

Book review essay

Evolution: A View from the 21st Century

James Shapiro

Upper Saddle River, NJ: FT Press Science, 2011

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Introduction

Nothing in biology makes sense, Dobzhansky famously claimed, except in the light of evolution.² Without qualification the statement is surely an exaggeration, but evolutionary issues loom sufficiently large in biology to cast a shadow that extends well beyond the discipline. They have long absorbed the energies of philosophers of biology, for instance. If we see evolution as the quintessence of biologicality, the process that in some sense lies at farthest remove from the physical sciences, then it is scarcely surprising that it was a central player in the consolidation from roughly the 1970s onwards of a biologically oriented branch of philosophy of science, with Hull³ one of its foundational texts.⁴ To notions of biological fundamentality and remoteness from physics, however, can be added – perhaps a little awkwardly – another idea of comparable plausibility: that evolution was also the biological topic most consonant with the formalist outlook of positivist traditions in mainstream philosophy of science. For in biological evolution we apparently have a phenomenon in relation to which techniques of mathematical analysis and theory construction have found ready and often fruitful application. To appreciate the point one need only think of the work of Fisher, Wright and Haldane in population genetics, and the subsequent development of mathematical biology.⁵

Why might evolutionary processes lend themselves to formal treatment? Relevant factors presumably include the relative simplicity of the neo-Darwinian conceptual framework and the fact (working assumption?) that biological populations can be partitioned in ways congenial to the operation of statistical methods under that framework. To recapitulate: small variations arise between the individuals within a species population as a result of random genetic mutation events, and cumulatively those variations give rise to functionally substantive phenotypic differences. Blindly but irresistibly natural selection, the heterogeneous set of pressures that favours some phenotypes and disfavors others within the context of a particular environment, acts to adjust the levels of representation of particular phenotypic characteristics within a population. As a consequence, the genes that give rise to those characteristics, so the story goes, flourish or are filtered out. Over long timescales, against a background of environmental dynamics and competition for resources, species tend to differentiate from one another. The tree of life – for we typically conceive of species relationships in arboreal terms – reflects the progressive divergence and distinctive elaboration of organismic lineages, as individual organisms succeed or fail in their battle with the environment according to the success they enjoy as mating machines. (That lineages

sometimes converge in particular functional or morphological respects must also be acknowledged.) In standard accounts along these lines – I am thinking especially of Richard Dawkins’ elegant popularisations – adaptation is a pretty passive affair. The process is essentially blind to the narrative details of individual history, admitting of no mechanism whereby an individual’s experience might modulate the resources its progeny inherit.

In a distinctive new scientific distillation, leading bacterial geneticist James Shapiro contends that much of this familiar picture needs to be rethought in the light of advances in biological knowledge.⁶ His book will thus be of considerable interest to philosophers of biology, as well as to social scientists concerned to understand where the boundaries lie between the endogenous, the individual and the biological on the one hand and the exogenous, the social and the cultural on the other.⁷ His treatment, besides being notably concise, is an unusually personal one: it is difficult not to see imprinted in its form something of the author’s own academic background, which began with a BA in English Literature at Harvard. The PhD at Cambridge that followed, on bacterial genetics and under the supervision of Bill Hayes, developed into an interest in transposable genetic elements, which Shapiro was the first to discover in bacteria, and into a more general pre-occupation with mechanisms of what he terms ‘natural genetic engineering’.

In order to be as useful to a broad readership as its author apparently intends, a book like this (especially when so titled) should accomplish three objectives. It should set out as clearly as possible the range and nature of the mechanisms in question; it should explain their broad biological significance; and it should highlight what in particular they mean for our understanding of evolutionary processes. Shapiro on the whole succeeds in meeting the first two of these objectives, although the third should I think be regarded as only partially fulfilled. Here the title is a little unhelpful, being likely to instil in the potential reader a variety of expectations which it is not the author’s priority to meet. As Shapiro suggests at the outset, his principal concern is with mechanisms that give rise to genomic variation that reflects an individual’s lived experience:

Innovation, not selection, is the critical issue in evolutionary change. Without variation and novelty, selection has nothing to act upon. So this book is dedicated to considering the many ways that living organisms actively change themselves. (p.1)

This means that for much of the book the emphasis is on the (physiologically) proximate rather than the (evolutionarily) ultimate, to utilise Mayr’s distinction.⁸

Cognition at all levels

The book is divided into four chapters (‘parts’). In the first Shapiro shows, using examples such as bacterial sugar sensing and the lac operon, how cell physiology depends on the coupling and integration of genetic mechanisms with other cell processes. These examples he sees in terms of an interwoven complex of cognitive

and informatic/computational parallels which at times are pushed quite hard, Shapiro arguing that “Life requires cognition at all levels” (p.7). Recognition sites on DNA are described as playing a genome formatting role which “can usefully be compared to data file formatting in computer systems because they are essential in both cases to accurate utilization of stored information” (p.10), while proteins are described as “conditional microprocessors in regulatory circuits” (p.11). Even the DNA replication proofreading process, we are told, amounts to a cognitive rather than a mechanical process, which at the same time Shapiro compares – and perhaps the comparison deserves to be explicated more fully – with fuzzy logic-based models of cybernetic control (p.14).

We learn of the sophistication of cellular DNA damage repair mechanisms. Rather than passively withstanding as best they can the damaging effects of mutagens such as UV radiation, bacteria sense them and mount an active response. This so-called SOS response involves two distinct repair systems: a precise process that selectively excises UV-damaged DNA without introducing mutations, and a mutagenic repair process involving the induced synthesis of error-prone DNA polymerases. Without the latter, cells unable to replicate past any DNA damage will die, and so the price of survival (if I understand Shapiro correctly) is the introduction of sequence mutations. The importance of the DNA damage response in relation to Shapiro’s overall message is that even the evolutionarily fundamental phenomenon of mutation – traditionally seen as the foundation for the organismic differences on which selection acts – must be viewed as one over which cells exert a significant degree of control. This, with other examples, leads Shapiro to reject the Central Dogma as originally formulated by Crick⁹ as being simplistic and misleading. Information does not flow unidirectionally from the genome, but rather a context-dependent dialogue takes place between genome and extra-genomic processes.

Genomic memory

The aim in Part II, we are informed in the book’s preliminary pages, is to address “the many ways cells inscribe information into their genomes”. The “diverse inscriptions” at issue “constitute a form of writing that modifies the cell’s genomic memory” (p.xvii). Textual, linguistic and computational metaphors come together in the idea of operations involving string-like data structures (although Shapiro does not use that terminology), and the chapter begins with a compelling metaphor:

... the view of traditional genetics and conventional evolutionary theory is that the genome is a read-only memory (ROM) system subject to change by stochastic damage and copying errors. ... [The new perspective based on cytogenetic and molecular evidence] treats the genome as a read-write (RW) memory system subject to non-random change by dedicated cell functions. (p.28)

Following a discussion of genome and chromatin formatting, which expands on what is said in Part I, come some technically dense sections dealing with a range of genomic processes and phenomena. The big picture is that particular kinds of genomic

change occur over different timescales, ranging from that of a single cell cycle, through the multiple cell cycles involved in the development of an individual organism, to the “countless” cell cycles over which evolution occurs. Within a cell cycle it is chiefly through the formation of transient complexes of proteins and nucleic acid that the genome reflects cellular circumstances, whilst over several cycles heritable – but also modifiable, e.g. during meiosis and gamete formation – epigenetic modifications come about through imprinting and chromatin formatting. In addition, in some cells, such as those of the mammalian immune system, genetic information is rewritten over the intermediate term by changes to DNA structure.

