Biology Is Not Postage Stamp Collecting

Ernst Mayr, the eminent Harvard evolutionist, explains why he thinks some physical scientists have a problem with evolution

"The people who come from the physical sciences have an enormous amount of difficulty with evolutionary biology," asserts Ernst Mayr, professor emeritus at Harvard's Museum of Comparative Zoology. "This was Karl Popper's problem. At first he said the 'just so' stories of natural selection cannot be proven, and evolutionary biology is not really scientific. He said this again and again. But in the last 2 or 3 years he has taken it back because he finally realized that evolutionary biology is a different kind of science from the functional sciences, from the experimental sciences, but it is nevertheless science. It is not, as the British physicist Lord Rutherford contended, just postage stamp collecting."

In the year when many evolutionary biologists are publishing more or less scholarly tomes on Darwin in commemoration of the century since the great man died, Mayr is bringing out a more wide-ranging work, entitled *The Growth of Biological Thought*, the first major history of ideas in biology.* We met on 19 April, exactly 100 years since Darwin died, on the fifth floor of the museum built by the United States' most dedicated anti-Darwinist, Louis Agassiz. The question I asked of Mayr was, why, 100 years after Darwin, do some people, especially physical scientists, still have so much trouble with evolution?

There are important differences between the living world and the inanimate world, which, says Mayr, are frequently not appreciated by physical scientists. Without a grasp of these differences, evolution must remain beyond comprehension.

"Few physical scientists understand the uniqueness of individuals," suggests Mayr. "I was at a conference at the Wistar Institute in 1967 where a group of evolutionists and physical scientists, including mathematicians, met to ask, was 4.5 billion years long enough for the evolution of diversity and adaptation seen in the world? The physical scientists said no, we can calculate that the time is nowhere near sufficient. And we evolutionists argued that it was indeed sufficient."

The two sides disputed for 3 days, and then dispersed with nothing resolved. Mayr says that it wasn't until about 9 months later that he realized what "mistake" the physicists and their companions had made. "They assumed that all the individuals in a species are identical, just as all atoms of sodium are identical, for example. For them, a mutation has to spread through all the individuals in the population, and this must be followed by another mutation, and so on. If one were to adopt such a process of tandem evolution, no amount of time would be sufficient to account for the diversity we see now."

For Mayr, selection operating on many genes in concert and, crucially in his view, on a small population of individuals, can indeed give rise to a new species rather rapidly and thus to increased diversity. "You and I differ by more than our location in space," says Mayr by way of emphasizing his basic point. "If this fundamental issue is not appreciated, one cannot understand the power of natural selection."

Population geneticists are also the object of some criticism along these lines. "Many geneticists still define evolution in terms of changes in gene frequencies, thus demonstrating that they do not understand that the individual as a whole is the target of selection, not individual genes." Mayr describes evolution as being composed of two parts. One is "vertical evolution," which might produce shifts in adaptation. And the second is "horizontal evolution," which leads to the origin of different species. It is horizontal evolution that generates the diversity of form so characteristic of the living world. "When you bring this to the attention of geneticists they will say, I agree with you, and then when they write their papers they will just ignore it again."

The domain of the origin of species, for Mayr, is in the real world of real populations of individuals. He is therefore frustrated by the experimental world of some population geneticists. "Their techniques determine the questions they ask," he says. "Most of them work with closed populations, flies in a bottle, mice in a cage, and so on. If gene flow occurs—a mouse escapes, for instance—the whole thing is thrown out. This is why more and more geneticists now study natural populations."

Such sharp criticism might surprise those who are aware of Mayr's role in the marriage between geneticists and naturalists in the 1930's and 1940's, known as the "modern synthesis," that marked the new age of Neo-Darwinism. "I had thought that with the modern synthesis everything was straightened out and that there were no more major problems," reflects Mayr, "but I was wrong in assuming that all geneticists understood the importance of individuals in selection. The discussions of the last 20 years, including some things in an issue of *Nature* I read today, show that they don't."

