Book Review

Evolution in Four Dimensions

Eva Jablonka and Marion J. Lamb.

MIT Press, Cambridge, MA, 2005.

The basic claim of Jablonka and Lamb is that "biological thinking about heredity and evolution is undergoing a revolutionary change. What is emerging is a new synthesis which challenges the gene-centered version of neo-Darwinism that has dominated biological thought for the last fifty years." They argue in the Prologue that

- there is more to heredity than genes;
- some hereditary variations are nonrandom in origin;
- some acquired information is inherited; and
- evolutionary change can result from instruction as well as selection.

The subtitle of the book is *Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life*; thus, the four dimensions of the title. "The challenge [this book] offers is not to Darwin's theory of evolution through natural selection, but to the prevalent gene-based unidimensional version of it." The audience to which the book is directed is revealed in the Preface in the following sentence: "We hope that the book can be read not only by professional scientists but also by the many people who are interested in biological ideas, and are fascinated (and sometimes worried) by the current ways of thinking about biology, especially about modern genetics."

The book is divided into three major sections. The first section (Chapters 1, 2, and 3) is devoted to the genetic system: how Darwin's theory became so gene centered; the relation between genes and characters; and evidence that not all genetic changes should be seen as random, chance events. The second section (Chapters 4, 5, and 6) deals individually with three other evolutionary dimensions.

- Through epigenetic inheritance, structurally and physiologically different cells with identical DNA content are able to transmit their phenotypes to daughter cells.
- Animals are sometimes capable of transmitting their behaviors and preferences through the mechanism of social learning.
- Humans transmit information through language and other forms of symbolic communication.

The third section (Chapters 7, 8, and 9) shows how the systems of inheritance depend on and interact with one another; it suggests how they may have originated and how they have guided evolutionary history, and considers some philosophical, political, and ethical issues associated with the four-dimensional view of life.

Each chapter ends with a "dialogue" between a mythical critic called Ifcha Mistabra (Aramaic for "the opposite conjecture") and the authors. The final chapter contains a "last dialogue" that helps to review, flesh out, and extend questions that had or had not been presented by Ifcha in previous chapters. Copious endnotes, containing the more specialized information, are organized on a page-by-page basis at the end of the book. An extensive bibliography occupies pages 417–446, followed by a well-documented index. Quaint drawings are peppered throughout the text to help the reader visualize the concepts presented therein.

Natural selection requires heritable sources of phenotypic variation to be effective. The most commonly known source of phenotypic variation is the genetically based differences between organisms in a population. The first three chapters review how Darwinism has been transformed by new discoveries, especially those emanating from molecular biology and developmental biology. In addition to gene mutations, this section outlines three additional sources of heritable diversity produced through sexual reproduction: (1) offspring receive equal (except for X and Y chromosomes) amounts of DNA from both parents, (2) each reproductive cell (egg, sperm) contains a sample half of the genes from each parent through the process of meiosis, and (3) the process of crossing-over during meiosis recombines genes that formerly were on different parental chromosomes.

I found the next three chapters to be most interesting. Chapters 4, 5, and 6 discuss how heritable phenotypic variations can be produced by epigenetic, behavioral, and symbolic systems, respectively. By way of a thought experiment, the authors demonstrate how a population of genetically identical organisms can evolve through "epigenetic inheritance systems" (EIS) into phenotypically different groups, without any changes at the genetic level (nucleotide sequences in DNA). "An 'epigenetic change' is a 'developmental change' that leads to an altered phenotype. The adjective 'epigenetic' does not mean that the change is heritable, i.e., 'epigenetic change' is not identical with 'heritable epigenetic change'." Differentiation of various cell types of a multicellular organism, during normal development from the fertilized egg (zygote), produces an individual consisting of genetically identical "somatic" cells (all body cells except egg and sperm) with different structures and physiologies such as those of muscle, bone, skin, and blood. If each of these cell types could survive as an independent organism and reproduce by asexual means (fragmentation, binary fission, budding, grafting, and aggregation), there would be numerous populations, each with their own characteristics (phenotypes, traits), yet all genetically identical both within and between the populations. Somatic cells become differentiated into different tissue types by activating specific sets of genes and inactivating others. Once early cells of an embryo undergo this differentiation process, their cell fates and those of their mitotically derived descendants normally become

irreversibly established by EIS. Understanding how these systems operate has been essential to the success of modern cloning and genetic engineering projects. Four broad categories of EIS are presented: (1) self-sustaining feedback loops, (2) structural inheritance, (3) chromatin-marking systems, and (4) RNA interference (RNAi).

