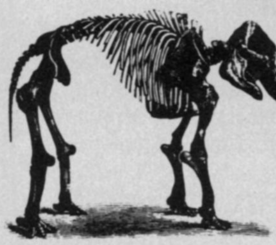
EVOLUTION



A THEORY EVOLVING

The neutrality theory, a 'non-Darwinian' alternative, has been fighting for survival in a hostile climate. Will it stand, fall or merge with existing theories?

by Janet H. Weinberg

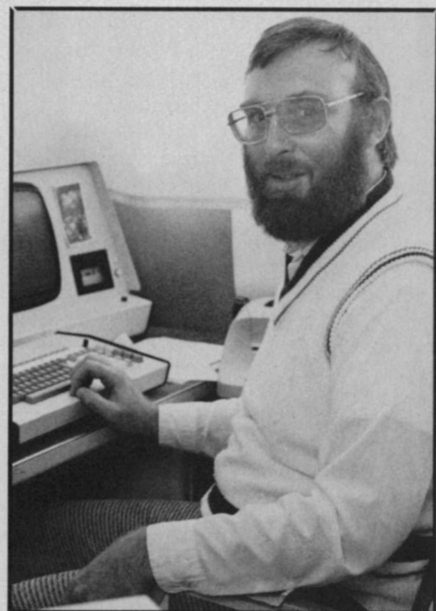
It stands as a testament to the genius of Charles Darwin and Alfred Wallace that the theory of natural selection is still a central concept in biology. Based only on observations of nature and on logic, the concept has held firm through a century of experimental probing on the organism, cellular and molecular levels.

Evolution is not a static field, though, and new theories arise and adapt to the existing scientific climates as surely as Darwin's finches adapted to the balmy Galapagos. Natural selection is now just one tenet, although a basic one, in a broader understanding of evolution, a synthesis of the generally accepted ideas on the mechanisms of change and adaptation.

One fairly new theory, the neutrality theory, challenges the dominance of natural selection and has teetered between extinction and acceptance for several years. It may go the way of the dinosaur and the dodo, or it may become another thread in the texture of evolutionary thought. Whatever the answer will be, it will probably come in the near future.

A brief overview of Darwinian evolution and the currently accepted synthetic theory establishes a framework for understanding the neutrality theory.

Both Darwin and Wallace formulated the theory of natural selection in the mid-1850's after traveling independently to tropical areas and observing the great diversity of animal and plant life. Although Wallace beat Darwin into print, the theories of both men were presented simultaneously before the Linnaen Society in 1858. The theory can be summarized in five main points: 1) All species produce offspring in excess of the number which can survive. 2) Adult populations in any region tend to remain constant (that has been largely disproven) and therefore there is an enormous death rate (this is generally true). 3) There must be a struggle for survival which the majority loses. 4) The competitors vary in many small characteristics and these will affect the chances for survival. 5) The result of these conditions is that the organism best able to survive the conditions transmits its more adaptive traits to future generations.



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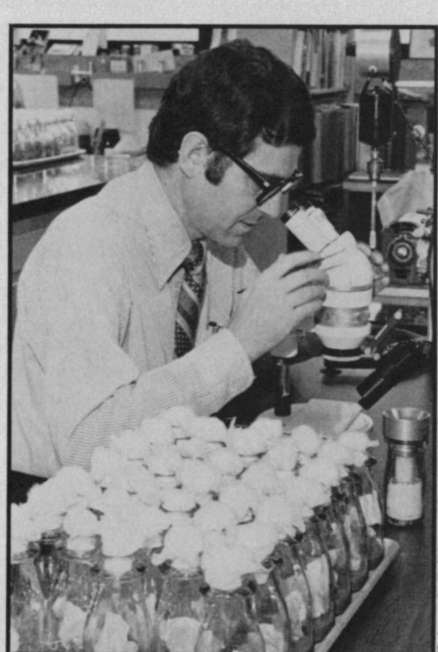
King: Questioning Darwin's dominance.



