On Ultimacy in the Life Sciences RDA: 29 Dec 03 –1 Nov. 08

Note This essay is incomplete and imperfect, including the references.

On Ultimacy in the Life Sciences

The nouns "ultimacy" or "ultimateness" do not appear in either of my dictionaries. The adjectival meaning is present in the term "ultima," as "most remote, final, farthest, last"; the same term, ultima, as a noun, is defined in my unabridged dictionary solely as "the last syllable of a word." Thus, it appears that a nominal concept of ultimacy or ultimateness, as extremeness, is at least unusual. Perhaps the topic of this essay, focused on both ends of at least one of the spectra characterizing the discipline of biology (the study of life, in all its forms, traits, functions, and history), is also unusual.

Recent technological advances have enabled reduction-minded biologists to expand their science impressively at the molecular level. One consequence is the working out of the human genome and the subsequent rise of the "Life Sciences Initiative," as mainly molecular biology and medical drug development, ostensibly driven most often by interest in reducing human pain and discomfort, and lengthening human lifetimes. Aside from athletics, this initiative sometimes appears to be the biggest current adventure on the campuses of many major research universities, these two programs yielding an apposition curiously relevant to the theme of this essay.

Individual Life Sciences laboratories receive tens or hundreds of millions of dollars to explore the ultimacy represented by molecular studies, often spinning off promising lines of research to start-up companies and corporations that seek profits primarily in developing and manufacturing medical drugs. The 1980 Bayh-Dole Act of Congress, as a prominent new connection between basic academic research in biology and practical applications, ". . .made it much easier for universities to own license patents on discoveries made through research paid for with public funds" (cf. Wohlgelernter 2005-6, pp.65-66).

The "Life Sciences," incidentally, once referred to all of the biological sciences (meaning the comprehensive study of all life), not merely, or even mainly, direct concentration on immediate and specific applications to human welfare. Installment of Life Science initiatives on university campuses have sometimes tended to bypass – and diminish -- the existing biology departments. This may not seem particularly surprising, because new technologies had already created separate departments of

molecular biology within most large universities. Molecular biology obviously includes an enormous array of possible break-throughs in medicine and other fields.

Everyone recognizes the current enterprises of the Life Sciences as admirable and highly promising. We already realize that virtually every step yields astonishing new discoveries. The point of this essay is that they are not the only admirable and highly promising enterprises in biology, and not the only kind of ultimacy in the life sciences. Indeed, the unity of development (ontogeny) and the corresponding functioning of all human affairs primarily at the organismic level suggest that the understandably attractive and novel ultimacy of molecular biology may not ever become the best or quickest route to lengthening and enriching human lifetimes and reducing human suffering and misery.

The chief analytical ultimacy in the new "Life Sciences" enterprise is the taking of scientific reduction to the smallest relevant structural and functional level for understanding life. From this beginning have come two initiatives: (1) seeking to apply knowledge about molecules directly at the highest level – that is, leaping all the way back with efforts to improve "whole ~~body~~ organism(s)" functioning (in the case of the human organism, especially with medical drugs) -- while also (2) initiating the incredibly difficult proposition of climbing step by analytical step back up the ladder of development (ontogeny) in structure, physiology, and behavior. This second goal (beginning with working out the array of proteins produced by the genes, the "proteome") is the almost incomprehensible one of eventually understanding ourselves as wholes by knowing how all of our bodily components interact across the entire lifetime.

The goal of tracing all the steps in organismal development have not yet been achieved for any form of life -- indeed, not even all of the ontogenetic steps *for any single behavior of any organism.* The principal reason, curiously only just now becoming broadly understood (e.g., Silverman 2004; Parens et al 2008), was presaged long ago by Theodosius Dobzhansky (1961, p. 111) when he said: "Heredity is particulate, but development is unitary. Everything in the organism is the result of the interactions of all genes, subject to the environment to which they are exposed. What genes determine is not characters, but rather the ways in which the developing organism responds to the environment it encounters."

