Educational Lessons from Evolutionary Properties of the Sexual Genome

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1 Introduction

With respect to biology, the histories of philosophy, religion, and science in essence have been the histories of mankind's attempts to understand why organic systems work as well as they do. Paradoxically, such understanding might seem at face value to have spiraled downward ever since Darwin and Mendel in the sense that we have many more unanswered questions today than we did in bygone times when almost everyone "knew" that supernatural agents orchestrated the organic world. My favorite metaphor about this paradoxical relationship between science and faith involves a balloon. Think of leading-edge inquiry in any scientific discipline as occurring at the outer surface of a balloon that encompasses contemporary knowledge. As the balloon expands via objective discovery processes, so too does its interface with the unknown, thereby exposing ever-broader horizons that beg further investigation. Thanks to technological and interpretative breakthroughs, the empirical balloon of molecular genetics is now bloating at a pace that is almost unprecedented in the history of any scientific discipline, so the cliché that science can be humbling (as well as enabling) is especially true today in the field of genomics. Sometimes it seems that each passing day brings genomic discoveries that challenge what we thought we knew (Table 1).

My goals in this chapter are to: (a) recapitulate conceptual paradigms that have given compass to mankind's effort to understand biological complexity; (b) consider how these traditional paradigms translate into the ongoing scientific revolution in genomics; and (c) emphasize ramifications of an emerging gene-centric view of the sexual genome that departs rather dramatically from all biological viewpoints that had gone before. Readers wishing to pursue these topics in greater depth should consult two of the author's books (Avise 1998, 2010a).

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K. Kampourakis (ed.), *The Philosophy of Biology: A Companion for Educators*, History, Philosophy and Theory of the Life Sciences 1, DOI 10.1007/978-94-007-6537-5_13,

Table 1 A few examples of 'paradigms lost' through startling discoveries about the genome[a]

(a)	The Central Dogma (that information flows only from DNA → RNA → protein) proved to be violated routinely with the discovery of reverse transcriptases that catalyze RNA → DNA.
(b)	Conventional wisdom that only proteins can be organic catalysts was proved wrong when RNA catalysts (ribozymes) were discovered.
(c)	The notion that most of the genome codes polypeptides was dismantled with the discovery of introns.
(d)	A standard metaphor of genes being arranged like tight beads along each chromosomal string was abandoned after geneticists came to appreciate the abundance of repetitive DNA.
(e)	The notion that all DNA in sexual species is routinely subject to recombination had to be revised with the elucidation of transmission genetics in cytoplasmic genomes such as mitochondrial DNA.
(f)	The notion that an allele was structurally autonomous had to be revised after the discovery of the phenomena of gene conversion and concerted evolution.
(g)	The traditional view that genes collaborate for the collective good of the individual had to be abandoned with the insight that DNA sequences in effect often behave selfishly.
(h)	Traditional concepts of gene homology had to be modified to accommodate the reality of different types of shared ancestry such as paralogy versus orthology.
(i)	The conventional use of particular DNA sequences to reconstruct a species phylogeny had to be revised when an appreciation was gained of a fundamental distinction in sexual species between gene trees and organismal phylogenies.
(j)	Conventional thought about the stationarity of DNA sequences was thrown out following the discovery of ubiquitous mobile elements.
(k)	Heritable changes in gene expression not attributable to alterations of DNA sequence per se have opened biologists' eyes to an array of previously underappreciated "epigenetic" phenomena.
(l)	Many examples of horizontal gene transfer across species have challenged the conventional wisdom that phylogenies invariably can be depicted as non-reticulate branched trees.

[a]These and countless lesser revelations in the evolutionary-genomic sciences might be viewed as inspirational or disturbing depending in part on each person's educational outlook. Science is not well suited for those who demand eternal truths

2 Religion and Science Before Genetics

2.1 Natural Theology: The Argument from Design

In the thirteenth century, the Dominican scholar Saint Thomas Aquinas invoked the "argument from design" (design implies a designer) as one of his Five Ways to prove the existence of a Creator. The design argument has a long and distinguished intellectual pedigree in science and philosophy. For example, in the fourth century BCE the Greek mathematician and philosopher Plato mused at length about how a conscious power must be responsible for organic complexity, and across the ensuing two millennia countless scientists and theologians expressly sought to glorify God's handiwork through their studies of nature. Late in the seventeenth century, the Christian naturalist John Ray encapsulated this approach in *The Wisdom of God* (1691), which in effect became a prequel to minister William Paley's *Natural*

Theology (1802) that further elaborated what many laypeople and intellectuals long had deemed to be self-evident: that nature offers powerful testimony to God's omnipotence (see also Lennox and Kampourakis, this volume). In his youth, Darwin apparently read both Ray and Paley (Barrett et al. 1987; Birkhead 2010) and became "charmed and convinced of the long line of argumentation" (see Darwin 1887) for intelligent design in their two eloquent treatises. Thus when Darwin boarded the H.M.S. Beagle in 1831, he too was a natural theologian at heart.