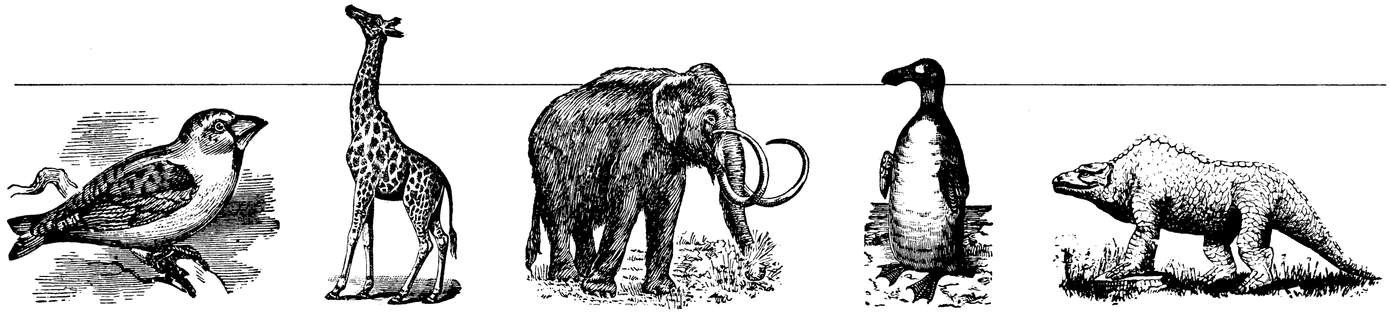
Univ. of Calif. at Davis

Ayala: Supporting Darwin's dominance.

Although Darwin and Wallace devised the hypothesis, it remained for experimentalists to prove it and determine the mechanisms of change, transmission and adaptation. The field of genetics, started by Gregor Mendel in his Moravian garden, has provided many of these answers. The growing body of experimental data at first seemed at variance with natural selection, but Theodozius Dobzhansky wove the ideas together in his 1937 book *Genetics and the Origin of Species.* His widely accepted synthesis states that variation is continually arising in all species by means of mutations in genes and chromosomes. These variations are shuffled and passed on by the mechanism of sexual reproduction into new patterns of variability in the offspring. These are then put to the test of natural selection and the fittest pass on the most adaptive traits.

The synthetic theory, too, is remarkable in that it was proposed before the discovery of DNA and the exploration of molecular biology, and yet still is consistent with much of the current experimental data. Where once naturalists looked for signs of evolutionary change by counting scales and measuring bones, population geneticists now search for amino acid substitutions and protein polymorphisms. (These are proteins with different structures but the same properties.)

But, some say, neither the synthetic theory nor Darwinian evolution can explain all of the minute changes that can be observed in nature. So, in 1968, the neutrality theory appeared and has fought for survival ever since.



One of the earliest proponents, biophysicist and geneticist Jack L. King of the University of California at Santa Barbara, explains the theory this way. The functional differences seen between individuals and species are the result of many small mutations such as the substitution of one amino acid for another in a large protein molecule. Many of these mutations seem to enable the organism to function equally as well as the individual without the mutation. Since so many small changes and substitutions occur in any species, if each one either augmented or decreased an organism's chances for survival, the rate of evolution would be much greater than is thought likely. Therefore, at least some of the mutations must be neutral and must become fixed in the population by genetic drift.

"What we are really talking about on the molecular level," King says, "is whether all of the fine detail of a protein is controlled by natural selection or whether you have gone beneath the resolving power of natural selection and are looking at random changes." This, he says, makes the concept of genetic drift more important to evolution.

Traditionally, genetic drift (the random fluctuation in the gene pool caused by chance events and mortalities) was thought to be exhibited only when populations are small and isolated. In such cases, genotypes that are uncommon in a large, original population but are common in isolated, secondary populations can become fixed into the gene pool in the new colonies after several generations. In contrast, the neutrality theory emphasizes the role of genetic drift even for large, stable populations. If many mutations are neutral rather than directional, then whether or not they become fixed in the population depends much more on the chance events of reproduction and survival than on the adaptive advantages or disadvantages the mutations provide.

Sparks flew when the neutrality theory was first proposed by Motoo Kimura of the National Institute of Genetics in Mishima, Japan (NATURE, 2/17/68, p. 624), and by King and biochemist Thomas H. Jukes of the University of California at Berkeley (SCIENCE, 5/16/69, p. 788). King and Jukes called their article "Non-Darwinian Evolution." This title was "deliberately provocative to get discussion going," King says. "However, opinion remains divided on whether that was a cool move or not." Vitalism, mutationism and Lamarkism are also called "non-Darwinian," and the association with these discredited theories polarized some synthetic theorists from the outset.

After some initial misunderstanding and acrimony, however, both sides have focused on the problem of how much importance shall be assigned to mutation, selection and drift during the evolution of any particular species. King and Jukes have mustered some experimental support for their position that mutation and drift play the larger role. Probably the strongest piece of evidence, Jukes says, is the "evolutionary clock" hypothesis. This states that the same protein in parallel lines of descent will have an approximately constant rate of change. Jukes cites a recently reported case in which a virus escaped from a monkey into a cat. After thousands of viral generations and mutations, the base changes were the same in both the monkey and cat. This constant rate of change illustrates that mutation is a moving force and that the mutations are neutral, he says.