The mechanisms of genome re-engineering to which we are introduced are numerous and diverse, and involve a plethora of molecular actors and genetic elements (including the transposons first discovered by Barbara McClintock and now known to be ubiquitous among prokaryotes and eukaryotes). Some microbes, for instance, switch between different ‘phases’, according to environmental context, with different sets of proteins being synthesised in the different phases. Phase switching is achieved, rather surprisingly, by DNA recombination processes that invert either promoter regions or coding sequences. Other cases are known in which genomic diversity arises as the result of a range of recombination-based mechanisms. Perhaps most bizarre of all is the case of macronuclear development in ciliate protozoa such as *Paramecium*, in which within a single cell generation a whole new somatic genome, controlling mitotic cell proliferation, is built out of a germline genome constructed in a quite different way. Here is a species in which massive genome restructuring plays a central role in the life cycle. That underscores an important point: that these diverse processes of natural genetic engineering should be regarded not as accidental, the results of limitations in the ability of cells to control what their molecules get up to, but rather as targeted, functional, and perhaps even in some sense intentional operations. Genomes, then, are complex, plastic and responsive cellular sub-systems, capable of sensing and adapting to a variety of stimuli and shocks through regulated reorganisation. Not only do genomes generally not behave randomly, Shapiro persuades us, but entrenched gradualist assumptions about genomic change are at serious variance with biological reality.

Against gradualism

The perils of gradualism are well-illustrated by the case presented at the start of Part III. In 1967 the US Surgeon General announced that “the war against infectious diseases has been won”. The pronouncement stemmed in part from the finding that under laboratory conditions bacterial antibiotic resistance depends on the occurrence of multiple successive mutations, each individually rather improbable and in serial combination exceptionally unlikely. As single mutations generally produce only incremental resistance increases, it seemed safe to assume that there was no chance of full-blown resistance arising in a bacterial population. We now know all too well, however, that bacterial antibiotic resistance spreads rapidly in clinical settings, thanks to the transmission between bacterial cells of mobile genomic elements such as drug resistance plasmids. Again, Shapiro stresses the often sophisticated and functionally

specialised nature of the mechanisms involved in the horizontal transfer of DNA molecules. A greater appreciation of the extent of this inter-cellular DNA trafficking is now stimulating a reappraisal of the tree-based conception of lineage relationships, and the material that Shapiro presents is very much of a piece with that revisionary project.¹⁰

Discussion of protein evolution lends further credence to saltationist points of view. Whereas at one time it was supposed that the amino acid was the basic unit of protein variation, particular functional significance is now known often to attach to the protein domain, or folded subunit. Particular protein domains are often associated with specific binding or catalytic properties, and when novel domain combinations are created through genetic engineering the individual domains typically retain their distinct chemical functionalities. Moreover, cells appear to possess the kinds of natural genetic engineering mechanism needed to manipulate protein domains combinatorially as a resource for adaptation and evolvability, leading Shapiro to speak of the “systems view” of proteins.

There is a connection here, I suggest, with Monod’s idea of *gratuité*, which adverts to the contingently mediated nature of the molecular interactions involved in cell processes.¹¹ The basis for the connection is that it is chiefly through the presence of domain recombination mechanisms and the like that the relevant contingency can meaningfully be said to exist. These notions of modular reconfigurability, of both genomes and proteins, encourage us to contemplate the cell simplistically in terms of somewhat stable building blocks, and this will likely be the interpretation of synthetic biologists as they attempt to reverse-engineer the functional logic taken to inhere in biological complexity. On the other hand, however, the modular decoupling of functional activities, and implied possibilities for radical reconfiguration of cellular and (hence) organismic functional architecture through relatively simple genomic rearrangements, may mean that cross-species comparisons will often prove illuminating as much for the differences they reveal as for the similarities. (Excepting, however, certain highly conserved, basic organisational features and operating principles.) In other words, making straightforward inferences from the presence of particular base sequences or molecular species to specific biological functions or phenotypic features may be harder than the simplified building blocks conception might at first glance seem to imply.

