Evolution Controversies and the Theory of Aging

An unresolved 150-year-old scientific argument is *still* affecting medical research.

Theodore C. Goldsmith

Why do we age? Surprisingly, there is still substantial scientific disagreement concerning even the fundamental nature of biological aging. The disagreement in turn can be traced directly to long-standing disagreement regarding details of the evolution process. This ancient academic argument may now be significantly detracting from research into age-related diseases and conditions.

In 1859 Charles Darwin published his theory of evolution in his book *On the Origin of Species*. The theory actually consisted of two distinct parts: First, species are descended from other, earlier species. There is currently no *scientific* disagreement with this part. The second part concerned the way evolution works. Survival of the fittest was an elegant yet simple explanation for the mechanics of evolution. Anyone looking at a giraffe or even a tulip could easily identify hundreds of organism design characteristics that clearly aided in surviving or reproducing, that is, in increasing evolutionary *fitness*.

However, Darwin's critics immediately noticed a nagging inconsistency. Different organisms, even very similar ones, had dramatically different life spans. Each species appeared to be *designed* to have a particular life span that was specific to that species. Among mammals there is a 100:1 range in life spans. Fish species have life spans that range between weeks and at least 205 years. A few fish and reptile species exhibit no measurable deterioration in survival or reproductive characteristics with calendar age, known as *negligible senescence,* and thus may have much longer maximum life spans. Darwin's mechanics theory says that all organisms should be trying, through the evolution process, to live as long as possible and to reproduce as much as possible so an organism design that purposely self-limited life span or reproduction was incompatible and unexpected. Yet if the life span limitation was not self-imposed why were life spans of species so different? Why would parrots live six times as long as crows or humans 100 times longer than some mice? Life span seemed to be as specific to a particular species as any evolved design characteristic.

Note that it is generally accepted that there are universal damaging processes such as oxidation and wear that lead to deterioration of any organized system. However, it is *also* generally accepted that living organisms, unlike automobiles and exterior paint, have very extensive internal maintenance and repair capabilities. Wounds heal, claws grow, and dead cells are replaced. Simple deterioration or "damage" theories could not explain the observed gross inter-species life span variation.

Even more inconvenient were more explicit examples of pro-active biological suicide provided by species that die suddenly following reproduction, rather than from gradual

deterioration, such as octopus, salmon, and many plants and animals including one mammal, the male marsupial mouse.

Darwin, in later editions of *Origin* that responded to "miscellaneous objections to the theory of natural selection" advanced by critics, suggested that a limited life span must convey some *benefit* that offset its otherwise adverse nature. He had no suggestion as to the nature of the hidden benefit. This has been a recurring theme since then and scientists still argue endlessly as to the nature of the compensating benefit.

The life span issue remained a total mystery, a completely "unsolved problem of biology", until 1952 when famous British zoologist Peter Medawar suggested that the evolution process is affected by the age of an organism as measured relative to the age at which it is first capable of reproducing. He proposed that even major adverse events, such as death of old age or other major consequences of aging, that occurred well after that age would have relatively little effect on the evolution process because they would have relatively little impact on the organism's ability to reproduce. Indeed, age of sexual maturity in different species correlates moderately well with life span. Because of Medawar's concept, a compensating benefit might be relatively minor. Medawar himself thought that the negative evolutionary impact of aging was negligible and that therefore no compensating benefit was necessary. Other theorists disagreed and contended that deleterious effects of aging somewhat affected survival and reproductive potential of even relatively young animals thus requiring a compensating benefit.

A series of theories of mammal aging based on Darwin's mechanics and Medawar's concept then appeared that each held that the compensating benefit was itself compatible with the traditional mechanics concept i.e. benefiting survival or reproduction of individual organisms. Examples: Aging somehow benefits reproduction; aging somehow acts to reduce incidence of cancer in younger animals, aging is an unavoidable side-effect of some unknown benefit, etc. These theories all had significant criticisms and competed with each other. Extensive efforts to identify an actual cause and effect relationship between an alleged individual benefit and aging have been generally unsuccessful. In addition, these theories have difficulty matching observational evidence. All these mammal theories ostentatiously disregard non-mammal species and especially the explicit instances of biological suicide as being "irrelevant" although they consider mammal life spans (except for the suicidal mammal) to be relevant to human aging. All generally ignore observations of human and other mammal characteristics except the life span variation. Critics call this "cherry-picking the data." These theories say that aging evolved as an unavoidable side effect of some benefiting characteristic and that, consistent with traditional mechanics, the life span limitation itself was not the benefit. In this context "unavoidable" means that for some reason, the evolution process was unable to find a way to accomplish the benefit without incurring the disadvantage of aging.

