Title
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Journal
Journal of Molecular Evolution, 35(6)

ISSN
0022-2844

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Publication Date
1992-12-01

DOI
10.1007/bf00160207

J Mol Evol (1992) 35:467–471

Journal of
Molecular Evolution

Book Selection

Wistar's Views

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Review of Leonard Warren and Hilary Koprowski, eds, *New Perspectives in Evolution* (Proceedings of a Symposium sponsored by The Wistar Institute), 1991, John Wiley & Sons, New York, xii + 258 pp.

> "Yet as the most quotable biologist J.B.S. Haldane . . . once said: 'It is, in my opinion, worth while devoting some energy to proving the obvious'." Richard Powers, *The Gold Bug Variations,* William Morrow, New York, 1991, p. 141.

If you happen to be reading this paragraph, you may consider stopping since you are performing an impossibly improbable act. There are 5×10^9 people in the world, 2.5×10^{11} paragraphs in the world libraries, $10^{1,061}$ possible letter combinations in a paragraph with 750 characters, and 8×10^{15} min have elapsed since the origin of the universe. Your reading this paragraph at this moment could not possibly occur because it has a probability of $10^{-1,098}$. Of course, you are reading it and thus showing my argument's fallacy, just as Samuel Johnson kicked the cat to prove its existence against Bishop Berkeley's idealism.

On April 25 and 26, 1966, The Wistar Institute held a symposium on "Mathematical Challenges to the Neo-Darwinian Interpretation of Evolution" (Moorhead and Kaplan 1967) in which some mathematicians and physical scientists, skippered by Dr. Murray Eden of MIT, held the neo-Darwinian account of evolution to be wanting because of the enormous improbability that, say, a particular protein consisting of 146 residues would arise by chance combination of the 20 possible amino acids. The critics failed to understand that (1) all events in the real world have infinitesimal a priori probabilities and (2) natural selection is not a random process.

Point (1) was well made by botanist Conway Zirkle, of the University of Pennsylvania, during the discussion of Eden's paper in the symposium's first session. I will quote Dr. Zirkle at some length:

> Mr. Chairman, I wish merely to indulge in a little improbability, one that is at least as great as that cited by Dr. Eden. If we can assume, I think quite reasonably, that our parents were heterozygous for about 10,000 loci, we can see how slight the chances are that any one of us would have been born instead of some nonexisting brother or sister. . . . The chances against any one of us having been born is [*sic*] practically infinite; and this forces me to accept a solipsism and to assume that this room is empty, except for myself, of course, and that the only existence any of you have is in my imagination. (Moorhead and Kaplan 1967, p. 19)

This comment elicited no response. Apparently neither the force of Zirkle's argument nor his irony was appreciated.

Point (2) was repeatedly made, but the notion of the nonrandomness of natural selection apparently remained impenetrable to Eden and others. In the symposium's final session Eden expressed his willingness to accept that evolutionary events with low probabilities can be measured in the laboratory: "I am told that nowadays a mutation with a frequency of about 10^{-9} can be detected. This obviously requires an awfully large number of Petri dishes." But he went on to say that it is impossible, now or "at any time in the future," to study experimentally events with probabilities of 10^{-14} to 10^{-16}, "unless you presumably agar-plate a great part of the surface of the earth" (Moorhead and Kaplan 1967, p. 99). Nobody bothered to contradict this claim by pointing out, for example, that a culture of *Escherichia coli* bacteria sensitive to streptomycin and dependent on histidine will yield billions of streptomycin-resistant and histidine-independent bacteria (two changes with joint mutation probability of 4×10^{-16}) if we first add streptomycin and obtain a culture of resistant bacteria, which can then be spread in Petri dishes with medium lacking histidine, so that only histidine-independent mutants will grow.

The notion that natural selection can yield extremely improbable outcomes by stepwise accumulation of moderately improbable events was, however, discerned by mathematician Stanislaw M. Ulam, of the Los Alamos Laboratories:

> A mathematical treatment of evolution . . . must include the mechanism of the advantages that single mutations bring about and the process of how these advantages, no matter how slight, serve to sieve out parts of the population, which then get additional advantages. It is the process of selection which might produce the more complicated organisms that exist today. (Moorhead and Kaplan 1967, p. 21)

What was to come at the symposium on mathematical challenges could have been anticipated from a position paper by Eden ("Inadequacies of Neo-Darwinian Evolution as a Scientific Theory") distributed to participants in advance. The first paragraph reads as follows:

> During the course of development of neo-Darwinian evolution as a theory, a variety of suggested universal postulates with empirical content have been invalidated. For example, the postulate that environmental influences on parents cannot affect offspring was invalidated by the discovery of induced mutations. In like manner, the notions that genes alone govern inheritance or that no morphological changes in a phenotype will propagate in its descendants have also been experimentally contradicted. In consequence the theory has been modified to the point that virtually every formulation of the principles of evolution is a tautology. (Moorhead and Kaplan 1967, p. 109)

Like this paragraph, the rest of the paper expounds bad biology, bad epistemology, and bad logic. I find it surprising that in view of such inauspicious forebodings, a number of biologists (including the likes of Ernst Mayr, Peter Medawar, and C.H. Waddington) willingly engaged in the symposium. Sewall Wright wrote a devastating critique of Eden's preliminary paper ("Comments on the Preliminary Working Papers of Eden and Waddington") but did not attend the symposium.

I opened the proceedings volume of the recent Wistar symposium on evolution with some apprehension, as might be expected in view of my experience of the earlier document. *New Perspectives on Evolution* is, however, quite unlike *Mathematical Challenges*. It sets forth to "discuss the astonishing advances that have been made in our knowledge and understanding of evolution since the 1960s" (p. ix). The first paper, by Ernst Mayr ("Introduction: An Overview of Current Evolutionary Biology"), exudes up-to-date knowledge, common sense, and wisdom, as it moves from examining the concept of natural selection to the enumeration of current problems in developmental biology, molecular evolution, and macroevolution.

One astonishing advance in recent evolutionary studies has been the discovery that the microbial world is overwhelmingly rich, surpassing in diversity the multicellular organisms more familiar to us. This was unexpected. Bacteria and protozoa had of course long been known. What was unforeseen was the diversity of microbial lifestyles and the ancient age of the microbial eukaryotic lineages. Paleoproterozoic (2,500–1,600 Ma) protistan fossils have been discovered in the Chuanglinggou Formation of China, dated at 1,900–1,800 Ma (Hofmann and Chen 1981; Zhang 1986). Biogeochemical data show that eukaryotic assemblages occurred in the late Paleoproterozoic. Steranes (derived from sterols, distinctive membrane components of eukaryotic cells) have been found in bitumen from the Barney Creek Formation in northern Australia (Hofmann and Chen 1981), dated 1,690 Ma.

The oldest eukaryotes are surely older than these fossil and geochemical traces (Knoll 1992). The molecular data suggest that the deepest branches of the eukaryotic tree are just about as deep as the oldest eubacterial or archaebacterial lineages. The eukaryotes are no less than three billion years old, rather than one-billion-and-a-half, as was generally thought just a few years back.

The early phylogeny of microorganisms has been reconstructed from rRNA sequence comparisons. The radical separation of the eubacteria and archaebacteria lineages was evidenced a decade and a half ago by Woese and colleagues (Woese and Fox 1977). Mitchell L. Sogin ("The Phylogenetic Significance of Sequence Diversity and Length Variations in Eukaryotic Small Subunit Ribosomal RNA Coding Regions") reviews extensive work, largely done by him and collaborators, showing the eukaryotes as a very heterogeneous and ancient evolutionary clade, perhaps as old as the prokaryotic lineages. The degree of sequence divergence is greater between some extant eukaryotic lineages, such as the parasitic protozoa *Giardia* and *Plasmodium* (0.325), for example, than between the most divergent eubacteria and archaebacteria (0.300, between *E. coli* and *Sulfolobus solfataricus*).

The *Giardia* lineage is the oldest-known branch of the eukaryotic tree. Its early divergence is underscored by lack of mitochondria and a fully formed endoplasmic reticulum. The geochemical record indicates that the endosymbiotic acquisition of mitochondria occurred at least 2,400 years ago, and perhaps much earlier (Knoll 1992). The sequence divergence of the rRNAs would thus indicate that the earlier branchings of extant eukaryotes are some three billion years old. Multicellular organisms evolved much later, after more than one, perhaps nearly two, billion years. The major diversifications of the animals, plants, and fungi are recent events on this scale: about 550 million years for the coelomate phyla.

The rRNA phylogenies show the protist phyla as paraphyletic, an assemblage of unrelated lineages, whereas the animals, plants, and fungi emerge as monophyletic lineages. The three higher kingdoms separate nearly simultaneously, at a late time in eukaryotic evolution when several major protist lineages (paramecia, acanthamoebae, plasmodia, and dinoflagellates) also arise. Sogin wonders whether this explosion of phenotypic evolution may have been prompted by evolution of a novel genetic mechanism such as controlling elements similar to the homeoboxes required for complex development, or RNA splicing, or vectors mediating genetic exchange. Alternatively, the trigger may have been some critical environmental shift, such as might result from a cataclysmic episode or from an increase in the partial pressure of atmospheric oxygen.