Just 2 years earlier (in 1829), the last will and testament of Reverend Francis Henry (Earl of Bridgewater) had directed the president of the Royal Society of London to identify and fund authors willing to write books "on the power, wisdom, and goodness of God as manifested in Creation." Between 1833 and 1840, Henry's directive eventuated in eight works (some in multiple volumes) that became known as the Bridgewater Treatises: *The Moral and Intellectual Constitution of Man* (Chalmers); *Chemistry, Meteorology, and the Function of Digestion* (Prout); *The History, Habits, and Instincts of Animals* (Kirby); *The Hand* (Bell); *Geology and Mineralogy* (Buckland); *The Physical Condition of Man* (Kidd); *Astronomy and General Physics* (Whewell); and *Animal and Vegetable Physiology* (Roget). These books now are remembered not for their scientific merit but rather because they were the last grand endeavors from natural theologians prior to the Darwinian revolution.

2.2 Theodicy and the Counterargument to Sentient Design

A conceptual dilemma for natural theologians always has been how to vindicate a God who would craft a biological world that is rife with imperfection as well as beauty. Therein lies the theodicic challenge, which refers to the difficulty of rationalizing the actions of a well-meaning omnipotent Deity who created grossly defective biological objects. Theodicy (from the Greek roots *theós* for God and *diki* for justice) also has a lengthy pedigree. The word was coined in 1710 by the German philosopher and mathematician Gottfried Leibniz in *Theodicic Essays on the Benevolence of God, the Free Will of Man, and the Origin of Evil*, but Leibniz certainly was neither the first nor last to wrestle with "the problem of evil". Throughout the ages, people have pondered why a caring all-powerful God countenances grotesque biological flaws and permits so much organismal (including human) suffering. In *Dialogues Concerning Natural Religion* (1779), the Scottish philosopher-historian David Hume managed to précis both the argument from design (natural theology) and its antipode (theodicy) in a pithy exchange between two fictional characters, Cleanthes and Philo. First, Cleanthes proclaimed, "the Author of Nature is somewhat similar to the mind of man though possessed of much larger faculties proportioned to the grandeur of the work he has executed […] By this argument alone, do we prove at once the existence of a Deity"; to which Philo simply responded, "What surprise must we entertain when we find him a stupid mechanic." (part VI, passages 166 and 167).

Hume could not have anticipated that within a century, the age-old dilemma registered in the theology-theodicy dialogue would be rendered largely moot by the Darwinian revolution.

2.3 Scientific Challenges to Natural Theology

In 1514, Poland-born Nicolas Copernicus began to question prevailing anthropocentric interpretations of the universe. Using mathematical arguments based on detailed observations of planetary movements, Copernicus concluded that Earth and several other celestial bodies revolve around the sun and thereby constitute a heliocentric system (perhaps one of many in the cosmos). No longer could the Earth and its inhabitants be viewed quite so comfortably as the focus of all Creation. The importance of the Copernican revolution lay not in the proof of heliocentrism but rather in the introduction of a powerful but then-radical epistemology not shackled to sacred texts or religious revelations. For nearly the first time, the sciences (in this case physics and astronomy) had begun to wrest from theologians some substantive measure of intellectual authority regarding nature's mechanistic operations. More than three centuries later, Charles Darwin would extend the scientific ethos into biological arenas by showing that natural forces amenable to objective analysis had shaped organismal phenotypes (morphologies, physiologies, and behaviors) that traditionally had been ascribed to supernatural agencies. The Darwinian revolution went on to transform the life sciences in analogous fashion to how the Copernican revolution had transformed the physical sciences (see also Ayala, this volume).

An Augustinian friar and contemporary of Darwin was the second most important figure in the history of biology. Gregor Mendel (1865) discovered the particulate nature of hereditary factors [but see the historian Olby (1985) for a different interpretation] that later (in 1909) would be named genes. Mendel's scientific breakthroughs in the mid-1800s went unappreciated during his lifetime but they provided the other half of the puzzle that during the first half of the twentieth century enabled a union of Darwinian and Mendelian principles (Provine 1971) into a so-called "modern synthesis" (now a bit worn and tattered and about the edges) that still provides the foundation for much of the biological sciences (see also Depew, this volume).