Blood types are another example of polymorphic proteins that appear to support the neutrality theory. The protein factors that give blood the characteristic types (A, B, O, etc.) are composed of different amino acid sequences, presumably mutated from one original sequence. But the different forms have all become fixed in the gene pool and give no apparent advantages or disadvantages.

King and Jukes will present a third piece of evidence in an upcoming issue of the JOURNAL OF HUMAN EVOLUTION. It has been noted that several animal species including birds, bats, guinea pigs and anthropoids (humans included) have lost the ability to synthesize ascorbic acid (vitamin C). According to traditional Darwinian evolution, the loss must be in some way adaptive. But King and Jukes argue that it is neutral or even deleterious. One theory is that animals with diets abundant in ascorbic acid could save biochemical energy by avoiding its production. But, King and Jukes argue, many herbivorous vertebrates with high ascorbic acid diets still retain the ability to make vitamin C, and this would be wasteful and therefore disadvantageous according to strict natural selectionists. Also, birds and mammals from various lines of descent have lost the trait while others retained it, none with apparent evolutionary advantage or disadvantage, they state.

Despite the neutralists' evidence, many remain unconvinced. Perhaps the theory's strongest critic is Francisco Ayala, formerly a student of Dobzhansky and now a professor of genetics at the University of California at Davis. He and his students have published more than a dozen papers attempting to refute the theory since it was proposed.

In several studies, Ayala compared the frequency of polymorphic proteins in natural populations of various fruit fly species. He found similar frequencies of polymorphisms in different species and geographically dispersed populations of the same species. The neutrality theory predicts, Ayala says, that different species and dispersed populations will have different frequencies of the mutated proteins, since only chance determines which form will become fixed in the populations. But finding similar frequencies implies that those frequencies must lend an adaptive value for survival.

In another major series of experiments, Ayala attempted to test the neutrality theory directly. He found two species of fruit flies with different amounts of two polymorphic enzymes (A and B for simplicity). In nature, most Species One individuals carry enzyme A, while only a few carry enzyme B. Most Species Two individuals carry enzyme B, but a few carry A. Ayala collected large numbers of flies and established laboratory colonies in which the natural frequencies were changed. Now, enzyme B was more common in the Species One colonies than in nature, and enzyme A was more common in the Species Two colonies. He then maintained the colonies under similar conditions for many generations.

If the neutrality theory were correct, Ayala says, then one would not expect A and B to return to their natural frequencies. If the enzymes were neutral mutations, Ayala reasoned, then only chance would determine which form would increase and which would decrease throughout the generations. After hundreds of generations, electrophoresis revealed that the frequencies had returned to those found in nature, an indication, Ayala says, that A is advantageous (not neutral) for Species

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One and B is advantageous for Species Two.

Considering all of the experiments and observations, then, where does the neutrality theory stand? Ayala says, "I have gone systematically about making observations and measurements, and it looks as if the hypothesis is not likely to be correct." It was valuable as a guide for experimentation, but it's still wrong.

Jukes sees things differently. Far from feeling defeated, he says, "I think the general principle of neutral mutations is still a dominant one in evolution, and with certain modifications, I see it being incorporated into evolutionary theory. In the field of population genetics, King's area, perhaps it hasn't been well accepted. But in the field of biochemistry, the general reaction is, 'Well, isn't this obvious? Why does anyone disagree with it?' " Besides this, he says, much of the work refuting neutrality may be wrong because of the limitations of certain experimental techniques, such as starch gel electrophoresis.

King takes a more moderate view, hoping for an amelioration and pointing to signs of a synthesis of the two positions. In recent theoretical work by Kimura's student Tomoko Ohta, she proposes a continuum of mutational effects from beneficial to deleterious, with most falling in the middle. She has also suggested that within one protein molecule, selection may guide the evolution of functional areas while mutations arising in less important areas have a neutral effect on the molecule's evolution.

An interested observer, physiological chemist Walter Fitch of the University of Wisconsin at Madison, agrees that there has already been some synthesis. "There is a difference between where people are and where they think they are, and I think both sides are now closer than they have been in the past. But many of them don't understand that." The question now is one of proportion, how much mutation pressure, random drift and natural selection are at work in each case.

"The field is still in ferment, and we are now at the period where what we need are facts. The reason there has been no resolution to the debate is that it's not altogether clear that any of the facts you may garner are going to be incontrovertible." And the question of proportion is "a difficult one to fix upon," Fitch says. The field seems quiescent on the surface, he says, because people are trying to determine what they can study that "will really nail something down."

When the hammering finally starts, it should soon be clear whether the neutrality theory will stand or fall. □