Engineering without an engineer, or shedding new light on feats in the junkyard of DNA

Evolution: A View from the 21st Century

James A. Shapiro

Financial Times Press Science, Upper Saddle River, NJ, 2011

J. Günter Grossmann

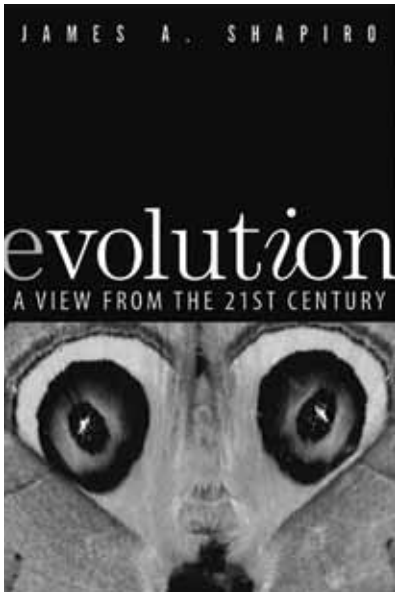
This is a thought-provoking book by a highly eminent expert in microbiology and bacterial molecular genetics. He developed the concept of "natural genetic engineering" over the last 20 years, and produced numerous publications in the relevant scientific literature. Thus one may perhaps be a little taken aback considering the number of published commentaries that have been offered since the appearance of his book.

Bearing in mind a variety of reviews in the very recent literature and a range of accessible appraisals of Shapiro's book (incl. a series of reports and exchanges from ID proponents since 2011[1]), I would like to restrict my brief review to a few principal observations. In view of the slender size of Shapiro's book (the actual length of main text consists only of 147 pages, including about 20 pages with tables), the length of all reviews taken together will soon match the extent of the original—this is also testament to the author's standing and naturally the high profile debate on departures from Darwinian evolution.

Cover, captured

A striking photo of the wings of a mimetic moth from Costa Rica adorns the cover of Shapiro's book and tenders a promising opening into an up-to-date scientific account of biology in general and evolution in particular. However, don't be baffled that there is neither the expected traditional discourse of evolutionary biology nor a specific reference to moths in the book other than mentioning them in two passages in passing. It's therefore all the more provocative considering that another moth—the peppered moth, *Biston betularia*—has been portrayed as the prime example for natural selection and thus one of the main accepted drivers for change according to Darwinian evolution in action. 'Industrial melanism' was the catchphrase to highlight the increase in the number of black versus speckled moths due to rising pollution in areas with developing heavy industries. Despite various criticisms from the evolutionary camp that it does not present such a well-understood example of natural selection in action after all,[2] this 'paradigm' still experiences resurrection[3] to underline its apparent unfaltering attractiveness.

Still looking at the front cover, a second feature stares at you. The 'e' of evolution is set apart in red colour from the rest of the word, which is printed in white on a black background (and with just the '*i*' written in italics). This pattern is to be understood as a play on terminology of the Digital Age and the inventiveness



of funding schemes using the 'e' as a placeholder for 'electronic' such as in e-learning, e-publishing or e-science. It is to highlight *e*volut*i*on as a subject matter that has come of age, which needs to embrace high performance computational and network resources as well as data handling and storage given the immense information ('*I*') content accumulated from structural and functional genomics as well as from computational systems biology since the beginning of the new century.

A novel thesis

The cover page sets the scene deftly for a "fresh look at the basics of evolution in the new century" as announced in the Introduction. Shapiro says that "we currently see only the tip of the iceberg" in view of our understanding of how such an incredible diversity of existing life arose. Despite this drawback, he introduces the stimulating idea of innovation through 'natural genetic engineering'. The latter is regarded as the driving force for generating genomic variation once basic/simple biological organisms have acquired their directives to evolve. According to the author's well-founded studies and

investigations integrating the modern genomic concepts, the "basic fact of life" is that mutations, i.e. genetic variations do not arise by chance. Consequently natural selection can no longer be the primary shaping force of evolution. Are we witnessing a paradigm shift in evolution according to Shapiro stating, "Living cells do not operate blindly"? In other words the colourful and dazzling parade of disguise of the moth's wings has been the result of a feedback mechanism that developed over time and eventually engraved in its genetic makeup in order to scare possible predators. However, so far the current understanding of evolution is still very much rooted in tradition—as is every so often voiced in influential journals.[4]

