Evolution: a view from the 21st century
James A. Shapiro
FT Press Science, 2011
ISBN: 0132780933
Pages: 272
Price: $23.09

In his book, *Evolution: A View from the 21st Century,* James Shapiro attacks as inadequate the 20th century idea of evolution as *essentially a selection biased random walk*. Several technological analogies are proposed to describe the required conceptual shifts including that genomes should be thought of, not as inert data storage objects, but as dynamic read-write devices and that evolution should be understood as a process through which organisms engage in natural genetic engineering. The latter idea is the most pervasive through the book and also likely to be the most controversial as it suggests and even involves an element of design and any hint of design sets off alarm bells for evolutionary biologists. Aware of this discomfort, Shapiro is careful to put distance between his scientific model and anti-scientific creationism although, interestingly, given that he views cellular processes that involve sensing and responding to the environment as a kind of cognition and organisms and cells as, in some sense, intelligent agents actively engaged in shaping their own evolutionary trajectories, the term intelligent natural genetic engineering would seem to come close to what he has in mind.

The intended audience is broad. Shapiro sets himself the challenge of being accessible and interesting to the non-scientist, but at the same time provocative and yet convincing to the more specialist reader with a background in molecular biology and evolution. To help bridge the gap and to satisfy readers with an appetite for greater detail there is a swathe of additional material available in the form of online appendices and an extensive list of suggested further readings, primarily directed towards stimulating and providing further background for the interested non-scientific reader. The book operates at a conceptual level, arguing the need for and describing new intellectual frameworks for evolutionary theory. Throughout, Shapiro's breadth of knowledge of contemporary biology and molecular evolution are impressive, made all the more compelling by his personal perspectives and reflections on several of the developments of modern biology that are relevant to his thesis and appear to have shaped his ideas. He draws inspiration, among other sources, from the ground-breaking work of his close friend and collaborator, Barbara McClintock, herself no stranger to controversy, and her scientific successors who were the first to demonstrate that genomes are not static and can undergo rapid and disruptive changes, mediated by mobile genetic elements. The book is stimulating and provocative reading, even if all of the views and perspectives it advances are not always shared.

The book opens with a discussion of how cells process information, with an emphasis on the similarities (and differences) between the microprocessors of computer science and mechanisms of information processing in living cells and organisms. Shapiro challenges a view of cell biology that would treat DNA as an information molecule, omnisciently directing cellular processes from the comfort of the nucleus. An obvious example of cells acting on their DNA comes from DNA repair: cells have mechanisms that sense and repair DNA damage. Shapiro interprets this as a contradiction of the central dogma of molecular biology. Here and elsewhere in the book, the zeal of the iconoclast to tear down intellectual edifices, perhaps gets the better of balance and even accuracy. For instance, mRNA splicing is posed as an example of information flow from proteins to RNA. While it is the case that proteins present in the cell modify the sequence information encoded in RNA molecules, it seems unlikely that Francis Crick, had he been aware of alternative splicing, would have considered this an example of the *transfer* of sequence information from proteins to RNA in the same way that sequence information is transferred from RNA to DNA in the process of reverse transcription, the discovery of which did bring about revision of the central dogma in 1970.

Despite any possible disagreements over the details, most contemporary biologists would probably share, broadly, the view of organisms and cells as complex systems, consisting of networks of interacting components that enable them to process information from their environments, their own states and other cells - in short, a systems biology view of life, with the genome as an interactive participant. Cells act on their genomes, maintaining and restructuring chromatin. For Shapiro this is analogous to the formatting of computer files and it is one of the reasons that genomes should properly be seen as read-write devices, rather than, more traditionally, as a form of read-only memory. Recent research has shown the extent to which cells are engaged in remodelling and marking chromatin and the importance of this for controlling many processes, including mRNA expression, especially the large-scale and stable changes in expression required as cells differentiate. Indeed, in some cases epigenetic changes are heritable, so that life histories can influence genetic inheritance sometimes for several generations, in a throwback to the Lamarkian model of evolution.