Andrew H. Knoll ("Environmental Context of Evolutionary Change: An Example from the End of the Proterozoic Eon") has much to say about this latter subject. Natural selection ensues from interaction between hereditary variation and the environment. Population genetics provides a calculus for describing this interaction and molecular biology supplies a picture of genomic change. However, the origin of genetic novelty and the historical role of the environment, avers Knoll, are left out of the picture obtained from these disciplines. This deficiency can be remedied by the geological record, which provides a "type of information central to understanding how the present diversity of life came to be; it provides a perspective on the environmental context in which phenotypic innovations have arisen, spread, and/or disappeared" (p. 77).

For the last 550 million years, the duration of the Phanerozoic Eon, most physical environmental change has consisted of oscillations in the configuration of continents, ocean currents, sea level, climate, and other nondirectional shifts. Not so in the earlier history of the Earth, says Knoll. Environmental oscillations occurred as they did later. But there also was a directional transformation from "a planet with little continental crust and almost no atmospheric oxygen to one characterized by large stable continents bathed by oxygen-rich fluids" (p. 78). What has been learned over the last three decades about this process provides much insight into the long history of life before the emergence of the major multicellular phyla in Cambrian times (Knoll 1992).

The most credible evidence supports the hypothesis that 800–900 Ma ago, just prior to the Ediacaran epoch, when the first traces of multicellular animals appear, there was a substantial increase in the oxygen content of the atmosphere and the hydrosphere. This resulted from extended periods of unusually high rates of organic carbon burial during the late Proterozoic. These higher burial rates of organic carbon were facilitated by tectonic and climatic shifts associated with the fractionation of the preexisting huge supercontinent(s). Oxygen-rich environments are necessary for the evolution of large animals but not sufficient. Control systems able to regulate complex developmental processes would also be required. The necessary genetic processes, says Knoll, were "either easily evolved or, perhaps more likely, already in place in minute, nematode-grade animals able to live in earlier Proterozoic environments with limited oxygen" (p. 82). I suspect that the riddle of the Cambrian explosive radiations may soon be resolved, thanks to the impressive strides that theoretical models and molecular biology are taking toward understanding complex development. An article by Rudolf A. Raff, Gregory A. Wray, and Jonathan J. Henry ("Implications of Radical Evolutionary Changes in Early Development for Concepts of Developmental Constraint") explores some consequential themes.

Knoll's larger message is that the broad pattern of the evolution of life on Earth can be discerned only by studying the biogeochemical cycles in which biological and physical Earth evolution are twined. The history of the planet has profoundly influenced and been influenced by biological evolution. Knoll's message should be heeded. Those who want to explore further how far geology can go, in the hands of an enlightened and well-informed practitioner, toward illuminating large-scale biological evolution, would do well to read Knoll's (1992) splendid (though it is slow going for the uninitiated) review article on "The Early Evolution of Eukaryotes: A Geological Perspective," recently published in *Science* (Knoll 1992).

The ways of evolution embody "tinkering" (Jacob 1977), a distinctive process that the critics at the earlier Wistar symposium failed to understand. Novelty in evolution does not come about as in engineering, where an object is designed from scratch to serve some function, and the best raw materials for the purpose are selected. Rather, readily available "materials" are combined and modified to meet new environmental challenges or to improve performance in the current environments. Paleontological, genetic, morphological and, most dramatically, embryological investigations have given wonderful insights into evolutionary tinkering.

Molecular biology has now shown evolutionary tinkering at the genome level: exons are recombined to produce novel genes (Walter Gilbert, "Gene Structure and Evolutionary Theory"); new proteins result from recombination of extant functional units rather than from successive single amino acid replacements (Daniel L. Hartl, "New Perspectives on the Molecular Evolution of Genes and Genomes"); genomes are "dynamic" owing to the occurrence of transposable DNA sequences that move from one genome to another or from one position to a different one (Margaret G. Kidwell and Kenneth R. Peterson, "Evolution of Transposable Elements in *Drosophila*"); the vast protein repertory of organisms is made up of modified duplications and recombinations of a few ancient proteins (Russell F. Doolittle, "New Perspectives on Evolution Provided by Protein Sequences").