Supportive of the notion of 'natural genetic engineering' is the more than 50 years of built-up evidence for the need of an overhaul of evolutionary mechanisms such as the random nature of mutations, natural selection, and gradual change. For this, one may also consider the experiments by Waddington as seminal.[5] The effective capabilities of cellular systems to restructure the genome by an abundance of masterstrokes (DNA insertion elements, DNA-based transposition mechanisms, mobile elements and RNA-based mutagenesis processes, to name only a few) reflect a 'fluid genome' prone to countless rewriting events through sensing of the environment.

Shapiro introduces the apt analogy from computing that the genome is not like a read-only but like a read-write memory, which can be formatted in numerous ways to suit the organism. Most interestingly this read-write concept is not only restricted to the small proportion of DNA (~2%) encoding proteins, i.e. the real workhorses of each organism (see figure 1), but also to significant amounts of DNA that had been written off as irrelevant ('junk' DNA). In this regard it is fitting to mention the very recent ENCODE project, which reported, after analyzing the functional elements of the human genome, that most of the so-called 'junk' is in fact very important.[6] For example, it is vital for delicate and dynamic regulatory and transcriptional functions. Of further interest is also a survey of the human microbiome project[7] recently revealing an immense diversity of microbes that live on and in our bodies with implications not only for medicine and public health but also for evolutionary processes. For instance theses microbes contribute to tutoring and education as well as protection of the developing human host. Yet another interconnected research area to evolution that only just glanced at the tip of the iceberg.

A well-known dilemma

Even if there is something like a cell's own life, the primary crux of the matter is that the author doesn't let us know the prerequisite(s) for his thesis. That is, an understanding of how the basic principles of life in a cell are defined and acquired so that at a specific stage the workings of evolutionary information processing, the 'natural genetic engineering', can take over. It is the latter that forms the core of the book and is described in a truly impressive, concise, and scientifically substantial manner. This will most likely be overwhelming and intense for someone who has neither a degree in modern biology nor is a scientist with interest in molecular/cellular biology or genetics. It remains debatable whether a layperson will get something out of this technical account. This is aggravated by the fact that a further 100 pages (in addition to the above mentioned 147 pages) contain an index, a glossary comprising 25 pages with basic terms (such as gamete, homeodomain, and retrovirus), and 1,162 references, which the enthusiast can upscale by an extensive and unique on-line referencing system. Furthermore, there are no figures, schematics or diagrams to help readers understand the main points! This seems out of place, considering visual aids would be very well suited to help illustrate the numerous and intricate ways in which DNA sequences can be modified.

A reasoned layout

In the four parts, Shapiro progressively builds up a mechanistic picture of "the capacity of living organisms to alter their own heredity" from cellular to multicellular life-forms and then going beyond Darwin.

In part I, we learn in detail about molecular descriptions of how bacteria, yeast, and mammalian cells acquire knowledge through their sensory systems. These are well elucidated by specific examples, such as the sophisticated cellular regulations of the bacterial sugar metabolism (one of the author's expert areas) and the complex cellular feats in identifying and correcting DNA defects (DNA damage repair).

Implications for the 'Central Dogma of Molecular Biology' formulated by Francis Crick in 1958[8] are revisited in the light of 21st century's knowledge. This 'dogma' states that there is a directional flow of sequence information from nucleic acids (DNA/RNA) to protein. It is clear that amino acid sequences of proteins cannot be reverse-read into nucleic acid sequences. Also, inverted ribosome action is unworkable due to the redundancy of the genetic code. So one has to question Shapiro's point of criticism. He puts the dogma's flow of information on a level with non-adjustability of DNA information towards external stimuli, reaching the usually understood view of the genome as a read-only memory.