Genes in genomes share their fates because for the most part they are incapable of changing genomes. As a result we may expect that natural selection will favor (though it is unlikely ever to achieve) what might be called complete genic cooperation in the construction and operation of the organism (e.g., Burt and Trivers

2006). Development is (organisms are) unitary in the sense that the organism's evolved function is singular: maximizing the persistence of its genes via all forms of reproductive acts, including kin-tending (Hamilton, 1964; Williams 1966; Trivers 1971). Presumably genes tend to be saved when their contributions to the positive effects of all the other genes in the genome, collectively, become more valuable (more reproductive) than their allelic competitors. Only genes and learning (the latter transmitted by learned learning, or culture) – and their left-behind traces -- persist across generations.

The complex and still almost entirely uncharted unity of development is the means by which organisms are able to carry out the ultimately incredible numbers and kinds of behavioral acts. Almost surely, the extreme case is that the brain of the 30- trillion-celled human individual enables us to make uncountable numbers of behaviorally appropriate decisions across our entire lifetimes in a succession of complicated and ever-changing social and physical environments, using millions or billions of changes in neural connections that can take place in split seconds, and in which the number of behavioral changes correlates with the number of effective environmental changes. The functioning of the behavioral changes resulting from the action of the brain's and the organism's entirety – meaning their consequences for the reproductive success of the genes of the organism in the environments of the organism -- can be regarded as an ultimacy at the opposite extreme from the ultimacy represented by the structural and functional details of the molecules of life themselves. The incredible distance between the two extremes still remains almost entirely unfathom~~able~~ed. ("-able" may be more correct)

Perhaps nothing currently known in the universe, living or non-living, is as complex as the behavioral consequences of the performance of the human organism across the average maximum human lifetime of 85-90 years, including the effects of the innumerable intrinsic and extrinsic environmental changes to which humans are subjected. The generation-by-generation process of evolution, after all, is incredibly simple; its products are complex because environments change, both independently of life's changes and – vastly more important – the multiplication, and coming and going across the past several billion years of history, of at least trillions of distinct species, each potentially and sequentially composed of up to uncountable numbers and generations of individual organisms; each species, and every assembly of species, also adding to the diversity of the environments of every individual member of every individual species. a little awkward

Molecular genetics has gone from an early and puzzling one-gene-one-product insufficiency of explanation to the realization that by turning on and off the ability to make that single product (protein) in the succession of different environments across

the lifetime of the organism, the nearly complete cooperation of the thousands of genes in the genome becomes capable of producing innumerable trait expressions. Yet every part of the human organism, including its marvelous brain and all the behavioral outcomes that result from it, begins from a single cell.

Behavior is an ultimate study partly because it is at the opposite end of the organizational spectrum of life from molecules, and is by far the most complex expression of the organism. In an analogy once used for a certain deodorant, behavior can be thought of as the ultimate shield – the first and most finely tuned line of defense – against what Darwin called the hostile forces of nature.

For humans, a specific form of ultimacy is self-understanding, a behavioral proposition that can be applied to both the individual and the whole of humanity. Efforts of humans at self-understanding are searches for meaning, including answers to "Why?" questions. The searches include identifying the ultimate reasons for the elaboration and continued existence of *evolved life functions*, as contrasted with immediate or proximate lifetime guides to such functions, such as pleasure and pain, which have been saved and elaborated because they help cause evolved functions to be realized; pain and pleasure are examples of the working components on the assembly lines of structural, physiological, and behavioral contributions that lead to the eventual acts of reproduction that cause proximate mechanisms to be saved, elaborated, and adjusted. Knowledge of such things enables us to decide which evolved life functions of ourselves we wish to promote and which ones we seek to alter or suppress as unnecessarily traumatic, or even pernicious. The concept of evolutionary adaptation has never implied that every evolved trait is either inevitable or desirable, "right," or even useful in today's world. Not all evolved adaptations are likely to be deemed desirable in today's world. "The challenge of Darwinism is to find out what our genes have been up to and to make that knowledge widely available as a part of the environment in which each of us develops and lives so that we can decide for ourselves, quite deliberately, to what extent we wish to go along. " (Alexander 1979, pp 136-137). But it will remain difficult to make and effect decisions on such questions so long as we lack clear understanding of the evolutionary backgrounds and changing environments of the expression of human functions.