From information talk to informatics talk

Much of the molecular and cell biology that Shapiro describes comports nicely with recent work by anti-reductionist philosophers of biology, in particular in its rejection of the Central Dogma and of genocentric thinking more generally.¹² (I have already noted the common interest in horizontal gene transfer and what that might mean for how we conceive of organismic lineage relationships.) However, Shapiro’s outlook differs from contemporary biophilosophical orthodoxy in certain respects, and to my mind this makes it all the more interesting. In particular, as we have seen, he frequently invokes an information-processing, cognitive/computational perspective on

cell processes. He is not alone in this: cell biologist Dennis Bray's recent semi-popularisation was subtitled *A computer in every living cell*.¹³ And even though the focus is largely extra-genomic, I suspect that when non-coding RNA regulatory networks are said to "form a highly parallel digital network that integrates complex suites of gene expression and controls the programmed responses required for the autopoietic development of multicellular organisms",¹⁴ Shapiro would endorse the overall figurative stance.

What we should make of these informatic, computational and cognitive parallels is not entirely clear. Should they be seen 'simply' as figures of speech, aimed at making intelligible to a broad audience the functional relations that hold between different cell structures and processes, or ought we to regard them as making somewhat stronger ontological claims? And to what extent does it make sense to seek to relate them to the other forms of information talk we see in biology and elsewhere? The prospects there do not look especially good, informational perspectives on biological systems having often proved to be scientifically unrewarding.¹⁵ It is noteworthy too that philosophers of biology have so far struggled to agree on a philosophically satisfactory assimilation of information talk, and have in the main been silent about cognitive and computational cell biological perspectives.¹⁶ However, a spirited millennial campaign to banish information talk from biology, driven by the proponents of Developmental Systems Theory (DST) and waged on several fronts, appears for now to have been unsuccessful.¹⁷ A recent paper has reinvigorated the debate about the nature of biological information,¹⁸ relevant workshops continue to be held,¹⁹ and books published exploring an impressively catholic range of ideas.²⁰

A common thread running through both earlier and more recent investigations into the nature of biological information is a tendency to view Shannon's mathematical theory of communication as the ultimate authority to which all debates about information must defer.²¹ How much does that theory really have to offer cell, and other, biologists, however? Evelyn Fox Keller has argued that the distinctive complexity of genomic and cellular processes may call for the development of new theoretical approaches to information.²² And if we find that it takes courage to be sceptical about the utility of Shannon's theory, perhaps we would do well to reflect on the by no means implausible claim that the theory, "with the immense exception of the definition of the bit, is not actually very important in most areas of computer science".²³ Scientific and philosophical progress may be more likely to result not from focusing on the concept of information itself, whatever that is, but rather from investigating more closely possibilities for turning Shapiro's informatic figurations and their ilk into something like an explicit theory of biocomputational systems. Ideally such a theory would be capable of relating the quasi-algorithmic nature of cell biological processes to computational systems as conventionally understood.²⁴ This is a goal Gunther Stent hinted at over 30 years ago, in relation to the development of an algorithmic understanding of organismic development.²⁵ More significantly, much of the intensive research currently being carried out in systems and synthetic biology is implicitly or explicitly predicated on the idea that cell processes are underpinned by a

logico-functional architecture of some kind. Indeed, some seek to adapt and exploit that architecture as a platform for performing novel biocomputations.²⁶

The thought that cells, and organisms, can be considered not merely to be like computational systems but *as* computational systems is an intriguing one. It also argues for shifting our attention from information talk to informatics talk of the sort for which Shapiro has evident sympathy. One of the charges sometimes levelled against information talk is that where it relates to genomic processes, it often betrays latent ontogenic preformationism, i.e. commitment to the belief that the genome encodes a representation of the developed organism. The charge is not a powerful one, however, for inasmuch as no one today really supposes that genomes describe the organisms that bear them in any straightforward (developmentally illiterate) way, it smacks of flogging a dead horse. But also, in that developmental processes are generally not blown hither and thither by every chance environmental factor, perhaps it is reasonable to think of genomes in their cellular contexts as hereditary “code-scripts”²⁷ – provided we interpret that term informatically rather than informationally. Just as a computer’s hard disk drive is a storage device that has functional capacity only in the context of the host computer system, so genomes play a comparable functional role only in virtue of their causal integration with the rest of the cell. If there is code in the genome, its role is not to specify outcomes so much as it is to participate, with other cell components, in sets of self-regulating processes that instantiate the flexible biological capacities needed by living systems.