Mayr is also puzzled by the mathematical geneticists' conviction that by doing calculations something meaningful necessarily results. He recalls a meeting almost 30 years ago when R. A. Fisher, one of the founders of the discipline, was being besieged by younger evolutionists who were fired by all kinds of recently discovered complex genetic interactions. At the end of the second day when, by Mayr's account, Fisher had been thoroughly beaten down by the Young Turks, Fisher said with a great sigh of resignation, "Well, if you are right about all these things, I no longer can calculate it."

Fisher's response indicates to Mayr the difference in outlook between a mathematician and a naturalist. The story reminds Mayr of another example. "Two years ago I saw a paper in the *Proceedings of the National Academy of Sciences*, and the author wrote, 'Let's assume the gene has a constant selective value; let's assume there is no gene flow from any other population.' He made about five such assumptions, each of which was equally unrealistic, and then he went on to prove something very beautiful mathematically, but it was meaningless."

Mayr realizes that a mathematical analysis is in many cases very valuable, but he feels that it is frequently extended

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beyond the cautious application that is necessary to obtain realistic conclusions.

Returning to the apparent disharmony between the biological and physical scientists, Mayr emphasizes that there is no conflict between the sciences concerning the applicability of physical laws. "Vitalism is dead and gone. There isn't a process in a living organism that isn't completely consistent with any physical theory. Living organisms, however, differ from inanimate matter by the degree of the complexity of their systems and by the possession of a genetic program."

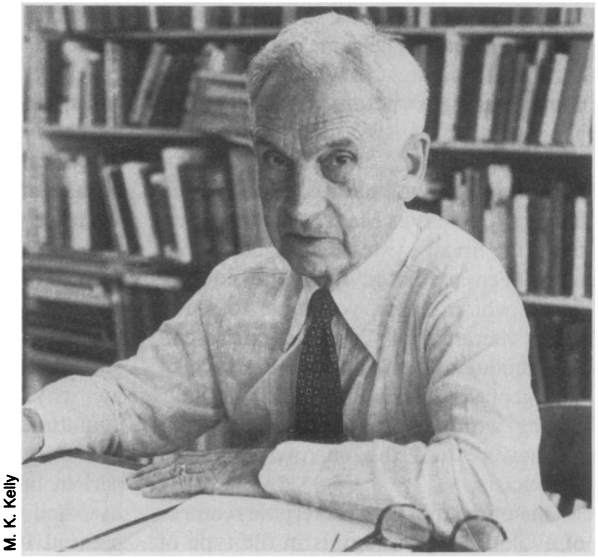
Complexity per se is not a mark of living nature but, by comparison with the inorganic world, complexity is highly developed. From the level of the macromolecule, through the components of the cell, the cell itself, organs and the individual, and up through the social mix and the surrounding ecosystem, complexity abounds. Moreover, says Mayr, it is a highly interconnected complexity, a mutual adaptation of parts that is unknown in the inanimate world.

The core of life is, of course, the genetic program that directs the formation of each individual. "The possession of a genetic program confers two special properties on living things," says Mayr, "history and teleonomy."

Before Darwin, scientists and philosophers believed in a direction or purpose in nature and its processes. The theory of natural selection removed teleology from nature, but nevertheless leaves the special property of teleonomy in the developing organism. The genetic instructions packaged in an embryo direct the formation of an adult, whether it be a tree, a fish, or a human. The process is goal-directed, but from the instructions in the genetic program, not from outside. Nothing like it exists in the inanimate world.

The genetic program that specifies the construction of an individual is not simply a package of instructions necessary for building a member of that species. It is the product of descent through evolution, a legacy that, for instance, is revealed in the transitory appearance of the gill arch stage in the development of every mammal. When the ancestors of the mammals were converted from aquatic to land animals they retained a lot of their ontogenetic pathways, particularly the early ones. To start from scratch and totally rebuild the ontogenetic process would have been far more expensive than to build on the old foundations.