Not everyone was persuaded by the science, of course, and many people even today view Darwinism as anathema. In some countries including the United States, religious disapproval or even wholesale rejection of evolutionary thought is a huge stumbling block against incorporating evolutionary science into biology curricula (Scott 2004). This situation is sadly ironic in at least two educational regards: (a) evolution is a core science without which "nothing in biology [otherwise] makes sense" (Dobzhansky 1973); and (b) Darwin's discovery of natural selection could be deemed a tremendous blessing in disguise for religion because it removes the need to explain the world's imperfections as failed outcomes of God's design (Ayala 2007).

Thus, when fundamentalists preach that evolution and religion are incompatible, they ignore the more uplifting possibility that the evolutionary sciences could partner

with religion in mankind's broader struggle to understand the ultimate nature of nature. Indeed, in some respects evolution might even be theology's salvation. Rather than blaspheme God for shoddy engineering, theologians after Darwin and Mendel could put the proximate blame for biological flaws on insentient natural selection and hereditary mechanisms. No longer need priests, ministers, and clerics agonize why a Creator God is the world's leading abortionist and mass murderer, nor question God's motives for debilitating innocents with horrific disabilities, nor anguish about the motives of an interventionist Deity who permits so much evil and suffering in His biological flocks. Evolution by natural causes can emancipate religion from many such theodicic dilemmas. Darwin simply discovered a scientifically decipherable process of nature (natural selection) that seems to eliminate the need to invoke direct supernatural intervention for apparent organismal design. Whereas many fundamentalists reject Darwinian notions as heretical, many scientists and scholars in the evolutionary-genetic era have welcomed the opportunity to explore uncharted waters that lie in the traditional gulf between science and religion and that thereby lap the shores of both (see also Ayala this volume; Alexander this volume).

There are many additional reasons why science and religion need not be archenemies. For example, even if all biological outcomes proved to be fully consistent with natural laws and intelligible processes amenable to scientific scrutiny, a non-excluded theological interpretation is that nature's ground-rules somehow were set into motion by a God. In 1973, the evolutionary geneticist Theodosius Dobzhansky issued a clear deistic statement: "I am a creationist *and* an evolutionist. Evolution is God's, or Nature's method of creation." This is the sort of deity that Albert Einstein tried to comprehend in his explorations of energy and matter, and it is clearly the kind of God that Darwin (1859) had in mind when he mentioned the Creator in the closing paragraph of the second edition of *The Origin of Species*. When scientists explore the nature of life including the human condition, they are not necessarily atheistic but they do strive to avoid the subjective and metaphysical explanations of theism by focusing instead on hypotheses that can be analyzed dispassionately and tested critically.

3 Science and Religion in the Genetics Era

3.1 Natural Theology Revisited

On the theological front, recent decades have been witness to the birth and growth of the Intelligent Design (ID), the latest reincarnation of religious creationism and natural theology (Numbers 2006). Proponents of ID insist that complex biological outcomes such as bacterial cells and humans beings offer incontrovertible evidence for purposeful design and direct craftsmanship by a supernatural force, and they often go further to claim that such arguments are based in science rather than faith or revelation. In the United States, ID advocates have been plaintiffs in several

high-profile courtroom cases (see NAS 2008) that to date have ruled that ID is a religious movement without scientific merit and as such should not be mandated equal time in science classrooms of public schools. Few biologists in the modern genetic era openly subscribe to natural theology ala Ray or Paley, but one notable exception is biochemist Michael Behe (1996) who in *Darwin's Black Box* issued a challenge to evolution by arguing that complicated biotic traits such as the vertebrate eye, the bacterial flagellum, or the sexual genome are "irreducibly complex" and could only have been constructed *ex nihilo* for their current functions by an intelligent engineer who in effect must be an interventionist Creator God (see Brigandt this volume).

3.2 Theodicy Revisited

On the scientific front, genetic findings in recent decades have extended the age-old theodicy dilemma to previously unexplored inner workings of the cell. Biologists now know that despite its many intricate features, the genome of humans (like those of other sexual species) also is riddled with structural and operational deficiencies ranging from the subtle to the egregious (Table 2).

These molecular defects register not only as deleterious mutational departures from some hypothetical genomic ideal but also as universal architectural flaws. Thus, whereas the theodicic challenge traditionally arose in the context of observable phenotypes such as serious disease conditions and overt medical disabilities that plague humanity, in times past a theological rejoinder always could be entertained that God's handiwork someday might be found in the finer details of human biological operations. However, now that human genomes have been dissected in astounding detail (Lander et al. 2001; Venter et al. 2001), that possibility is no longer scientifically tenable. Furthermore, rampant imperfection inside the human genome is hardly unexpected if indeed non-sentient evolutionary processes generally are in charge of biological outcomes (Table 3). Thus contrary to Behe (1996), molecular findings offer only a Lilliputian challenge to evolution when compared to their Gargantuan challenge to intelligent design.