Proximate means and ultimate ends

The idea that genomes are protean in their ability to respond to circumstances to which they are tightly coupled via a wide variety of epigenetic cell processes, and hence have the capacity to influence the evolutionary trajectories of the lineages of organisms that bear them, is one which Shapiro imparts effectively enough. A weakness of the book, however, is that his enthusiasm for biological detail sometimes makes the going hard and the overall message more elusive than necessary. Bulleted lists and numerous tables provide useful summaries, but one sometimes wishes for a more discursive and measured assimilation of what by any standards is an exceptionally rich corpus of scientific data and findings. Unusually, this is a biology book entirely devoid of figures, and I fear that this will limit Shapiro’s comprehending readership to those already possessed of a reasonably strong background in basic genetics and cell biology. This is a pity. What there are, in abundance, are references to the relevant literature. Supplementary online resources are also provided on the publisher’s website, including additional references, suggested readings for ‘non-professionals’, and several appendices (which include – hurrah! – a number of figures). These extras could be seen as a useful bonus, or one could feel slightly cheated that they were not integrated into the printed book.

While the various examples that Shapiro discusses all serve to reinforce the point that genomes are more plastic than we tend to think, the evolutionary significance of the various genome-reengineering mechanisms is sometimes not made sufficiently

obvious at the points where they are introduced and discussed. That said, Parts III and IV do, in the end, come round to reflect on big evolutionary issues and themes – although not to the degree that one might expect from the title. However, it is probably unreasonable of me to complain about that deficiency now, for towards the start of this review I set out (and tacitly accepted) what I took to be Shapiro's more proximately oriented objectives. Perhaps, therefore, it should be deemed a measure of his success in meeting those that it is now possible to see more clearly the space that I think remains in the literature. This is for a synthesis even more ambitious than Shapiro's, one that having taken fully on board the biology he sets out then goes on to explore in detail what it all means for neo-Darwinism and evolution-oriented mathematical biology. What, if anything, do the biological complications to which Shapiro introduces us mean for our understanding of the levels of selection debate²⁸ or our ability to model evolutionary processes and phenomena? To what extent do they call into question the competence of population genetics?²⁹ Are such questions naive? (If nothing else, the synthesis I am advocating should provide a sense of an answer to *that* question.) If they are not naive, then perhaps these are questions as much for philosophers as biologists, for the symbiosis between biology and philosophy can be a fruitful and transforming one. As it is, Shapiro deserves the thanks of many for providing such expert guidance into the complex literature of some fascinating biological realms.

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² T. Dobzhansky. Biology, Molecular and Organismic. *American Zoologist* 1964; 4: 443-452; T. Dobzhansky. Nothing in Biology Makes Sense Except in the Light of Evolution. *The American Biology Teacher* 1973; 35: 125-129.

³ D. L. Hull. 1974. *Philosophy of Biological Science* Englewood Cliffs, NJ: Prentice-Hall.

⁴ P.E. Griffiths. 2008. Philosophy of biology. *Stanford Encyclopedia of Philosophy*. <http://plato.stanford.edu/entries/biology-philosophy/> (accessed 6 February 2012).

⁵ Represented today in the work of Angela McLean and Martin Novak, for example.

⁶ J. Shapiro. 2011. *Evolution: A View from the 21st Century*. Upper Saddle River, NJ: FT Press Science.

⁷ Shapiro summarises much of the material included in the book in J.A. Shapiro. A 21st century view of evolution: genome system architecture, repetitive DNA and natural genetic engineering. *Gene* 2005; 345: 91-100.

⁸ E. Mayr. Cause and Effect in Biology. *Science* 1961; 131: 1501-1506.