There is a tendency among life scientists to see evolved functions as either flexible or unchangeable. The latter are sometimes referred to as hard-wired, instinctive, hereditary, genetically determined, or "biological," when "unchangeable" or "biological" is contrasted with "cultural" or "learned." Dobzhansky's last sentence in the quote given earlier points up the inadequacy of such dichotomies. Organisms are not complex because their genes have been favored in unchanging environments but

because genes have been favored for their ability, collectively in the genome, to respond reproductively in (or despite) an enormous range of differing environments. Humans, perhaps more than other forms of life, have evolved an expanding ability to create and thrive in increasingly diverse and complex environments. Some of these possible environments – more accurately, perhaps, the vast majority of them – have not yet occurred, or become significant. In some sense human behavior (or any function of the whole organism) is complex because, as already noted, environments have changed continually, sometimes rapidly and successively in multiple directions, so as to become a virtually countless proposition, even within and across the lifetimes of individuals. This is why it is inadequate to think of genes "for" specific evolved functions – for example, a gene for murder -- or a gene for any complex system of behavior -- say, monogamy, polygyny, or polyandry -- being either "natural" or "unnatural" (the closest to a counter example might be a mutation with deleterious effects that make it temporary because in current environments it has only or primarily ~~a~~deleterious effects). There are environments in which murder is likely and others in which it is not; similarly, environments in which different forms of mating (marriage) systems are more or less likely. The result is phenotypic flexibility, which is why Dobzhansky said that genes do not determine characters but the ways in which the developing organism responds to the environment it encounters. Many kinds of phenotypic variations can only be studied, or at least satisfactorily introduced, by directly behavioral studies. Such studies can be virtually essential, even if only as introductions to the most importantly consequential affairs of humans.

The most general and destructive of evolved behavioral responses to environments – and the most broadly influential of all uniquely human traits -- is surely the human tendency to take inter-group competitiveness to levels resulting in incredible rates of deliberate killings within our own species (_____ has calculated that across the recorded history of our species, there have been no more than 29 days when not a single war was going on in the world – I have to identify the person to whom the senior editor of the Washington Post – Rick Atkinson -- attributed this conclusion in a discussion of his new – second – volume on WWII: *The Day of Battle*). Wars and genocides that destroy large numbers of people (50-150 million in the 20th century alone – cf. National Geographic ???; Scaruffi 2006), including not only military personnel but all the others who for one reason or another find themselves in the wrong places, are started by the behavior of individuals or cooperative groups of individuals. How much have the behaviors resulting in the premature deaths of the many millions of people murdered in various parts of the world in recent years altered the average human lifetime? What numerical figures describing the collection of expected lifetimes of all people alive at any given time do deliberate killings erase? How much have such killings added to pain, suffering, and misery? There is not

much likelihood that any of the answers to these questions will deny that inter-group competition is the central trait-expression characterizing the human species.

Fries (1980) showed that average maximum life lengths of Americans did not change significantly between 1900 and 1980; instead, changes resulting from virtually the entire practice of medicine have resulted primarily in lowered rates of early (including infant) mortality such that more lifetimes are approaching the average maximum life length (if, in a population of two, one individual lives to be 80 and the other dies at birth, the average age of the population is 40). It is worth asking how all of the effects of medical practice on life lengths, pain, suffering, and misery compare with all of the same effects caused by the deliberate killings – i.e., behaviors of whole organisms (humans and their cooperative groups) -- that we have evidently failed to diminish greatly. There is the connection with the (team) sports – intergroup competition in play — and consider its intensity + popularity *

Enlightened searches for ways to change human behavior carry promises of far greater and potentially quicker alleviation of misery, and reduction of premature deaths, than does any other enterprise. This is true not only because multiple forms of destructive behavior continue to be prevalent and often disastrous -- from individual conflicts of interest to international strife -- but also because all use of knowledge in all fields is necessarily mediated by human behavior. For example, as we all are aware, everything useful and effective about medical drugs is influenced by the behavior of scientists, manufacturers, medical advisors, vendors, and users, and by (behavioral) intervention or lack of intervention by courts, lobbyists, governments, and many others.