Again, however, the more important point is that evolutionary-genetic science interpreted properly could in principle help open-minded theologians escape the conundrums of ID and thereby return religion to its rightful realm—not as the interpreter of the biological minutiae in our physical existence (as Behe seems to wish), but rather as a philosophical counselor on much grander matters such as ethics, morality, the soul, spirituality, sacredness, and other such issues of "ultimate concern" to nearly everyone (Dobzhansky 1967). For this reason too, it seems logical that evolution should be welcomed not only into houses of worship but also into academic curricula of the humanities as well as the biological sciences.

Table 2 Some of the many lines of evidence (often overlapping) for suboptimal design in sexual genomes, including those of humans

(a)	Mutations with oft-disastrous consequences for a person's health arise de novo in protein-coding genes as well as in essentially all other classes of loci.
(b)	Many older mutations with deleterious effects continue to segregate in populations long after their evolutionary origin.
(c)	Much of the molecular complexity of the human genome is gratuitous rather than functionally effective.
(d)	Much of the molecular complexity of the human genome is astonishingly wasteful of cellular resources.
(e)	Breakdowns in gene regulation routinely underlie genetic disabilities ranging from inborn errors of metabolism to various cancers acquired during an individual's lifetime.
(f)	Malfunctions in gene-based energy metabolism often underlie physiological deterioration.
(g)	Many DNA sequences ranging from short to lengthy routinely proliferate at organismal expense or at best at organismal indifference.
(h)	Many genes are deceased in the sense that they no longer perform an active function for the cell.
(i)	Even when not overtly deleterious, many alternative alleles scattered throughout the genome are selectively neutral or nearly so.
(j)	Genomes themselves in effect recognize that they are flawed, as gauged by the fact that they have evolved sophisticated yet far-from-infallible repair apparatuses.
(k)	Many genomic features go well beyond merely poor design and into the realm of downright ludicrous design by almost any engineering standard.
(l)	Many suggestions for improvement of genomic design can be imagined readily even by mere mortals with just a modicum of intelligence.
(m)	Genetic disabilities strike even the most innocent and helpless among us, and indeed are especially likely to target embryos, fetuses, and the elderly.
(n)	Everyone is afflicted with at least some genetic ailments at one stage or another of life.
(o)	Senescence and death themselves are inevitable and have evolutionary-genetic etiologies.

See Avise (2010a) for details and elaboration

3.3 Natural Selection: The New Holy Grail

Given that natural selection in the modern era in some ways became a surrogate for God's hand as a proximate sculptor of biological design, perhaps it is not too surprising that scientists ever since Darwin have embarked on missions to understand the operation of natural selection with a zeal almost reminiscent of the fervor with which natural theologians had pursued their earlier quest to understand the mind of God. For example, much of the modern synthesis involved developing (Fisher 1930; Wright 1931; Haldane 1932) and then translating (Dobzhansky 1951) mathematical models that describe how natural selection operates in conjunction with other evolutionary processes to effect genetic changes in populations through time (see Depew this volume). Population-genetic theories remain essential for interpreting molecular data, including those that later would emerge from detailed analyses of

Table 3 Some reasons why evolution often yields sub-optimal biological outcomes

(a)	Natural selection is a non-sentient natural process, as uncaring and dispassionate as gravity.
(b)	Natural selection is not all-powerful, but instead is just one in a nexus of evolutionary forces, others of which can override the adaptation-promoting power of natural selection in particular instances and thereby yield products that fall far short of designer perfection.
(c)	Random mutations continually arise, most of which are either deleterious or fitness-neutral.
(d)	Harmful mutations (especially those that are only slightly deleterious individually) often fly below the radar screen of purifying natural selection, especially in small populations.
(e)	Genetic drift can alter the genetic composition of populations in ways that are uncorrelated with adaptive benefits.
(f)	Sexual selection on particular traits often operates in direct opposition to natural selection.
(g)	Genetic correlations and conflicts are common such that deleterious alleles linked to host-beneficial alleles at other loci can hitchhike with the favorable alleles and thereby at least temporarily escape eradication by purifying selection.
(h)	Pleiotropy and fitness tradeoffs are common, meaning that a genotype often has multiple phenotypic consequences some of which benefit and others may harm the organism.
(i)	Natural selection acts not only at the organismal level but also at the level of genes, so selfish DNA sequences can persist and proliferate in a sexual genome without enhancing the wellbeing of the host population.
(j)	Phylogenetic constraints are ubiquitous and natural selection at any point in time can only work with the genetic diversity presented by lineages that have survived from the past.

After Avise (2010b)

sexual genomes (Lynch 2007). Indeed, ever since molecular technologies were introduced to population biology in the mid-1960s (see Avise 2006), the fields of molecular ecology and evolution have been preoccupied with elucidating the multifarious roles of selection in shaping "the genetic basis of evolutionary change" (Lewontin 1974).

