Molecules Come to Darwin's Aid

Evolutionists welcome the support of molecular biologists, but insist that the newcomers must first learn something about evolution

"I used to think evolution was just a question of history having nothing to do with my kind of work," comments David Baltimore, a molecular biologist at the Massachusetts Institute of Technology. "But when you look at the detailed structure of the mammalian genome you can't help but realize you are looking at history. I now find myself puzzling over evolutionary questions continually."

Baltimore was speaking at a recent meeting of the American Academy of Arts and Sciences which addressed the issue of "Darwinism: The expanding synthesis with molecular genetics." The current explosion of information about the detailed structure and organization of genes as revealed by DNA sequencing has brought molecular biology face to face with evolutionary biology with peremptory speed. "Anyone who wants to sequence DNA had better be an evolutionist," cautions Baltimore.

There is no question that molecular biology will be a highly effective new tool for analyzing some important questions in evolutionary biology, and undoubtedly it will allow entirely new questions to be addressed too. But what is currently in some doubt is, now that the two disparate disciplines confront each other directly, will there be a rapid and harmonious marriage? Or will there be a period of uneasy bickering while each gets to know the other a little better?

The meeting was held as the academy's commemoration of the centenary of Charles Darwin's death. "We wanted to honor the event in some way," says Bernard Davis, one of the organizers, "but we wanted to focus on new directions rather than review the past. It seems obvious to me that molecular genetics is not just strengthening evolutionary biology. It is also providing a new foundation. We are at the beginning of a grand new synthesis in evolutionary biology." Davis is a microbiologist at Harvard Medical School.

When geneticists and natural historians resolved their differences and combined their efforts in studying evolution in the 1930's and 1940's, there emerged the powerful "Modern Synthesis," a term coined by Julian Huxley, which became a unifying theme in biology. Selective inheritance of genetically based variation then became accessible to scientific analysis. Genetic variation was seen to be rooted in reassortment of genes through meiosis and sexual reproduction; later, point mutations in the DNA code of the genes was recognized as another source of change. Evolution then came to be viewed in part as a shift in the frequency of genes within a population, according to the differential beneficial effects of those genes.

The advent of recombinant DNA technology permitted a previously unattainable dissection of genetic material through DNA sequencing, an attack that has revealed the extraordinary nature of genomes in higher organisms. "Genetics has changed from being an inferential science to being a direct visual science," says Philip Leder, a molecular biologist at Harvard Medical School. "We can now look at genes and determine their structure in detail."

This ability to examine genetic material in close focus may, as Davis anticipates, lift the established Modern Synthesis to a fundamentally new level, to a grand new synthesis. But there is a palpable concern on the part of evolutionists that the newly accessible stories written in fine molecular print will present an irresistible—but not necessarily useful—reductionism at a time when pluralism is reasserting itself with beneficial effect in evolutionary biology.

> "... the beginning of a grand new synthesis in evolutionary biology."

"Darwin was interested in diversity in the natural world," says Lawrence Bogorad of Harvard. "Now, we are looking at the same problem at the molecular level." This statement might be taken to imply that the grand new synthesis is already complete, but its reductionist claim is challenged by Lynn Margulis, an evolutionary biologist at Boston University. "The big question is the relation between what molecular biologists measure and the processes of evolutionary change in populations of organisms," she cautions.

There is no doubt that data on the difference in nucleotide sequence on DNA's between related species will provide a valuable access to the molecular clock, an access that will be used in more accurate reconstruction of phylogenies, once the highly complex kinetics of the clock have been resolved. But, says Margulis, "The changes in the molecules do not necessarily directly reflect the evolutionary history of the group from which they were taken."

David Pilbeam, a paleoanthropologist at Harvard, is delighted that molecular biologists are beginning to think about evolution and anticipates tremendous advances from it. But he also believes that molecular biologists have a very naïve view about evolution. "They have the simple notion that it is all beads on a string," he says. "The important answers will be much more complex than they imagine."

The same kind of reservation is expressed by Rudolf Raff, an evolutionary biologist at Indiana University. "Evolutionary biologists are interested in the shape and behavior of organisms. Molecular biologists are much too reductionist for this. They try to reduce everything to a linear sequence and yet what we want to know about is something three-dimensional through time."

Davis counters the accusation of reductionism by saying that "evolution proceeds at every level, and each level is part of the whole problem. You have to study every part if you are going to solve it." Bogorad agrees, and says that "the organism is an integration of all levels of evolution. You can't say that any particular one of them doesn't count."

The exchanges at the recent meeting clearly exposed the reductionism-holism axis as a key point of contention in the tentative marriage between molecular biology and evolutionary biology. Evolution is a hierarchical process operating at several levels, each important in its own right. Nevertheless, it is prudent to ensure that analytical tools are applied only at appropriate levels. The trick is to agree which levels are accessible to which tools.

0036-8075/82/0604-1091$01.00/0

Edward O. Wilson, an evolutionist at Harvard, marvels at the emerging picture of higher genomes. "It surely impinges on the wider issues of evolutionary biology," he says. "We cannot fail to be excited and stimulated by it. But first you can wonder at it for its own sake." With his adept gift for graphic metaphor, Wilson describes the traditional, and now superseded, view of the genome as "a relatively uniform, unchanging landscape of stable elements." Now, he says, you have to think of "a rainforest with many niches occupied by a whole range of elements, all parts of which are in a dynamic state of change."