Unfortunately -- partly because natural selection has excluded so much knowledge from consciousness -- easy routes to important changes in human behavior do not present themselves as plainly as have the recent advances in technology that have fueled advances in molecular biology. Nevertheless, as indicated above, there is an accessible and also essential ultimacy that continues to be generally ignored or downplayed. It is the ultimacy of meaning that comes from surmounting our historical ignorance about evolved functions of human traits, and from removing the consequent errors and self-deception in contrived explanations generated across human history. Such errors and self-deception, even when they are understandable and seem unavoidable, have thwarted us in fully comprehending ourselves, not only as individuals, but as well at all levels of human social and political organization, including spousal bonding, family and kin relations, and friendships all the way up to international alliances.

* I think I'll start my next lecture by asking the audience why we are the only species that plays competitively group-against-group (commenting on its intensity + popularity), then ask the audience what they think is the most central + influential human trait or adaptation or practice. Then give figures on the nos. (maybe this is the adaptation that culture has improved. The most people killed in wars + genocide)

Ultimacy of meaning may have little possibility of being understood, except through working out the frequently surprising evolved functions of identifiable human traits in current environments. Ultimacy in the form of reasons for the existence and persistence of trait expressions has, of course, been recognized as a useful goal for centuries by religious and philosophically-minded thinkers. Until recently, however, such thinkers have been doomed to one or another kind of failure because they had no way of understanding humanity via the cumulative effects of the evolutionary process responsible for our existence and our nature. During the last half century, our understanding of evolution developed rapidly through a series of enlightening theories (see references in Alexander 1990, 2008, and in press). Unfortunately, the kind of academic thinking and analysis that has been most productive in this biological enterprise does not typically require huge amounts of taxpayer money, with the accompanying generous overheads of federal grants on which large research universities have come to depend. Sizes of external grants have increasingly become the most comfortable substitute for more direct judgments of the worth of science faculties and their research.

In expense of pursuance, evolutionary biology – in particular evolutionary study of behavior -- has not been remotely competitive with its opposite biological ultimacy, molecular biology. During the last few decades, awareness of this financial fact seems to have generated the attitude in many university administrators that an appropriate way of dealing with ever-more difficult budget problems is to downsize and replace all those enterprises -- at least within the discipline of biology -- that neither require huge research grants nor interface with patentable discoveries and royalties from profit-making corporations. As an example of the insufficiency of this attitude, consider the lifetime of a single evolutionary biologist, the late William D. Hamilton (1937-2000). Often regarded as the greatest 20th century student of the evolutionary process, Hamilton literally changed our entire view of biology, including our understanding of the evolutionary background and patterning of human social behavior, and the evolutionary reasons behind ease and speed, or difficulty, therefore patterning, in virtually all social learning. Yet I doubt that he ever sought or received a grant providing one penny of overhead to his universities (University College of London, University of Michigan, and Oxford University) (Alexander 2000).

Departments of biology traditionally do not hire faculty to study the human species, leaving this task almost entirely to the medical and social sciences. This situation, which might at first be regarded as entirely reasonable, has contributed to the medical and social sciences remaining almost devoid of knowledge or interest in the evolutionary process. For example, the 1957 theory of George C. Williams, accounting for senescence and the patterning of lifetimes in all organisms with

disposable soma, including humans, was for decades almost totally ignored by gerontological investigators based in medical and social science departments.

Similarly, cancer was studied across the same decades in a virtually non-evolutionary fashion, as if it were a disease that could be cured with a magic bullet approach, even though the basic components and predictions of current general theory about the causes and nature of cancer were well understood a third of a century ago by many evolution-minded biologists (e.g., Cairns 1975). Radiation, a principal cause of mutations, therefore ultimately of cancer, was employed by medical and dental practitioners in needless – sometimes reckless -- manners across decades during which it was widely known by biologists to be cancer-inducing. The current general theory of cancer accounts for it as a consequence of mutations largely induced by radiation and various environmental (and medicinal) chemicals, combined with the ability of body cells to continue multiplying, evolved as an aspect of tissue growth and repair but incidentally keeping organisms like ourselves scant steps away from facilitation of metastasis (e.g., Weinstein and Ciszek 200?).

