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# LET US APPRECIATE EVOLVING GENES[1]

JODY HEY
*Department of Genetics, Rutgers University, Nelson Biological Labs, 604 Allison Road, Piscataway, New Jersey 08854-8082*
*E-mail: jhey@mbcl.rutgers.edu*

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Once upon a time biologists would lament their imprecise profession, and their physics envy—their wish for a more quantitative and predictive science—was a palpable undercurrent of epistemological dialogues (often with beer-enhanced erudition and insight). But in fact, and for well over a century, biologists have had something that physicists still lack—a ''grand unified theory''. In some respects this grand theory is not much (the gist of it only takes five words: ''evolution proceeds by natural selection''), but it is the conceptual root of a still exponentially growing transformation of the life sciences, and of human thought and human culture. Biologists have long had a firm handle on real ''superstrings'' (i.e., DNA) and our physics envy just is not what it used to be.

The discovery and elucidation of the role of DNA hit different parts of biology at different times in different ways. For the express study of evolutionary pattern and process, the DNA age began in the early 1960s when Emile Zuckerkandl and Linus Pauling compared and aligned homologous protein sequences, mused about molecular clocks, and built evolutionary trees (Pauling and Zuckerkandl 1963; Zuckerkandl and Pauling 1962). They gave the label ''semantides'' to polymers that were either DNAs or descended directly from them (Zuckerkandl and Pauling 1965), and they called the task of evolutionary reconstruction that relied upon them ''paleogenetics'' (Pauling and Zuckerkandl 1963). Those terms have not endured, but the field has thrived and today the study of the evolution of molecules that either contain the genotype (i.e., the DNA sequence), or are direct translations of the genotype, is exciting and turbulent and at the center of the modern genomic extravaganza.

For Austin Hughes, the author of *Adaptive Evolution of Genes and Genomes*, the key historical antecedents are not the very earliest days of molecular evolution, but rather the development in the 1970s and 1980s of the neutral theory of molecular evolution (Kimura 1968; Kimura and Ohta 1974). Regardless of how much it explains, the neutral theory is a mathematical model of divergence *and* polymorphism, and it is *the* null model for statistical assessments of natural selection on DNA and protein sequences. Evolutionary biologists are sometimes faced with a classic skeptical challenge: *if evolution proceeds by natural selection, then is not all of life a Panglossian utopia of adapted forms* (Gould and Lewontin 1979)? This question can be difficult in some contexts, but not for those who study the evolution of molecules, because they have an arsenal of statistical weapons for deciding when there is evidence of natural selection. In the opening chapter, Hughes nicely tells how the neutral model has allowed evolutionary biologists who study genes and proteins to make specific predictions of how DNAs change over time in the absence of natural selection, and thus to have power to detect the signal of natural selection and to infer the kind of selection that has been operating on genes.

Hughes has written a methodical survey of methods and studies. It does not present an argument, but rather is a useful resource for anyone needing to get a basic grounding in how one studies the adaptation of genes and of the details of some of the most interesting discoveries. Some of the examples will be familiar to many (e.g., the evidence of balancing selection on MHC genes), but most of the cases reviewed will be news to anyone who is not a molecular evolutionist. Lecturers needing examples and case studies will be grateful. Hughes writes from intimacy. He has been a leader in this field since he teamed up with Masatoshi Nei over a dozen years ago.

For an uncloistered biologist having to face creationists or others skeptical that evolution could be an engine of creativity, the best part of the book is the chapter on the evolution of new protein functions. New functions really do evolve, and they have new genes to prove it. Hughes reviews the evidence for the diversification of functions that arises following gene duplication and other cases where new genes have been shown to arise. He concludes, reasonably, that typically the first step in the acquisition of new function is specialization among different duplicated genes of functions once carried out by a single generalist gene.

The letdown of the book is the chapter on adaptive characteristics of genomes. Unlike the rest of the book, which is all about discerning alternative evolutionary hypotheses, this chapter simply reviews codon bias, genome size variation, and the reconstruction of gene duplication events. A more ambitious writing effort would have foreseen that the same kind of critical questioning and hypothesis testing that has become the tradition in the study of the adaptation of genes will also come to be applied on a broad scale to the study of how genomes have been structured.

In closing, Hughes provides an answer to one biologist's commentary that molecular evolutionary studies have merely supported and confirmed the findings of earlier evolutionary studies on organisms. The rebuttal lies in the richness and the novelty of discoveries made at the molecular level. That sumptuousness is on display throughout this book, and it could not have been predicted prior to the molecular age. What is sometimes overlooked in our appreciation of the

[1] *Adaptive Evolution of Genes and Genomes.* Austin L. Hughes. 1999. Oxford University Press, New York. 288 pp. HB $60.00; ISBN 0-19-511626-7.

modern synthesis is how very incomplete it was. Ronald Fisher, Sewall Wright, and J. B. S. Haldane did not (at least early in their careers) know of the fundamental role played by DNA, and only Wright's work played a significant role in the development of the neutral theory (Kimura 1983). The modern synthesis was a theoretical and analytical triumph, but it was not very much a statistical one. The conjunction that began in the 1970s, between the molecular sequence data and the neutral model, led to a kind of rigorous, reductionist evolutionary analysis that was essentially impossible with other kinds of genetic and phenotypic data. Hughes does not trumpet the discoveries that followed, but he lays them out nicely for all to appreciate.

## Literature Cited

Gould, S. J., and R. C. Lewontin. 1979. The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. Proc. R. Soc. Lond. B Biol. Sci. 205:581–598.

Kimura, M. 1968. Evolutionary rate at the molecular level. Nature 217:624–626.

Kimura, M. 1983. The neutral theory of molecular evolution. Cambridge Univ. Press, Cambridge, U.K.

Kimura, M., and T. Ohta. 1974. On some principles governing molecular evolution. Proc. Natl. Acad. Sci. USA 71:2848–2852.

Pauling, L., and E. Zuckerkandl. 1963. Chemical paleogenetics: molecular restoration studies of extinct forms of life. Acta Chem. Scand. 17:89.

Zuckerkandl, E., and L. Pauling. 1962. Molecular disease, evolution, and genetic heterogeneity. Pp. 189–225 *in* M. Kasha and B. Pullman, eds. Horizons in biochemistry. Academic Press, New York.

Zuckerkandl, E., and L. Pauling. 1965. Molecules as documents of evolutionary history. J. Theoret. Biol. 8:357–366.

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