Every genetic program therefore carries with it the experience of its ancestors, an experience upon which natural selection builds and which must constrain innovations that are possible. "This is central to biology and unique to it," says Mayr.



Ernst Mayr

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M. K. Kelly

Evolution is of course a historical process, and its extreme dependence on stochastic as against deterministic process makes prediction impossible. "If you had stood on the earth at the beginning of the Cretaceous [135 million years ago] and seen dinosaurs all over the place, you could not have predicted that the miserable little things that came out only at night would eventually take over when the Cretaceous came to an end. You can predict the next appearance of Halley's comet, but you can't predict changes in biological diversity. Such uncertainty is typical of evolution."

Physicists are interested in evolution too, the evolution of the universe and the solar system, for instance. But, insists Mayr, the processes in the physical and biological worlds are not the same. "I've been to several conferences where physicists have claimed that evolution in the universe is the same as biological evolution. I finally rebelled against that, and eventually tabulated some of the differences."

For instance, says Mayr, rates are quite different in the two realms. "In physical phenomena, rates are rather constant, whereas in biological evolution they are incredibly variable. Look at the Isthmus of Panama, which, when it was formed about 3.5 million years ago, divided into two what previously was a single ocean. Some species on either side of the barrier have remained indistinguishable whereas others have evolved so far as to become different genera.

"There are lagoons around Lake Victoria in Africa, one of which was separated from the lake about 4000 years ago. Of the six species of Lake Victoria fish in the lagoon, five have become new species. At the other extreme there is *Limulus* (the horseshoe crab) and *Nautilus*, neither of which has appreciably changed for at least 100 million years and perhaps as long as 250 million. You can see, the rates of biological evolution are extraordinarily variable, differing by three to five orders of magnitude. This would be extremely unusual in a physical process."

Another point of departure is in the mode of change. "In cosmic evolution changes are generally continuous," suggests Mayr. "Every once in a while there might be the origin of a nova or something, but generally it is a continuous process. In biological evolution, when each new generation arises, the formation of a new individual results in a new assembly of genetic material, and the process of selection starts anew." In this important sense, says Mayr, biological evolution is a discontinuous process.

Mayr is supremely skeptical of the dominant role of the reductionism which is the hallmark of the physical sciences. "This reductionism has led to what David Hull calls 'the arrogance of the physicists.' They say, yes, you biologists deal with complex things, but the ultimate explanation will be supplied by the level at which we study." The tremendous emphasis on particle physics, he says, is supposed eventually to make everything make sense. "I strongly disagree. They might find out all about particle physics, but it won't shed a single bit of light on, for instance, how the nervous system works or how ontogeny works. Complex systems have to be studied at high levels of complexity."

Complex systems are usually more than a simple sum of their parts. A set of genes, for instance, interacts to yield an intricate and integrated product that cannot be discerned from a shopping list of the components. The same can be said of a troop of primates, in which a deep and complex social structure forms. "Popper has recently said, 'We live in a world of emergent novelty,' and this is very important in studying nature, especially in biology," observes Mayr. "New properties turn up in systems that could not have been predicted from the components, which means you have to study things hierarchically. Reductionism can be vacuous at best, and, in the face of emergence, misleading and futile." Strong words, both for the "arrogant physicists" and the narrowly focused geneticists.

One of the most characteristic features of evolutionary biology is in the type of questions it asks. Every issue in biology has two facets: a functional facet, in which one asks, "what?" and "how?" questions; and an evolutionary facet, in which one asks, "why?" questions. "You can ask, why are certain organisms similar to each other, while others are utterly different?" says Mayr. "You can ask, why are there two sexes in most species of organisms? Why is there such a diversity of plant and animal life? Why are the faunas of some areas rich in species while those of others poor? Asking 'why?' questions is the major task of evolutionary biologists."