The view of evolution as a gradual, random walk in DNA sequence space, under the influence of selection, is challenged not only by the fact that cells modify or *reformat* (sometimes heritably) their DNA in response to external cues but also by the fact that changes to DNA sequences are often abrupt and substantial, rather than consisting of point mutations. Understandably, much space in the book is given over to the discussion of processes through which DNA sequences undergo large modifications. However, this makes for less compelling reading, feeling at times like a litany. For the author, these are the tools at the disposal of a process of natural genetic engineering, and they include genomic freeloaders, such as DNA transposons and various classes of retroelements. Some of these are extremely abundant, and movements of these elements have been shown to have the potential to bring about major phenotypic changes, for example bringing a gene under the control of different cis-regulatory elements or modules. Large genetic changes can also occur through duplication of tracts of the genome or even complete genomes, giving rise for a period following duplication, to opportunities to innovate new protein functions and even to bring about substantial rewiring of genetic networks. Shapiro discusses the evidence for whole genome duplications and some well-known examples - the role of genome duplications in vertebrate evolution and the diversification of flowering plants.

That abrupt changes make a substantial contribution to genomic and sometimes even phenotypic evolution (*e.g*. tetraploidy), in contrast to Darwin's gradualist view, is no longer controversial. Less clear cut is the extent to which the cell's natural genetic engineering toolkit can be activated in response to environmental signals, so that in some sense, evolution can be seen as a process that is actively managed by the cell. At least in the case of microorganisms this was demonstrated through cell stress experiments. In many such experiments cited in the book, including work by the author, the activity of mobile elements, capable of bringing about major phenotypic changes, increases in the stress condition. The genome becomes more labile precisely at a time when it is important for a population of microorganisms to explore possible alternative solutions in a challenging environment. But, more importantly, not only can the cells arrange it so that their genomes mutate more rapidly and more aggressively under stress conditions, but they can bring about directed genomic changes. To demonstrate this idea Shapiro points to the fascinating CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) system in prokaryotes, a defence against viruses that involves incorporation of fragments of viruses into the prokaryote genome. Such directional changes to the genetic material of the cell do push evolutionary theory towards a requirement of major conceptual shift. Mutations are supposed to be stochastic and not directional, but if prokaryotes have the means to incorporate viruses into their genomes, thus enabling them to become resistant to the virus, we are forced to accept that heritable genomic change within a single individual can sometimes be a directed process which occurs as a response to the environment. Instead of restricting to specialist examples of focussed or directional mutation, often involving defence against infection, Shapiro makes the broader claim that, truly random mutation would be the exception. But, this is somewhat disingenuous, given that very little in biology is truly random, and the mutational processes described may still be largely stochastic, even if sites at which these mutations occur are not randomly distributed through the genome. The question of whether regulated and directed/non-random mutation is the exception or rule is key to the central thesis of the book, that evolution requires a new conceptual framework for the 21st century.

Overall, at least for microorganisms the author's case that new theoretical frameworks are required is compelling. The promiscuous uptake of genetic material by prokaryotes can be evolutionarily advantageous and it is not too surprising that mechanisms exist to ensure that this uptake occurs, such as the CRISPR system mentioned above, and is directional - this does not fit neatly with a notion of discrete species, evolving gradually through random mutation and selection. Researchers involved in phylogenomics of prokaryotes have long had to grapple with this poor fit. It is not surprising that the parameters of the evolutionary process themselves are tuned by evolution. A species that managed to evolve a perfect mechanism to replicate DNA would ultimately die out as it failed to adapt to the inevitable changes in its environment; an excessive mutation rate would result in too many unfit progeny. Shapiro points to a set of observations that require a changed mindset in evolutionary theory: that evolution is not predominantly gradual, but includes a major contribution from abrupt, disruptive events; that mutation is regulated by cells, frequently in response to their environment; and that genome changes can be a directional, targeted result of a process of natural genetic engineering, rather than stochastic mistakes. The last of these is the strongest and is probably restricted to few, very specific examples. The first is the weakest and would not be too much of a stretch for an early 20th century evolutionary biologist to accommodate. The incidence of the second observation is difficult to quantify and the extent to which evolutionary theory requires a radical overhaul may depend on this. It is clearly the case that evolution colours outside the lines of evolutionary theory, but in many and perhaps most settings it seems unlikely that thinking of evolution as a process of directed natural genetic engineering would be helpful. Whether existing models and theories can accommodate modifications and exceptions to the rules, or whether the exceptions are the rules in some or all branches of the tree of life, remains to be seen.

Cathal Seoighe