The simplest example of a self-sustaining feedback loop is one in which a temporary cue (e.g., an external environmental change or an internal developmental or regulatory factor) turns on (activates) a gene, and the product of that gene action (RNA or protein) ensures the continued activity of itself (page 119). The authors state that such examples have been found in bacteria but give no specifics about any of them. However, the Notes for page 119 cite four articles about self-sustaining feedback loops that can be found in the Bibliography. It is the state of the loop that is transmitted from one generation to the next as a heritable entity. If every cell has multiple autonomous loops, each of which has two states ("on" or "off"), a large number of functional variants of the cell are possible, some of which might be substrates for natural selection.

An often cited example of structural inheritance is that found in ciliate microorganisms such as *Paramecium*. The outer surface of this organism is called the "cortex." Cilia are hairlike appendages of the cortex, arranged in rows. By microsurgery, a piece of cortex can be excised and reinserted after rotation through 180°. Offspring of such a cell inherit this change. It is hypothesized that the structure of the cortex serves as a template that directs the assembly of the protein components of cilia in a daughter cell. It is noted that some heritable architectural variants of normal proteins, called prions, also appear to have templating properties. The term "prion" indicates that it is a "proteinaceous infectious" particle. Once such a particle is present in a cell, the structure of normal forms of the same protein can be changed into prion conformation by contact with the mutant protein acting as a template. A prion is responsible for a neurological disease in cattle known as bovine spongiform encephalopathy (BSE) or "mad cow disease." Cattle fed supplemental feed containing sheep or cattle prion proteins can develop BSE as an acquired trait. Some yeast and fungal prions seem to do no harm, but some might have adaptive roles. For example, a strain of yeast carrying the prion PSI^{+} is better able to tolerate harsh conditions than the genetically identical strain without the prion.

Chromatin markings are a third kind of EIS. Chromatin consists of DNA plus all the RNA, proteins, and other molecules associated with it in chromosomes. In eukaryotes (nucleated cells), a group of proteins called histones help compact the DNA during cell division and generally inactivate genes in regions of the DNA to which they are attached. The same DNA sequences can have different patterns of association with histones in various cell types and at different times of a cell's life. Alternative heritable differences in the non-DNA features of chromatin are known as "chromatin marks." A methyl group (CH_3) often becomes attached to certain DNA nucleotides (e.g., cytosine bases in CG doublets or CNG triplets; N = any of the four nucleotides). Methylated DNA is found in all vertebrates and in many invertebrates, fungi, and bacteria. Densely methylated genes are usually inactive (not transcribed into RNA). How precise methylation occurs is incompletely known, but once it is established methylation might act directly by interfering with the binding of regulatory factors to the control region of a gene or it might act indirectly through a set of proteins that bind specifically to methylated DNA and thereby interfere with translation. Since a CG doublet on one DNA strand always pairs with a GC doublet on the opposite strand, a methylated cytosine (C^{m}) on one strand can be recognized by a methyltransferase enzyme that attaches a methyl group to the unmethylated C on the opposite strand. Thus, both daughter cells will usually receive the methylation pattern present in the mother cell. One of the best plant examples of a fairly stable epimutation (methylation pattern) is found in the peloric (Greek for "monster") flower form of the toadflax *Linaria vulgaris*. Carl von Linnaeus (1707–1778) thought that it was a new species. Today, it can still be found in the same region where Linnaeus found it. One of the most outstanding examples of an EIS in animals is found in the hair color of laboratory mice. Using genetically identical individuals, it was found that some of them are yellow, others are mottled, and still others develop a pseudoagouti pelage pattern. When the same genotype allows the production of more than one phenotype, the trait is said to exhibit "developmental plasticity." Surprisingly, yellow mothers tend to produce yellow offspring, mottled mothers tend to have mottled offspring, and pseudoagouti mothers tend to have more pseudoagouti offspring compared to the other two types of mothers. This variation was correlated with the methylation pattern on an extra bit of DNA (originating from a transposon or mobile genetic element) in the regulatory region of a coat-color gene.