Interestingly, however, an audacious theory that arose near the dawn of the molecular revolution focused on natural selection's scientific antithesis. Architects of the neutrality theory (Kimura 1968; King and Jukes 1969; Kimura and Ohta 1971) proposed that most sequence changes at the level of DNA are attributable not to natural selection but rather to the random fixation of fitness-neutral (selectively equivalent) genetic variants that arise via mutational processes (see Dietrich this volume). Across the ensuing decades, the neutrality-selection controversy has resurfaced time and again as biologists contemplated each new type of molecular data provided by the latest laboratory method. Research always proceeded on two fronts: testing mathematical or statistical predictions of neutrality theory against observed magnitudes or patterns of molecular variation; and addressing functional properties of particular genotypic traits by critical observations or experiments.

Several points should be made clear. Neutralists did not deny the conclusive empirical evidence for high genetic variation at the molecular level but rather they questioned the selective relevance of such variability. They did not suggest that most genes are dispensable (of course they are not) but rather that different alleles at a locus often are functionally equivalent. Neutralists never denied that highly deleterious mutations tend to be eliminated or kept at low frequency by purifying selection

but rather they focused on genetic variants that escape selective elimination. Finally, they did not challenge adaptive Darwinian evolution for organismal morphologies and behaviors but rather they explicitly confined their attention to variation at the molecular level (Kimura 1983).

Neutrality theory seemed radical when it was introduced in the late 1960s, but within two decades and continuing today it had become molecular evolution's gigantic null hypothesis: the most straightforward way to interpret molecular variability and the basic theoretical construct whose predictions must be falsified before invoking balancing or other forms of selection to explain a particular molecular polymorphism or evolutionary outcome. This is not to say that all molecular evolution is neutral; the truth undoubtedly resides somewhere between the extreme poles of pan-selectionism and pan-neutrality.

3.4 Levels of Natural Selection

Another recurring scientific debate during the twentieth century addressed the question: At what level or domain does natural selection operate with greatest efficacy? Although the notion of group selection occasionally gained some traction (Wynne-Edwards 1962), most evolutionary biologists remain convinced by the Darwinian argument that natural selection normally acts not for the benefit of an extended group or species but rather via fitness differences among individuals (Williams 1992). In 1964, William Hamilton introduced a more palatable adjustment to individual selection (or perhaps to group selection) when he advanced the concept of kin selection based on inclusive fitness. Whereas genetic fitness traditionally had been defined as an individual's personal reproductive success, inclusive fitness incorporated the novel insight that copies of an individual's genes may be transmitted indirectly through genetic kin as well as directly through genetic parenthood. Kin selection is now accepted as a plausible route for the evolution of at least some otherwise enigmatic traits (such as extreme sociality in ants and other hymenopteran insects). Hamilton's spotlight on the fate of replicate copies of genes also offers a useful segue here into another biological domain for selection: the differential proliferation of particular DNA sequences inside sexual genomes.

4 Neo-Darwinian Selection at the Level of Genes

In any sexual species, unlinked genes have quasi-independent evolutionary trajectories because the Mendelian processes of segregation and independent assortment (due to meiosis and syngamy) tend to shuffle alleles during each round of organismal reproduction, thereby partially randomizing genetic associations across loci and affording little opportunity for any allele to establish stable long-term relationships with particular compatriots. Yet the routine dissolution of potential cliques of

genes would seem to run counter to the desirability of evolving coadapted genic alliances that might be of benefit to the host organism. Ergo the longstanding evolutionary question (Turner 1967; Maynard Smith 1977): Why does the sexual genome not congeal? This enigma is tantamount to the monumental puzzle of why sex (as opposed to asexuality or parthenogenesis) is so prevalent in much of the biological world. Standard evolutionary answers appeal to various fitness advantages that arise via the genetic variety and adaptive flexibility that genetic recombination promotes (Bell 1982; Maynard Smith 1978).

4.1 Consequences for Genomic Architecture and Operations

Sexual reproduction also has major consequences for the level at which natural selection operates because recombination in effect decouples the fates of different DNA sequences within the sexual genome. As a result, genes in recombining genomes sometimes can increase their odds of survival and proliferation by acting in disharmony with the broader collective of genes (and hence against the interests of the genome and the host organism). Richard Dawkins (1976) elaborated and popularized the image of the "selfish gene," a concept that is now well ensconced in evolutionary thought. The realization that natural selection operating at the level of the gene can oppose natural selection operating at the level of the organism was a major conceptual breakthrough that has helped to clarify many otherwise enigmatic molecular features of sexual genomes. Indeed, if all forms of life forever had been strictly asexual, then genomes undoubtedly would be structured very differently than they are today because there would have been no evolutionary conflict of interest between loci, no conflict between what is best for the gene and what is best for the organism, and no opportunity for the evolution of selfish genetic elements.