⁹ F.H.C. Crick. On Protein Synthesis. *The Symposia of the Society for Experimental Biology* 1958; 12: 138-163.

¹⁰ M.A. O'Malley, W. Martin and J. Dupré. The tree of life: introduction to a philosophical debate. *Biology and Philosophy* 2010; 25: 441-453; M.A. O'Malley and E.V. Koonin. How stands the tree of life a century and a half after the Origin? *Biology Direct* 2011; 6: 32. <http://www.biology-direct.com/content/6/1/32> (accessed 9 March 2012).

¹¹ J. Monod. 1971. *Chance and Necessity*. Harmondsworth: Penguin.

¹² J. Dupré. 2012. *Processes of Life*. Oxford: Oxford University Press.

¹³ D. Bray. 2009. *Wetware: A computer in every living cell*. New Haven, CT & London: Yale University Press.

¹⁴ Mattick Laboratory 2010. Laboratory wiki pages (Research tab). <http://matticklab.com/index.php?title=Research> (accessed 5 February 2012).

¹⁵ See, for example, L.J. DeFelice. Information Isn't Everything. *Science* 1999; 284: 1935.

¹⁶ A partial exception is P. Godfrey-Smith. 2007. Information in Biology. In *The Cambridge Companion to the Philosophy of Biology*. D. Hull and M. Ruse, eds. Cambridge: Cambridge University

- Press: 103-119. In addition, a growing movement seeks to understand the roots of higher cognition in terms of the biology of simple organisms (see e.g. <http://www.hss.adelaide.edu.au/philosophy/cogbio/>).
- ¹⁷ P.E. Griffiths. Genetic information: a metaphor in search of a theory. *Philosophy of Science* 2001; 68: 394-412; S. Oyama, P.E. Griffiths and R.D. Gray. 2001. *Cycles of Contingency: Developmental Systems and Evolution*. Cambridge, MA: MIT Press; L. Moss. 2003. *What Genes Can't Do*. Cambridge, MA: MIT Press.
- ¹⁸ C.T. Bergstrom and M. Rosvall. The transmission sense of information. *Biology and Philosophy* 2011; 26: 159-176; see also C.T. Bergstrom and M. Rosvall. Response to commentaries on "The transmission sense of information". *Biology and Philosophy* 2011; 26: 195-200.
- ¹⁹ A one-day workshop on 'Natural Information' was held at the University of Aberdeen on 13 February 2012, for example.
- ²⁰ See for example P. Davies and H. Gregersen. 2010. *Information and the Nature of Reality – From Physics to Metaphysics*. Cambridge: Cambridge University Press.
- ²¹ C.E. Shannon and W. Weaver. 1949/1998. *The Mathematical Theory of Communication* Urbana, IL: University of Illinois Press.
- ²² E.F. Keller. Rethinking the Meaning of Biological Information. *Biological Theory* 2009; 4(2): 159-166.
- ²³ E. Davis. The life of information, from drums to Wikipedia. Review of James Gleick, *The Information – A history, a theory, a flood* (Fourth Estate, 2011). *Times Literary Supplement*, 23 August 2011.
- ²⁴ For a sketch of what some of the bases for such a theory might be, see A. Powell. 2009. *Molecules, Cells and Minds – Aspects of Bioscientific Explanation*. PhD thesis, University of Exeter. <http://hdl.handle.net/10036/95416>; 171-174.
- ²⁵ G.S. Stent. The genetic approach to developmental neurobiology. *Trends in Neurosciences* 1980; 3(2): 49–51.
- ²⁶ M. Amos. 2006. *Genesis machines: the new science of biocomputing*. London: Atlantic Books.
- ²⁷ E. Schrödinger. 1944. *What is Life?* Cambridge: Cambridge University Press.
- ²⁸ S. Okasha. 2006. *Evolution and the Levels of Selection*. Oxford: Oxford University Press.
- ²⁹ P. Gildenhuys. Righteous modelling: the competence of classical population genetics. *Biology and Philosophy* 2011; 26: 813-835.