For obvious and appropriate reasons medical scientists, and to a lesser extent social scientists, tend to focus on injuries, deficiencies, and pathologies in humans. As a consequence, however, perfectly normal distinctive and unique human traits essential to human self-understanding have often been misinterpreted as non-functional or pathological, or as disadvantageous consequences of processes such as aging. Menopause, the cessation of ovulation approximately midway through the maximum average lifetimes of women, is an excellent example (e.g., Alexander 1990). Menopause is unique to humans, a species that doubled the length of individual lifetimes after separating from its closest relatives, the great apes (because the human ability to reproduce at later ages by helping kin caused selection that pushed deleterious pleiotropic effects leading to senescence into later years of life – cf. Alexander 2008).

Astonishingly (at first), that 45-year extension of the human lifetime seems to have added little or nothing to the ages during which ovulation persists. How could this have happened if, in evolution, traits can succeed only by serving the reproduction of their bearers, or by being inevitable concomitants of other such traits: how, indeed, if, as Darwin (1859) implied, only reproductively positive traits can be furthered by the "numerous, successive, slight modifications" that necessarily underlie trait expressions such as menopause? The answer has to be that menopause serves reproduction late in a woman's life in a way that has not been obvious. Many evolutionary biologists now accept menopause as an evolved function, or adaptation, which turns off the production of offspring in favor of assisting those already

produced, and as well assisting grandchildren and the extended family or clan. This hypothesis accords with the fact that each new human offspring requires – or profits immensely from -- a very long period of parental attention, and, because of our complex and intense social behavior (which includes the great significance of differential status of older adults with respect to access to resources), is able to benefit from significant help from parents across much of even its adult life (Alexander 1990, 2008, in press).

Menopause is thus related to human traits such as intensive and long-term parental care, altriciality (helplessness) of human babies, lengthened periods of juvenile life, the extraordinary importance of social learning by juveniles, and our apparently long history of prominent differential nepotism directed toward extended families or kin groups. All of these traits in turn contribute to explaining the signature trait of humanity: its huge, complex, and calorically expensive brain, currently regarded by many evolutionists as having evolved as primarily a social tool, almost certainly directly or indirectly evolved in the context of inter-group competition (references in Alexander 1990, and in press).

Menopause appears to have evolved as a way of lengthening, not shortening, the lives of older women, and of making post-menopausal women, not non-reproductive, but more effective in reproduction. It is worth mentioning that the unique form of human concealment of ovulation enables both the longer human life length and menopause by providing opportunity for establishing parenthood on both sides of each individual's family, thereby enabling the establishment of the complex kinship systems characteristic of all pre-technological human societies, in the multi-male social groups of humans generated as a consequence of inter-group competition and aggression (Alexander 1990, 2008).

Menopause no longer can be viewed legitimately as merely a deleterious side effect of aging that shortens lives and reduces reproduction. Instead menopause seems to turn women into increasingly astute parental and political beings who pay attention to who gets what from whom, and when and why, and who, historically at least, became increasingly influential in the social affairs of their extended families and clans. The same general pattern occurs with men, but it has caused less attention because there is not such a dramatic alteration of the reproductive mode (retaining the ability to produce sperm, therefore to continue to produce offspring, is a triviality compared to pregnancy and motherhood).

Treating menopause as a pathological or deleterious aging condition that needs to be reversed or "cured," especially using laboratory-made drugs almost certain to have

life-shortening side effects, ignores the insights of biologists who specialize in how the evolutionary process causes cumulative changes in traits (e.g., Alexander in press), necessarily misguides with respect to the pain and inconvenience of symptoms of menopausal onset, and does grave insult to the nature and significance of womanhood. Yet identifying drugs to reverse the symptoms of menopause may be the major grant-acquiring initiative in medical programs devoted to menopause. The attitudes responsible provide one tiny glimpse of the broad consequences of ignoring the ultimacy of evolved functions in efforts at human self-understanding.

It is worth emphasizing here that adverse medical drug reactions are a leading cause of death in the United States. They are responsible for the death, hospitalization, or serious injury of more than 2 million people in the U.S. each year, including more than 100,000 fatalities. These figures are almost certainly highly conservative estimates. If the expense of purchasing both prescribed and unprescribed *unnecessary* "medical" drugs were included, we might legitimately wonder exactly what is the major "drug problem" in the United States (figures from Wolfe et al 1999).