Sexual genomes, however, are riddled with evidence for selfish DNA. Perhaps the most compelling testimony comes from the ubiquity and abundance of mobile elements (also known as jumping genes) that have proliferated to great numbers in the genomes of nearly all plant and animal species. These DNA sequences evolved the capacity to produce and distribute copies of themselves across multiple chromosomal locations within a cell lineage, thereby enhancing their prospects for transmission across the generations and eventually accumulating to vast numbers in most sexual genomes. In the human genome, for example, active or deceased mobile elements outnumber functional protein-coding genes by approximately 100 to 1 and altogether constitute at least 45 % of our DNA.

Researchers distinguish several categories of jumping genes. Some are cut-and-paste elements that move by excision and insertion of DNA whereas others locomote via a copy-and-paste mechanism of reverse transcription from RNA intermediates. Within the latter category are several subclasses (including *LINE*s, *SINE*s, and *LTR*s) each of which in turn is composed of subfamilies of elements. For example, in humans *L1* is the largest subclass of *LINE*s, with each intact *L1* element being approximately 6,000 base pairs long and with much smaller pieces of more

than 500,000 such elements collectively comprising about 17 % of the human genome; and *Alu* sequences constitute a major subcategory the *SINE*s, with each *Alu* sequence being about 300 base pairs long and with more than one million copies of *Alu* cluttering the human genome.

Many mobile elements house genes that encode proteins for reverse transcription and integration into a new chromosomal site whereas others hijack the necessary enzymes from other mobile elements or from the host genome. Mobile element replication can be a sloppy molecular process, so many jumping genes have lost bits and pieces that compromise their competency to code for the proteins that once enabled their own intra-genomic movements. Degenerate mobile elements are called non-autonomous elements, in contradistinction to active mobile elements that proliferate within the host genome much like quasi-autonomous and self-serving intracellular parasites (Hickey 1982).

In addition to being parasitic on cellular resources of the host organism, any newly arisen mobile element may cause serious harm by several mechanisms (e.g. Cordaux et al. 2006): by landing in an exon in which case it can ruin the protein encoded by a functional gene; by jumping into an intron-exon boundary in which case it can alter how RNA is processed; by inserting into a regulatory region in which case it also can disrupt proper gene expression; or by inserting almost anywhere in which case it can cause genetic instabilities including deletions of useful parts of the host genome. Apart from such examples of "insertional" mutagenesis, old as well as new mobile elements often promote genomic disruptions via non-allelic homologous recombination that also can disrupt cellular operations and result in serious metabolic disorders (Lupski 1998).

In short, mobile elements routinely invite and trigger genetic disasters for their hosts. For example, some expressions of heart disease, colon cancer, breast cancer, hemophilia, diabetes, and numerous other life-threatening conditions in humans are known to result in various instances from the activities of mobile elements (Prak and Kazazian 2000; Hedges and Deininger 2007). Although most data on mobile elements in humans have been acquired only recently, the list of serious metabolic disorders associated with these proliferate DNA sequences already is long and rapidly growing (see Avise 2010a). Still, any such list provides only a minimal estimate of the collective toll of jumping genes on human health because most of the serious medical difficulties undoubtedly arise so early in embryonic life as to cause miscarriages of undocumented etiology. Indeed, most mobile elements are especially active in cells of the germline, so many of their deleterious effects probably register in gametic deaths and lowered fertility.

From an evolutionary perspective, the ubiquity of transposable elements relates to their spreading nature, some of which reflects multiple historical invasions of germlines by infectious retroviruses but much of which also reflects each element's subsequent selfish proliferation within the genome. In any sexual species, a DNA sequence that gains a capacity to disperse copies of itself across chromosomal sites in germline cells almost inevitably enhances its prospects for passage to succeeding generations, even when the element harms its host. If the host instead were asexual, a mobile element would gain no transmission advantage by dispersing copies of

itself across a clonal genome. Thus, mobile elements also can be regarded as sexually transmitted genomic diseases.

As with any host/parasite association, evolutionary games of give-and-take are played across time. Namely, host genomes come under selection to evolve mechanisms that silence or suppress any harmful mobile element activities, and selfish mobile elements are under selection to avoid such strictures. Also, some degree of self-policing by mobile elements might be expected because it is not in the element's selfish interest to harm its host. The net long-term result of such co-evolutionary contests is likely to be a truce or balance wherein mobile elements and their host genomes manage to live together with varying mixes of amicability and hostility.