Some amino acids of histone molecules can be modified by enzymes that add or remove a small chemical group such as an acetyl (H_3–C=O) or a methyl group. The addition of acetyl groups to histones usually loosens chromatin structure, thereby enhancing transcription. Removing acetyl groups and adding methyl groups to histones contributes to condensation of chromatin fibers and inhibition of translation. These chromatin marks are often highly specific and localized. They can be induced by signals that a cell receives during embryological development or in response to changed environmental factors. Once induced, the information carried via a chromatin-marking pattern can often be transmitted from one cell generation to the next long after the inducing stimulus has ceased.

RNAi is a phenomenon that leads to the stable and cell-heritable silencing of specific genes. It is mediated by small double-stranded RNA molecules known as small interfering RNAs (siRNA). Healthy cells do not produce double-stranded RNA molecules. However, viruses and transposons ("jumping genes" or mobile genetic elements) tend to produce double-stranded RNAs. It is suggested that RNAi is a cellular immune system that helps protect the cell from these foreign sources of DNA. The association of siRNA molecules with the gene that produced it sometimes leads

to a stable methylation or protein-binding chromatin mark that is transmitted to subsequent cell generations. Silencing via the RNAi system destroys the existing abnormal double-stranded RNA and inactivates the gene that produced it. Gene-specific silencing by RNAi has been shown experimentally to be transmitted through several generations in the roundworm *Caenorhabditis elegans*. It has also been used in the development of tomatoes that deteriorate at a relatively slow rate after ripening.

Since epigenetic patterns may have a relatively high rate of generation and a good chance of being beneficial, the authors opine that "adaptation through the selection of epigenetic variants may be quite rapid compared with adaptation through genetic change." However, on page 153 the authors admit that "there is no direct evidence for adaptive epigenetic variants." But "if you accept that heritable variation is possible, self-evidently some of the variants will have an advantage relative to other variants. Even if all epigenetic variations were blind, this would happen, and it's very much more likely if we accept that a lot of them are induced and directed." Whether or not the authors have supplied sufficient evidence for the reader to "accept" these provisions requires studying the text and the cited references.

Three types of "behavioral inheritance systems" (BIS) are discussed in Chapter 5: (1) behavior influencing substances, (2) nonimitative socially mediated learning, and (3) imitation. The authors admit (page 185) that there are no observations or experiments that unambiguously show purely cultural speciation, but the same is true for most of the suggested mechanisms of speciation in animals. The Notes for page 184 state that "Many possible cases of environmentally induced speciation events in plants and animals are described" elsewhere in the references cited. Pregnant female rabbits fed juniper berries produce offspring that prefer these berries to normal food. Chemical cues reach the pups before birth through the amniotic fluid and placenta or after birth through the mother's milk. In the case of English tits, some birds discovered how to open milk bottle covers. Other tits, seeing this process, learned that food was inside these bottles. However, they did not learn how to open the bottles by imitation because each bird developed its own technique for doing this. Nonimitative social learning can occur by seeing or hearing others, usually through their parents and relatives, but sometimes through unrelated individuals. Learning by imitation involves not only what to do but also how to do it. Vocal imitation occurs in some birds, dolphins, and whales. Different populations may have distinctive dialects. The information transferred by imitative learning can occur in a modular manner, unlike the other two BIS. This allows many variant patterns of behavior to develop. The authors acknowledge that although examples of socially learned and transmitted changes in behavior patterns, skills, and preferences are known, most behavioral innovations are ephemeral and do not manage to become established, let alone spread, in a population. Even if there is genetic variation affecting a specific behavioral pattern, this does not negate the possibility that other factors, such as social learning, are less important. Likewise, if social learning is found to be an important source of variations between groups, it does not exclude genetic differences.