This "microbiogeography of the genome" must be understood in its own right, says Wilson, who helped organize the academy meeting. "It is a microcosmic world. It is of equal interest to evolutionists as is the problem of speciation." Genes and alleles can no longer be thought of as simple entities. The genome is a mélange of replication units, some of which constitute the encoding of an organism while others might be the product of the innate replicating ability of certain nucleotide configurations.

The immediate image derived from a glimpse into this microcosmic world is that genetic variation—and ultimately, phenotypic variation—is supplied from a deeper pool of variable elements than had previously been supposed. There is striking potential for modular change in the assembly of new proteins through the shuffling of coding regions in split genes. The propensity of some genes to produce copies of themselves which are then located at distant parts of the genome generates raw material that might be available to the processes of evolution. Some of these copies might retain their function, but perhaps be expressed at a different time in development or in a different tissue, depending on where they are relocated. Others might accumulate structural mutations that inactivate them, and so become pseudogenes. Still others might lose their noncoding regions en route back to the genome, and thus become "processed genes" (*Science*, 28 May, p. 969). The eponymous transposable elements can shift sections of DNA from one part of the genome to another, switching genes on or off as they pass. And huge families of repeated sequences seem able to multiply and move with alacrity.

"All of this appears to imply that the genome is in a state of turmoil in evolutionary time," says Leder. "The dynamic state of the genome will have to be taken account of in any new evolutionary synthesis." Leder's description of the genome's apparently endless capacity to change caused some people to wonder how genotypic identity might be maintained. "Selection is merciless," he responded. "It preserves what is necessary for survival."

In addition to movement of genetic elements within the genome, it is clear that the evolution of cells in higher organisms has involved the migration of genes between the genome and organelles such as mitochondria and chloroplasts. The entangled operations of nucleus and organelles betray a long and complex history. In Margulis' view, the cell is like a community of organisms, the integrity and history of which are too often ignored by molecular biologists, she says.

Molecular biologists still don't understand evolution.

Although Wilson is excited by the current revolution in molecular biology and professes himself optimistic that "within a few years we will begin to see some answers to evolutionary questions at the molecular level," he considers the major issues in evolutionary biology to be as yet beyond the reach of molecular analysis. "It doesn't have much to say about speciation, about macroevolution or about the rates of evolution." Davis, naturally, is bullish about prospects for tackling these issues and predicts, for instance, that "molecular biology will shed more light on the kinetics of evolution and its mechanism than paleontology will." Harvard's most vociferous spokesmen in support of paleontology, Ernst Mayr and Stephen Jay Gould, unfortunately were out of town and therefore unable to respond to the challenge.

Perhaps the key focus of evolutionary thought at the moment concerns the limits of natural selection. "Is it all powerful?" asks Wilson. "Can it mold anything in an organism under the right circumstances? Or are there important constraints in the embryological development of organisms that proscribe the range of possibilities?" The answer to this crucial outstanding question, says Wilson, lies between molecular biology and traditional biology.

"The point of contact," offers Raff, "is through embryology. That is the black box in which genes make organisms." Comparison between the product of structural genes in humans and chimpanzees shows a similarity compatible with their being sibling species, says Raff, and yet morphological differences have led taxonomists to assign them to different families. "It is clear that the important events of organismal evolution must affect the developmental program, and it begins to look as if these are under the control of relatively few genes."

The meeting found ready agreement that, yes, the mechanism of development is the key to important evolutionary change. And there was equal agreement that so far molecular biology possesses little with which to prise open the black box. The homoeotic mutants in *Drosophila*, in which the morphology of one segment might be transformed to that of another, are a start, says Raff. "Ultimately, evolutionary mechanisms will probably be explained in terms of gene structure and rearrangements," he guesses, "but there is a very long way to go."

In championing this new synthesis between molecular biology and evolutionary biology, Davis is hoping for more than just a productive marriage between disparate disciplines. "The public focuses on the fossil record and its imperfections," he says. "Perhaps it would be better to refocus on the new foundation provided by molecular genetics, with its directly testable predictions about evolution. Molecular genetics surely gives a much better defense of Darwinism than is offered by paleontology."

Armed with the weapons of molecular biology, evolutionists can feel emboldened enough to regard as outdated the phrase "the theory of evolution," says Davis. "We should refer to Darwin's law, as we do to Newton's law," he asserts. "It might be subject to modification in detail, but it has as solid a foundation as one could wish for."

Strong words, and ones that will give heart to many biologists worried by the prevailing unease over the teaching of evolution in the United States. But the new synthesis that Davis aims for will not be achieved readily. For one evolutionist at the meeting, the fact that Davis spoke about "Darwin's law" was yet another demonstration that molecular biologists still don't understand evolution. "There can be no such laws in biology as there are in physics. The nature of the processes are quite different."

Problems of semantics and lack of familiarity of one world by another will make for a slow and difficult beginning to the relationship, but eventually it will surely thrive.—ROGER LEWIN