Sometimes host organisms can even profit from mobile elements in at least two ways. First, mobile elements are powerful mutagenic agents (as mentioned earlier), and mutations are the ultimate source of genetic variation that is necessary for continued evolution. However, it is doubtful that jumping genes evolved expressly for their mutagenic behavior because natural selection lacks foresight (and also because many if not most random mutations are deleterious). Second, host genomes occasionally convert parasitic DNA into host-beneficial functions. Many mobile elements carry DNA sequences that have the capacity to regulate gene expression, so host genomes sometimes manage to capitalize upon ("exapt" or capture) the regulatory potential latent in mobile elements for the cell's own purposes. Such arrangements also can benefit the mobile element directly, which after its functional conversion then experiences selection for evolutionary maintenance as an integral part of the host genome.

The notion that the function of a trait often shifts during evolution was well appreciated by Darwin, but it was not until much later that the terms "exaptation", "cooptation", (Gould and Vrba 1982) and "co-opted adaptation" (Buss et al. 1998) were introduced to encapsulate the sentiment that a character shaped by natural selection for one adaptive function might later assume an altogether different role. Thus, even if it proves to be true that many mobile elements in the human genome now play useful roles in cellular operations, this does not necessarily mean that they evolved to perform these functional tasks from the outset. Instead, they might be exaptations that originated as selfish genetic elements but later were secondarily captured into host-beneficial services (for the concept of adaptation see Forber this volume; for the concept of function see Wouters this volume).

Although mobile elements clearly have been important evolutionary drivers of the sexual genome, they are merely the most conspicuous among many structural and operational properties of sexual genomes that motivate modern evolutionary thought about "genes in conflict" (Burt and Trivers 2006). Table 4 outlines several other recently discovered categories of selfish DNA.

4.2 Evolving Genomic Metaphors

Metaphors can be powerful images that capture complex ideas and educate audiences to new (and old) ways of thinking (Keller 2002), and perhaps nowhere has

Table 4 Several additional lines of evidence (apart from mobile elements described in the text) for genetic conflict within the sexual genome

(a)	Autosomal killers: Known in various animals, fungi, and plants, these are nuclear genetic elements that kill or disable gametes that do not carry copies of themselves, thereby eliminating potential competitors for successful fertilization events.
(b)	Selfish sex chromosomes: These are sex-linked genetic elements that distort the segregation process in ways that bias in favor of their own transmission to the next organismal generation.
(c)	Genomic imprinting: This is a common phenomenon in mammals and plants wherein a gene involved in an embryo's acquisition of maternal resources is expressed in progeny when inherited from one parent but not from the other. Such imprinting appears to be the evolutionary outcome of genetic conflict between the effects of natural selection on genes expressed in fetuses opposed by the effects of natural selection on genes expressed in mothers (Haig 1993).
(d)	Selfish mitochondrial DNA: Because mtDNA normally is inherited maternally rather than biparentally, it often plays by different evolutionary ground rules than those for autosomal genes and accordingly has evolved several properties and tactics (such as promoting male sterility) that bring it into conflict with the consensus interests of nuclear genes.
(e)	Biased gene conversion: These are recently discovered molecular processes (often related to DNA repair) by which particular DNA sequences convert alternative sequences or alleles to their own structure.
(f)	Female drive: This is a specific form of selfish genetic behavior in which a gene or chromosome engaged in meiosis in females disproportionately inserts itself (at the expense of competitors) into a fertilizable egg or ovule as opposed to the soon-to-be discarded polar bodies.
(g)	B chromosomes: These are additional chromosomes (distinguished from the normal or "A" chromosomal set) that are not a necessary part of the genome but nonetheless are maintained in populations because they possess "self-accumulation" mechanisms.
(h)	Genomic exclusion: This is a category of drive-like genetic situations in which individuals discard (rather than transmit to offspring) some or all of the genes inherited from one parent, thereby giving a huge selective advantage to genes from the alternative parent and once again fostering conflicts within the genome.

See Burt and Trivers (2006) for elaboration and for more examples

that been more evident than in the field of evolutionary genetics (Condit 1999; Brandt 2005). The sciences of heredity and evolution are steeped in evocative metaphors (Table 5), so much so that it often becomes difficult to distinguish simile from facsimile, or to disentangle what is real from our perception of what reality might be. Indeed, the most effective metaphors in science in effect become immortalized when they get incorporated so fully into conventional wisdom and language as to be accepted as the actual truth rather than as utilitarian caricatures of whatever reality might be. Furthermore, metaphors themselves can and do evolve under the force of new evidence.