The "why?" question has little or no part in the world of the physical scientist, and the taboo against it was impressed on the biologists. "It was regarded as an Aristotelian question and quite out of place," says Mayr. "But it is now legitimate, as well as necessary, to ask, why?"

Many physical scientists have inferred a tendency to vitalism in their biological colleagues' insistence that living nature is different from the inanimate world, and until a few decades ago this might have been correct in some cases. "Physical scientists must understand that biologists are not disclaiming physical phenomena," urges Mayr. "We are not setting up vitalism. We are not trying to produce a metaphysics. We simply claim that in complex, historically formed systems things occur that do not occur in inanimate systems. That is all that is being claimed."—Roger Lewin

Gene Family Controls a Snail's Egg Laying

The marine snail Aplysia *displays a stereotyped egg-laying behavior which appears to be under the control of a family of related genes*

The application of recombinant DNA technology to neuroscience is still in its infancy, but its promise of novel products is already being fulfilled. A recent example, tantalizing in its putative generality, comes from the combined efforts of the laboratories of Richard Axel, James Schwartz, and Eric Kandel, at Columbia University, New York. Early results* reveal insights into the organization and expression of a gene that is important in behavior of the marine snail *Aplysia*.

One of neuroscience's most fertile areas of research is in the discovery and characterization of behaviorally important peptides, of which the list stands currently at around 25. And one of the most intriguing features of neuroactive peptides is that, in a surprising number of instances, several peptides are coded for by the same gene, the resultant polyprotein being processed to release the individual peptides. A great deal remains to be discovered about the scope of action of neuropeptides, but it seems likely that under certain circumstances different combinations of such peptides might produce subtle variations on behavioral themes.

What the Columbia researchers have discovered is a family of genes in *Aplysia*, each member of which apparently has the potential to code for a small complement of neuropeptides. The genes are related in that each codes, among other things, for a peptide that initiates egg laying, or at least codes for something similar to the so-called egg-laying hormone (ELH). Axel, Schwartz, Kandel, and their colleagues think that different aspects of the snail's reproductive behavior might be elicited by the expression of different members of the gene family, depending on the nature of the peptides produced in association with ELH.

Aplysia is a simple organism, being blessed with only 20,000 central nerve cells which are arranged in four symmetrical pairs of ganglia—the cerebral, buccal, pleural, and pedal—and a single asymmetrical abdominal ganglion. With so limited a nervous system, it has been possible to relate the function of specific cells to certain behaviors. The extensive documentation of *Aplysia* behavior has been particularly useful in Kandel's earlier work. But perhaps the greatest advantage the snail has to offer is the large size of its nerve cells and the very large amount of genetic material each contains. For instance, one nerve cell may carry more than 1 microgram of DNA, which is up to 200,000 times more than that in other somatic cells.

In spite of *Aplysia*'s special endowments, conventional neurochemistry still has a problem in addressing some of the most important questions. Many of the interesting peptides are active at astonishingly small concentrations, and so it is difficult to learn very much about them when normal techniques are used. The tricks of recombinant DNA technology offered a way around this problem and so Axel, Schwartz, and Kandel began mulling over the idea of some kind of collaboration more than 2 years ago. When Richard Scheller arrived in Axel's laboratory from the California Institute of Technology late in 1980, he initiated a project that rapidly yielded results. The Columbia team was joined later by James Jackson and Linda Beth McAllister.

Egg-laying hormone was chosen as the target peptide in the project for a number of sound practical reasons. The peptide was known to be released from the bag cells, which are a pair of homogeneous clusters of neurons attached to the abdominal ganglion; access to source tissue would therefore be relatively easy. There is a rich background of information on the behavioral effects of ELH. The hormone is manufactured at relatively high concentration; therefore the chances were excellent that the messenger RNA could be isolated and the search for ELH genes could be undertaken.

Success was swift in coming. ELH messenger was used to fish out an ELH gene from fragmented DNA. And this gene was then used as a very specific

*Cell 28, 707 (1982).