionary one. But nonetheless, it seems to offer a reasonable hypothesis.

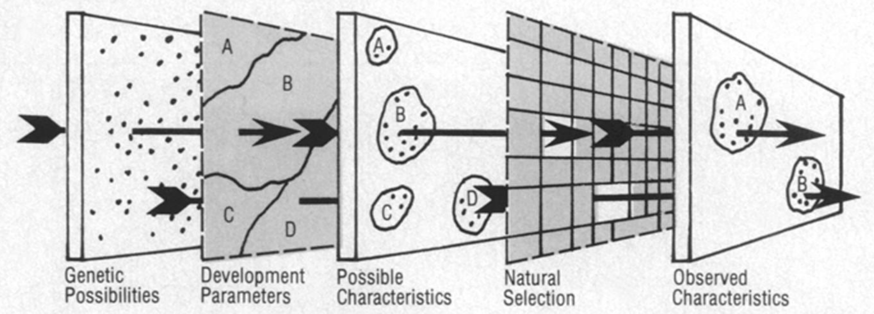
To some extent, the link between evolution and development lies in an organism's genes. One group of scientists considered whether current information about the organization of genes can offer insight into evolution of an organism's characteristics. Recent discoveries in molecular biology are promising—the surprising split genes, rearrangements during development, movable sequences and gene clusters. Still, in summarizing, Igor Dawid of the National Institutes of Health says, "We do not know the mechanisms by which gene activity affects the development of an individual animal; therefore, we cannot come to useful, specific conclusions regarding genomic correlates of evolutionary change at the morphological level."

The important advances yet to come in understanding development and evolution will have little to do with genes, predicted other scientists at the meeting. They say that new principles must be found at the more complex levels of organization. John C. Gerhart of the University of California at Berkeley summarizes this position: "...the role of genes is at too many removes from the developmental processes that actually give rise to the animal to provide an appropriate conceptual framework for posing the developmental questions that need to be answered." He draws an analogy to the 1930 quantum mechanical approach to genetics. That approach insisted that heredity could be best accounted for in terms of the interatomic forces that govern chemical bonds rather than in terms of the macromolecules, which later proved to be more important.

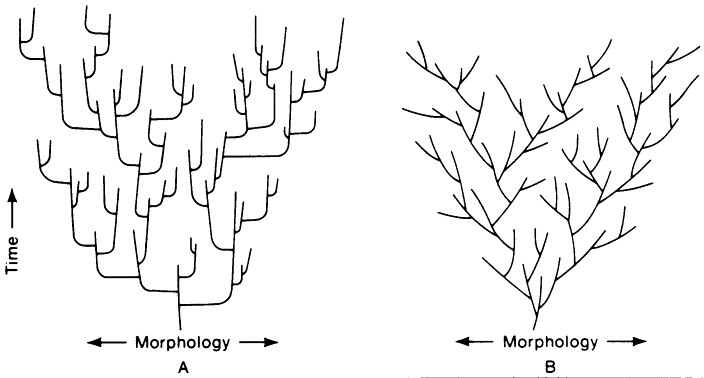
Turning from the chicken to the egg, it should be possible not only to learn about evolution from development, but also to learn about development from evolution. "Embryos participated in evolution too," explains Paul Maderson of Brooklyn College.

Different periods in the life cycle of an organism may be differentially sensitive to environmental influences. A complex lifestyle, for example that of metamorphosing animals, allows separate adaptations to the many biological demands—the need to feed, rest, reproduce and disperse. Most frogs and insects, for example, are adults before they disperse from their place of hatching, but bottom-living marine invertebrates usually disperse as larvae.

Alberch proposes that a continuum of genetic possibilities is limited first by the available modes of development. The resultant set of discrete and discontinuous characteristics is then pared further by the forces of natural selection.



Extreme theories of evolution: Punctuated equilibrium (A) and gradualistic evolution (B).



Macroevolution, Pattern and Process by Steven M. Stanley W. H. Freeman and Company ©

A striking example of the effect of evolution on development occurs among frogs. An amazing array of tadpole types all result in basically the same form of adult animal. At the meeting, Rudolf Raff of Indiana University described a recent reevaluation of data collected 40 years ago on a terrestrial tropical frog called Eleutherodactylus (see cover). This frog has no tadpole stage. Instead, a tiny adult the size of a house fly emerges from the frog egg. This major change in development frees the frog from needing a stable body of water for breeding and has allowed it to invade a new habitat.

A constellation of changes have occurred in development of this land frog, including some that have no discernible relationship to the absence of a tadpole stage. There is, for instance, dramatic change in the development of the blood vessels called the aortic arches. At different times during development most frog embryos display the six arches found in primitive vertebrates, but only three arches remain in the adult. Raff reports that the Eleutherodactylus avoids this recapitulation of the primitive form; only the adult structures are ever observed in the embryo. Timing changes of the land frog include a delay in the development of some skull bones and unusually early development of limbs. The limb buds appear before the formation of either the brain or the tail (which is lost before the tiny adult hatches).

Siamese cats are another example of unexpected linkages between traits. Gunther Stent of the University of California at Berkeley described work connecting abnormalities in the visual pathway of the cats to the pigment abnormality responsible for their distinctive coloration. Ray Guillery of the University of Chicago has shown that albino mutants of such disparate mammalian species as tigers, mice, rats, ferrets and mink have similar visual abnormalities. However, they are defective in a different gene involved in the synthesis of pigment. Stent says the most likely developmental link is provided by the pigmented cells that underlie the retina and shield the photoreceptors from stray light. Such traits linked in development pose the question whether they were linked in evolution.

Raising questions rather than answering them was the stated intention of the meeting. In that it certainly succeeded. Paul Maderson summed it up: "The most important thing we have done is simply being here. The embryo has been expressly invited back into the melee of evolutionary biology." □

A report of this meeting, including background papers and discussion group reports, will be available in November from the Dahlem Conference, Delbruckstrasse 4c, D-1000 Berlin 33, West Germany.