For example, one traditional set of metaphors pictured each genome as carefully coded text in a book of life that was scripted (either by natural selection or perhaps by God) expressly for organismal wellbeing. But recent molecular discoveries about the sexual genome have challenged this standard textual imagery in many ways. Contrary to earlier notions, DNA sequences are not always like intelligible words

Table 5 Examples of the many metaphors that are used routinely in genetics and evolutionary biology[a]

Evolutionary and population-genetic metaphors
Tree of life
DNA as hereditary sap in the tree of life
Phylogenetic branches
Evolutionary pathways
Fabric of life
Web of life
Life's evolutionary ladder
Streams of heredity
Gene pool
Gene flow
Genetic drift
Genetic draft or hitchhiking
Gene or genomic metaphors
Textual metaphors (e.g., genetic book of nature; encyclopedia of life; genetic code; genetic sentences; the genetic alphabet and its letters; the language of DNA; genetic text or scripture).
Genetic engineering, biotechnology
Germplasm, tissue banks, gene banks
Biological atlases (or maps, cookbooks, recipes, instructions, operating manuals)
Informational or occupational metaphors (e.g., DNA blueprints; genetic programs; gene circuits; gene batteries; housekeeping genes; jumping genes; selfish DNA; junk DNA; parasitic DNA; developmental switches; ontogenetic pathways).

For any such metaphor, a useful classroom exercise for students and teachers alike is to address the following types of questions: (a) how and when did the metaphor originate?; (b) how well does it capture our current understanding of biological reality?; (c) to what extent is it helpful or misleading?; (d) might it promote or inhibit further scientific inquiry? and (e) can you think of a different or perhaps better metaphor for the topic in question?

[a]Nelkin (2001) categorized contemporary genetic metaphors in popular discourse into four groups centered on notions of: essentialism (genes as essences of personal identity); religiosity (genes as sacred entities); fatalism (genes as determinants of destiny) and commerciality (genes as commodities)

tightly woven into coherent chromosomal sentences and paragraphs, all working smoothly and collaboratively to translate genetic code in life's instruction manual into meaningful cellular operations. Instead, protein-coding exons and other functional DNA sequences now seem like small islands suspended in rivers of intronic and extra-genic gibberish that flow through each species' hereditary channels. The precise volume of genomic flotsam (junk DNA, selfish DNA, parasitic DNA, or neutral DNA) mixed with host-beneficial DNA in various evolutionary watersheds remains to be determined by monitoring the ebb and flow of genomic operations in each species. Whole-genome sequencing (which has recently become almost routine) is merely a first step toward such characterizations. Far more difficult is the laborious follow-up challenge of genomic annotation—assigning functional roles or otherwise attaching useful biological information to each gene or other segment

of genomic sequence (Stein 2001). Genomic annotation (characterizing the genome functionally rather than just structurally) in humans and other model and non-model species is an immense enterprise that will keep geneticists fully occupied for the foreseeable future (see Marcos and Arp this volume for information in biology; see Burian and Kampourakis this volume for a proposal to replace gene concepts).

To help motivate such laborious genomic analyses as well as to tie them to evolutionary thinking, lively new metaphors might be useful too (Avise 2001). One such adaptable genomic metaphor would liken each sexual genome to a community of genes whose behaviors mirror those of humans entangled in a network of social arrangements. These behaviors would include cheating and arbitration (conflict resolution) as well as various expressions of cooperation for the common organismal good. Another such metaphor might envision each sexual genome as a miniature intracellular ecosystem extended through time, complete with different niches for genes that act much like parasites, symbionts, commensals, agents of disease, or that assume other roles traditionally reserved for organisms and species in natural macroscopic biological communities.

5 Conclusions

The field of evolutionary genetics lies at a unique crossroads between science, religion, philosophy, and education. Not only have organisms and their genomes evolved through time but so too have human perceptions about the etiology of biological design. Whereas pre-Darwinian religious philosophers typically focused on natural theology and its theodicic challenges, later scientific perspectives based on Darwinian and Mendelian principles in effect removed the requirement for divine intervention to justify biological outcomes including the complex molecular architectures of sexual genomes. In recent years, a social movement known as intelligent design (ID) has reintroduced natural theology in a form that needlessly seems to pit science against religion over matters of ultimate concern (such as the origins of sophisticated biological traits). Although ID (like traditional creationism) is strictly a religious movement, it has had negative impacts on science education in the United States (and elsewhere) through its overt hostility to evolutionary principles that otherwise provide a unifying conceptual foundation for all of the biological (including medical) sciences. Furthermore, within the scientific arena itself, several genetic controversies continue to swirl regarding precisely how selective processes shape genomic structure and genomic operations. The history of the science-religion interface as well as the ongoing trajectory of evolving scientific notions about the sexual genome both provide rich educational material for curricula in the humanities and in the biological sciences.

Acknowledgments The author's research and writing are supported by funds from the University of California at Irvine.

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