Mechanisms of genetic change are central to part II. Shapiro tries

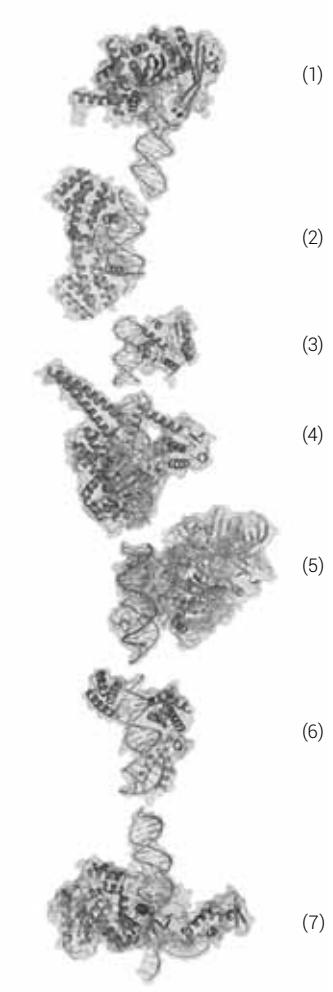


Figure produced using PyMOL (www.pymol.org), using protein data bank entries 1muh, 1fdq, 1t39, 1a36, 3pt6, 1o4x, and 3os1.

Figure 1. Homing in on DNA–regulatory signalling and DNA modification (molecular genetic engineering) require an enormous and intricate amount of distinct operations. Proteins, the cellular workhorses, accomplish this masterpiece through an amazing sequence of work. The schematic shows an example of seven DNA segments (DNA double helices are arranged vertically) being worked on by proteins (represented as ribbon models within their transparent molecular surfaces) during specific tasks. These include e.g. **(1)** DNA transposition (movement of DNA segments, so-called transposable elements), **(2)** prevention and **(6)** activation of transcription (for protein production), **(3)** nucleotide flipping during DNA repair, **(4)** relaxing DNA during winding and unwinding, **(5)** transfer of a methyl group to DNA (adjustment without changing the original DNA, an example of epigenetic DNA modification) and **(7)** viral DNA insertion into the host genome (retroviral DNA integration).

to underline the aforementioned comparison of the genome being a read-write storage memory that is part of the normal life cycle.

One may wonder, however, about the evolutionary potential of some of the examples presented. The adaptive immune system is indeed a textbook example for 'natural genetic engineering', yet there is a difference between somatic and germ cells. The adaptive immune system is associated with the former cell type, which means that genetic modifications or mutations will not be passed on to offspring, whereas there is the potential for germ cells to do so.

In contrast, part III provides higher-level discoveries in complex organisms, such as symbiotic cell fusion, horizontal DNA transfer, and the nature of protein evolution in the form of modular building blocks. These building blocks are known as (protein-) domains and represent elementary components—like parts in a construction kit—which are assembled depending on the desired overall function. They further delineate the remarkable manufacturing properties of cells and cellular constituents.

The data from molecular genetics and genome sequencing appear in favour of abrupt and saltational genomic changes "at key moments in evolution". The last part formulates a new and radical conceptual basis for evolutionary research after reviewing and summarizing the principal directions of gathered evidence for the postulated idea of sudden, non-Darwinian 'natural genetic engineering'. This contrasts with traditional neo-Darwinian, a slow, "selection-biased random walk through the limitless space of possible DNA configurations". According to the author, the new concept will attract and include physical and computational scientists not being biased by the formal education in the life sciences.

Concluding remarks

Evolution—A view from the 21st century presents a modern and different view on evolution based on current genetic analyses. It is certainly of interest for scientists with aspirations in the area of modern molecular biology and genetics as well as intra- and intercellular signalling and regulation. Coincidentally it is also appealing to note the formation of two camps in evolutionary biology divided over the question of the importance of the 'creative' concept of natural selection in transforming organisms. Even though the title appears a bit presumptuous, it is clear that the remaining decades of this century will surely bring many more amazing findings. Some will be from serendipitous observations;[9] others will result from well planned investigations such as those by large consortia.[6,7] In addition emerging natural genetic engineering tools will be exploited for studying and reshaping genomes of many species.[10] Not surprisingly the author highlights that there will be exciting and challenging years ahead. Yet new concepts will come and go.