Knowing what menopause is all about, and using such knowledge in our everyday lives, is a single example of how human self-understanding can reduce unhappiness and increase life length, and how behavioral change can quickly increase the average life length of humans and simultaneously turn negative misunderstandings into positive and hopeful insights. How would human self-understanding be promoted by a similar self-understanding of, say, 50 or 100 basic or unique human traits, including, most importantly, the almost certainly evolved human tendency to generate and exploit we-they confrontations at every social level within our species (cf. Alexander 2008)?

Like philosophy, religion is an enterprise which, across centuries or millenia, has sought human self-understanding and ultimacy of meaning. As in philosophy, medicine, and the social sciences, influential thinkers in religion have until recently proceeded without guidance from a deep understanding of the cumulative evolutionary process – indeed, while typically seeing evolutionists as the most dire of all adversaries in the seeking of ultimate explanations. This failure of cooperation is unfortunate, because evolutionary, philosophical, and religious thinkers presumably all share the goal of spreading happiness and harmony, and expanding the fullness of human existence. The persisting mutual aloofness or antagonism of these groups is, like others discussed earlier, a hindering behavioral problem involving interpretations, motivations, special interests, and all of the obvious reasons for inattention or resistance to new information and arguments from others. This adversarial relationship has come about partly because religious thinkers long ago expanded their

concept of gods from early concerns about death, security, cooperation, and unity within small human groups to a vision of God as creator and mediator of not merely human morality but all aspects of life on earth and the physical universe as well. This perhaps understandable extension, and the centrality of authoritatively maintained and relatively inflexible moralities, created an inevitable – and unnecessary – conflict, not only among different religions but between religion and any expanding analytical human activity directed toward deep comprehension of the physical nature of the universe, and the background of life in general and humans in particular. It is not trivial that within-group religious unity maintained by authoritative moral rules, starting from small groups dominated by kin (and, along with kinship systems and other forms of group cohesiveness, directly or indirectly serving the passions of the central human adaptation of intergroup competition and aggression), is virtually a methodological opposite of the hypothesizing, testing, re-thinking, and repeating in the efforts of what we now call science to "get things straight."

Improved human self-understanding is surely the most crucial of all life science research goals. Its scientific aspects include a call for armies of open-minded, competent, and cooperative analysts in a long overdue life sciences initiative devoted to problems of behavioral and evolutionary ultimacy. As new conceptual tools and perspectives continue to generate in evolutionary biology, such an initiative could serve the human species at least as fruitfully and immediately as nanotechnology. But, as a result of the recent profound change of direction in the philosophy of academia, described earlier, the needed armies continue to diminish rather than grow. This happens, not because such armies have little likelihood of serving dire human needs around the world, but for at least five related reasons: (1) seeking to change human behavior is so immensely more daunting than technological advances that, rather than marshal our forces, we tend to turn away in despair (consider, for example, how non-conscious conflicts of interest can result in conscious disagreements about right and wrong – Alexander 1987); (2) humans tend to reject explanations of their behavior that involve unfamiliar backgrounds or agents, such as a history of differential reproduction of genetic alternatives, or unfamiliar interpretations of familiar behaviors with familiar, if flawed, explanations; (3) unlike the most recent technological arrivals within biological science, the research of evolutionary biologists does not typically return large profits immediately and directly to the general funds of universities (which, as with all corporations, are plagued with new and formidable costs, such as health care for employees); (4) although there have been some encouraging recent changes, social and medical scientists remain largely isolated from – and often adversarial toward -- advances in knowledge of the evolutionary process, and (5) there is a widespread tendency to believe that evolutionary scientists concerned with human behavior are to an unacceptable extent "genetic determinists"

who only wish to describe and explain human behavior, not contribute to the means of changing its most inhumane features..

Perhaps some day the major research universities, now almost pathologically dependent on the government grants that began largely as a result of World War II, will return to the recognition that the cost or technological complexity of biological investigation does not always correlate with its likelihood of contributing to human life, liberty, and the pursuit of happiness. Our approach to this question is central to the entire mission of academia, which in human terms means the broadest possible nurturing of the growth of basic research and fundamental knowledge critical to all our futures.

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