The Triple Helix: Gene, Organism and Environment

By Richard C. Lewontin

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Soon we will know the sequence of the human genome, or some humans' genomes, anyway – and then what? The sequence alone will not tell us which parts function as genes, much less what those genes do. We are deluged by new knowledge in cell and molecular biology but, this book by evolutionary biologist Richard Lewontin argues, we know much less than we would like to believe we do. The Triple Helix stands back to look at the whole of biology as we practice it at the turn of the century. A key question remains in development and evolution: how to explain variation. Genes may account for why you are different from a chimpanzee, but not for why you are different from me. Are we headed toward the answers? John Maynard Keynes once wrote, "The difficulty lies, not so much in developing new ideas, as in escaping from the old ones." This book takes on that difficult task for biology.

Lewontin argues that we have come up against the constraints of the reigning metaphors in biology. Metaphors are necessary because we cannot see most of the things we study, but when we believe the thing actually is the metaphor, we are in trouble. We speak of genes as a blueprint, program or code, and so come to see development as the unfolding of a predetermined set of instructions. But the same genes have different products in different environments. Amino acid sequence does not fully determine protein structure and thus function; instead, protein structure is influenced by a diverse set of entities in the cell[1]. For example, a protein can take on a toxic or non-toxic form depending on the shape of pre-existing proteins. The outcome of development, what particular organism develops, is affected by noise from random molecular events within cells, and by the environment in which the organism grows. How organisms come to vary is the starting point for the study of natural selection, because without variation, there is nothing to select. Lewontin's best known work in population genetics, studying evolution in fruit flies, led to new techniques for examining variation in populations.

A naïve view of evolution equates function with adaptation; if we can identify a function of a trait, that function must be why natural selection put it there. One of Lewontin's most famous conceptual papers (with S J Gould) (ref. 2) points out the foolishness of this assumption. A trait might be irrelevant to natural selection, or it might be an inevitable consequence of another trait under selection, or it might actually be detrimental, in which case natural selection might be working to eliminate it. Facile adaptive explanations for human behavior are one weakness of sociobiology and its offshoots, which Lewontin has vigorously opposed; there is little evidence to link natural selection with the observation that some people are smarter, richer or happier than others. If *ad hoc* accounts of adaptation are inadequate, how then can we understand natural selection? Lewontin discusses the Darwinian metaphor of the organism adapting to an environment that is independent of it. He points out that environments are in fact constructed by organisms, through the organism's activities (where it goes, its physiological effects on the space around it, and more explicit construction such as building a nest); its perceptual abilities that determine which environmental signals it picks up; and its interactions with other species.

The last part of the book asks how we should proceed. Unlike machines, which can be separated easily into independent components, any piece of a biological system we choose to study is likely to be causally linked to parts not studied. Lewontin's advice is to look carefully at the strands of the causal web that are outside the spotlight. He argues vehemently against "obscurantist holism", the attempt to understand a system without examining the operation of its components. He has made many contributions to the mathematical theory of evolutionary change, but he is not optimistic that new theoretical advances will provide general laws applicable to all complex biological systems. To those ready to escape the old ideas, Lewontin counsels patience and empiricism. His examples draw on the relation of form and function: how cells in a developing organism make body parts of a particular shape, how protein folding transforms DNA sequences into particular gene products, how minor mutations map onto small variations among individuals, and in a more abstract notion of "shape and form," how organisms change their environments as they evolve, thus changing the conditions of evolution.

The dust jacket says this is "vintage Lewontin" but it would be more accurately described as distilled Lewontin, concentrating a career's worth of thinking about genetics and evolution into a small, elegant and powerful book. It will stimulate passionate discussion in a journal club; bring relief to students who sense that the textbooks aren't telling the whole story; annoy anyone who promotes simple generalizations about development or evolution; and inspire new ideas.

1. Feldman, D. E. & J. Frydman. Protein folding in vivo: the importance of molecular chaperones. *Current Opinion Struct Biol*. **10**, 26-33 (2000).
2. Gould, S.J. & Lewontin, R.C. The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. *Proc. Roy. Soc. Lond. B. Biol. Sci*. **205**, 581-598 (1979).