The book tries to clarify that the cell is its own engineer—that there is no need for an external agent—i.e. that genomic change, remodelling, formatting, however named, represents an intrinsic vital cellular characteristic. Still what is evoking the engineering capacity, to give rise to new properties? Where does the necessary training come from? And when does a cell graduate as an engineer? Are these the key moments of evolution? According to Shapiro, random natural selection has nothing to do with it.

Remarkably, the Introduction informs about Rudolf Virchow, a contemporary of Darwin and one of the big figures in pathology. He coined the phrase *omnis cellula e cellula* (every cell originates from

another cell). Obviously Virchow also doubted Darwin's theory of evolution. Yet Shapiro neither accepts Darwinian selection nor a supernatural force but is in favour of a 'third way' (the latter is not spelled out in the book but in subsequent exchanges with ID proponents[1]). Startling but at the same time still encouraging, therefore, is the phrase from his book, "It requires great faith to believe that a process of random, accidental genome change could serve this function." Thus there is still hope since great faith can accomplish much.

However, sitting on the fence is of little avail either.

> "I know your works, that you are neither cold nor hot. I could wish you were cold or hot. So then, because you are lukewarm, and neither cold nor hot, I will vomit you out of My mouth" (Revelation 3:15–16, NKJV).

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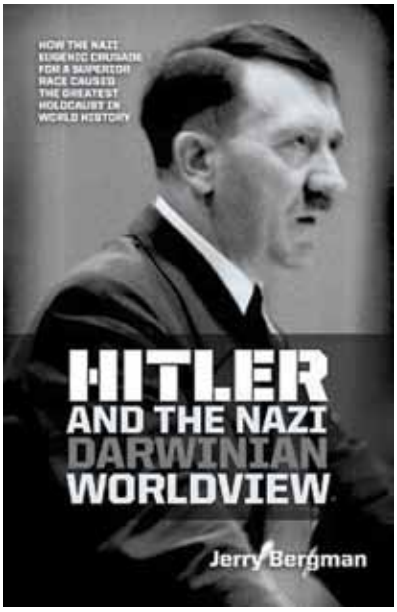
The Darwinian core, and fundamentally anti-Christian character, of Nazism

Hitler and the Nazi Darwinian Worldview
Jerry Bergman
Joshua Press, Ontario, 2012

John Woodmorappe



This work is a *tour de force*. It is *the* definitive book on the relationship of Darwinism and Nazism. It finds painstaking support from hundreds of references to studies in Nazism, the Third Reich, Darwin, eugenics, and related subjects. The authorities on Nazism cited in this work include Richard Breitman, Christopher R. Browning, John S. Conway, Joachim C. Fest, Ian Kershaw, Leon Poliakov, Bryan Mark Rigg, Paul Roland, William L. Shirer, Hugh R. Trevor-Roper, Richard Weikart, and many others.

Some unbelievers, obviously interested in attacking Christianity, have insinuated that Hitler and the top Nazis were devout Christians. This is very far from the case, as shown decisively by Bergman.

One common misconception about 'social Darwinism' is that it was some kind of intellectual fad. Perhaps this was so elsewhere, but not in Germany! There it was taken very seriously, as made so obvious by this book, and made into *the* central factor animating German political philosophy and action.

The history of Pan-Germanism, or *Deutschtum*, followed the same path. While it long predated Darwin, it also only became genocidally virulent when connected to, and synthesized with, Darwinism. The same was true of German racism and German anti-Semitism.

Many victims of Nazism

In contrast to the usual works on Nazism that focus primarily or entirely on Jews, Bergman considers other victims. The first victims of the gas chambers were not Jews: they were the 'Darwinian unfit' Germans, such as the mentally retarded (p. 258).

The Nazis also had genocidal plans for the Slavs. The Poles, and other Slavs, were *Untermenschen* (subhumans) who would live only as needed as helots for the Third Reich (pp. 44–45). The siege of Leningrad was planned to cause the starvation of the population (pp. 33, 215), whose surrender was not to be accepted even if offered. Martin Bormann (p. 166) pictured the German invasion