The "symbolic inheritance system" (Chapter 6) is peculiar to humans. A pattern of behavior can only be transmitted or acquired through a BIS if it is displayed. By contrast, symbols and genes can transmit latent information (nonexpressed genes, unimplemented ideas) and can skip generations without being displayed or used. Symbolic systems are hierarchically organized, e.g., letters make up words, words make up phrases, and phrases are used to construct sentences. Each of the components can be organized in a vast number of ways, but they only have meaning if the framework for interpreting symbolic information has been learned through active instruction.

Chapter 7 deals with the interactions of genetic and epigenetic systems. One of the most interesting concepts (to me) in this chapter is the problem of how induced developmental or physiological changes can be transformed into inherited characters that appear without an inducing stimulus. Studies of fruit flies have shown that most of their traits in a wild population have very little phenotypic variation even though it contains a remarkable amount of unexpressed genetic variation. Development of these wild-type characters is said to be well "canalized" or "buffered" against minor perturbations caused by genetic or environmental differences. Abnormal flies called "crossveinless" have all or a portion of the tiny cross-veins in their wings missing. Exposing normal (wild-type) flies to an unnaturally high temperature for a few hours during their pupal stage caused about 40% of them to develop the crossveinless phenotype. If only heat-shocked crossveinless flies were allowed to breed, the frequency of the crossveinless trait was shown to increase to over 90% in fewer than 20 generations. However, as early as generation 14, some of the flies developed the crossveinless trait even in the absence of heat shock. Breeding only from these unshocked crossveinless flies in a normal environment, produced strains in which the crossveinless trait was almost 100%. Thus, the crossveinless trait, which was originally an acquired character, had undergone almost complete "genetic assimilation" by selection to become an inherited character that developed in normal environments (without heat shocks). This experiment shows that exposing an organism to an unusual environmental factor can reveal the cryptic genetic variation of a trait on which selection can act to produce recombinants that develop an acquired trait even without the environmental stimulus that was initially required for its production. No evidence was provided for the adaptive value of the crossveinless trait in wild populations.

On page 312, the authors state "[B]oth genetic assimilation and selection for increased flexibility involve the same basic principles—the unmasking and selection of previously hidden variation. West-Eberhard, in particular, has stressed the generality of such processes in evolution, and has suggested the term 'genetic accommodation' for the genetic stabilization through selection of new phenotypic responses." I found this explanation of genetic accommodation wanting. A much better explanation is presented by Suzuki and Nijhout (2006) in *Science* 311:651.

> Genetic accommodation is a mechanism of evolution wherein a novel phenotype introduced through a mutation or environmental change is molded into an adaptive phenotype through quantitative genetic changes. Genetic accommodation differs from genetic assimilation in that the latter results in canalization of the new phenotype so that it is no longer affected by environmental variation, whereas genetic accommodation can result in an increased environmental sensitivity of a plastic phenotype.

Interactions between behavior, genes, and language are presented in Chapter 8, while Chapter 9 looks into the origins of the systems that introduce instructive elements into evolution. In Notes for page 307, we find "Most innovations, whether genetic, epigenetic, behavioral, or symbolic, are ephemeral, even when they are potentially beneficial. The conditions for the establishment and regular transmission of an innovation are quite demanding." The existence of four dimensions of variation in biological populations is undeniable. Compared to genetic inheritance systems, however, the potential importance of epigenetic, behavioral, and symbolic inheritance systems for adaptive evolution is relatively unknown at present and needs further study. Whether or not the four aims of the book, presented in the Prologue, are sufficiently backed by scientific evidence to convince the reader of their importance for adaptive evolution may lie in the subjective eye of the beholder.

The Bibliography shows that Jablonka and Lamb have coauthored four journal articles as well as a previous book titled *Epigenetic Inheritance and Evolution: The Lamarckian Dimension* (1995). M. J. Lamb was Senior Lecturer at Birkbeck College, University of London, before her retirement. Eva Jablonka's biodata is on the Internet at http://www.tau.ac.il/humanities/cohn/staff/eva-jablonka.htm

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