These authors for the most part do not show any awareness of the issues raised at the earlier Wistar symposium or of how far their recitations go toward confuting the riddles that had stifled the critics. Hartl is an exception in that he refers to the earlier volume and then goes on to affirm that "a great shift in emphasis [has occurred] in evolutionary biology since 1966 . . . toward reductionism" (p. 124). I would disagree: much of significance that has happened in evolutionary biology over the last 25 years is definitely antireductionist. The article by Knoll and those by Steven M. Stanley ("The Species as a Unit of Large-Scale Evolution") and Keith Stewart Thomson ("Parallelism and Convergence in the Horse Limb: The Internal-External Dichotomy") in *New Perspectives* are definitely antireductionist in vein. And so is Hartl's own piece, as it shows that the function of polypeptide segments depends on the protein context and that the adaptive significance of genetic variants is not an absolute property but is determined by environmental variables. But perhaps my disagreement with Hartl is nothing but a semantic quibble. If he means that much by way of detailed knowledge and precise understanding has been gained in evolutionary biology since 1966, I would surely agree. Detailed knowledge and precise understanding is what is needed to dispel ignorance, and also to confute obscurantism of the sort egregiously exemplified by the sorry story of Lysenkoism in the Soviet Union.

In February 1935, the agronomist Trofim Denisovich Lysenko—an opportunist charlatan with pretensions of being a great revolutionary scientist—addressed the Second Soviet Congress of Collective Farms on the shameful status of Soviet agriculture. Lysenko castigated Soviet geneticists, accusing them of being enemies of the people who were destroying Soviet agriculture by relying on abstract theories imported from the capitalistic West. Stalin, presiding over the event, expressed his approval: "Bravo, comrade Lysenko, bravo!"

Stalin's public approval consummated Lysenko's meteoric rise to fame and power. For three long decades, until the fall of Kruschev in October 1964, Lysenko and his partisans presided over Soviet agriculture, imposed their ideas on biology, and completed the elimination of Soviet genetics (and of numerous Soviet geneticists, who were sentenced to death, sent to concentration camps, or at best removed from their research and teaching positions). The Soviet Union, a country with enormous agricultural potential, would as a consequence become, for many years extending into the present, agriculturally insufficient and backward in biology (contrary to its successes in other disciplines, like physics and mathematics).

The story of Lysenko's frightful impact on Soviet biology is told by Mark B. Adams ("Through the Looking Glass: The Evolution of Soviet Darwinism"), a historian at the University of Pennsylvania who has studied Soviet biology for more than two decades, and by Nikolai N. Vorontsov ("Current State of Evolutionary Theory in the USSR"), a Russian theorist and experimentalist, whose lasting evolutionary contributions include the reconstruction of the complex chromosomal evolution in *Citellus* ground squirrels (Liapunova and Vorontsov 1970). "I remember 1948 very well," writes Vorontsov. "That fall, in all universities, in all institutions, three thousand biologists lost their jobs and all possibility of research—three *thousand*" (p. 68).

(Ernst Mayr comments after Vorontsov's paper: "What a pleasure it is to have a Russian evolutionary biologist among us!" And Mark Adams notes that, a few weeks after delivering the paper, Vorontsov was appointed to Gorbachev's cabinet as minister of the environment, "the first non-Party figure in Soviet history to achieve ministerial rank" [p. 75]. The euphoria of perestroika has since wilted, Gorbachev is gone, and alas! the ministry of the environment has been abolished. Vorontsov, Adams had noted, "is a scientist first and foremost, not a politician." Yet, as I write this, Vorontsov has said to me that he will remain politically active, as a member of the Russian Parliament and otherwise. Several decades of official abuse and neglect have deteriorated the Russian environment to an unimaginable extent, he says.)

Lysenko saw himself as a great successor of Darwin who was extending Darwinism as he denounced genetics, a capitalistic science that perpetuated the notion that there are qualitative differences—claimed to be rooted in the genes—in plants, animals, and people. Such immutable differences do not exist, Lysenko claimed; rather, differences between individuals are due to environmental effects and can be radically modified by exposing organisms to appropriate environmental challenges. Therefore, the production of new crops, or their adaptation to new habitats, need not be the long process of selection of suitable genotypes claimed by the capitalists, but can be simply and rapidly accomplished by exposing seeds or young plants to suitable conditions. At the height of his power, under Stalin's protecting approval, Lysenko advanced a "phase theory" that included the claim that "the conversion of one species into another takes place by a leap" (p. 51). In the appropriate environment wheat plants produce rye seeds.

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