At the time these theories originated, there were no scientific alternatives to Darwin's mechanics concept and so traditional mechanics was a "given" in developing a theory of aging. These "traditional" theories are still the most popular theories of human aging among gerontologists and other medical researchers.

It is important to mention that if there were some fundamental limit to the maximum age at which a particular organism could reproduce, there would be no evolutionary motivation to develop a life span substantially longer than that age. This is commonly cited as an explanation for aging: "Eighty-year-olds don't have babies so evolution doesn't care what happens to them." However, all the theorists and theories mentioned here agree that an organism design that self-limited reproduction would, like self-limited life span, be incompatible with traditional mechanics. Medawar assumed that a hypothetical non-aging animal would continue to reproduce indefinitely. Decline in reproductive ability with age is seen as a *symptom* of aging rather than an evolutionary *cause* of aging. Indeed, the negligibly senescent animals have negligible decline in reproductive ability with age.

Despite the logical issues and internal disagreements the traditional aging theories were widely seen as at least steps in the right direction. ***However***, in the meantime, a number of ***other*** apparent discrepancies with Darwin's mechanics were observed. *Animal altruism* refers to observed inherited behaviors of animals that are not in the animal's best interest from a survival of the fittest point of view. *Sexual reproduction* represented a quandary because it is massively reproductively adverse relative to *asexual reproduction* and yet sexually reproducing organisms evolved from asexually reproducing organisms. Other problems with traditional evolutionary mechanics were observed. Example: Age of sexual maturity in some species (especially males) appears to be unnecessarily late, a reproductive disadvantage. Theorists began thinking about potential adjustments or modifications to traditional mechanics in an effort to explain the other discrepancies.

In 1962 another British zoologist, Vero Wynne-Edwards, suggested that benefit to survival of a group (herd, tribe, even species) could offset "individual" fitness disadvantage and allow evolution of a group-benefiting organism design even if the design was somewhat adverse to individual survival or reproduction. The *group selection idea* was subsequently and currently refined in many books and papers by Wynne-Edwards and others. Traditionalists, especially George Williams, author of a 1957 mammal aging theory based on traditional mechanics, vigorously disagreed.

In 1975, Richard Dawkins proposed a *gene-oriented* mechanics theory in his book *The Selfish Gene* under which fitness-adverse characteristics could evolve. Dawkins was primarily interested in explaining altruism but the theory could be applied to other fitness-adverse observations. Others also developed gene-oriented theories.

Beginning in 1995, various *evolvability* theories arose in which design characteristics that benefited an organism's ability to evolve could offset an individual fitness disadvantage. Advances in genetics, some very recent, also suggested that, in general, the evolution process was more complex than previously thought. The biological inheritance process is rather central to evolutionary mechanics because any mutational change first occurs in a single individual and then propagates by inheritance. Both the gene-centered theories and evolvability theories explicitly propose that specific characteristics (e.g. genes, paired

chromosomes, meiosis, etc.) of inheritance mechanisms affect evolutionary mechanics. The feasibility of group selection also benefits from genetics discoveries.

None of these proposed adjustments suggest that survival of the fittest (individual fitness) is not the most important factor in the evolution process but rather that it is not the *only* factor and that other, more subtle natural factors can also influence evolution. All of the alternatives expand the definition of evolutionary benefit beyond individual survival and reproduction. Group selection and evolvability theories and probably also gene-oriented theories support aging theories in which life span limitation and even gradual deterioration are the "beneficial" characteristics and propose that aging or other life-span-limiting design feature therefore purposely exists because it provides an evolutionary benefit of its own, i.e. *genetically programmed aging*, *adaptive aging*, *pro-active aging*, or *aging-by-design*. Proposed evolutionary benefits of self-limited life span: increases genetic diversity by limiting ability of a few individuals to dominate the gene pool; assists evolution process by reducing the generation cycle time; aids group survival by reducing tendency toward wild swings in population size; many others.

Traditional mechanics theory says that *individual* organisms that survive longer and breed more *propagate* their personal characteristics in a population. All of the alternatives involve more complicated and less intuitive propagation concepts. Traditionalists generally do not object to the idea that an organism characteristic could produce a group or evolvability benefit, nor object to specific benefits proposed, but rather contend that it is impossible for a group or evolvability benefit (no matter how large) to override an individual disadvantage (no matter how small). It is a propagation issue. Propagation is dependent on inheritance. Inheritance is dependent on genetics. Genetics is rapidly developing science. Keep in mind that according to Medawar's concept, accepted by traditional aging theories, the evolutionary disadvantage of aging is somewhere between negligible and small. Therefore a compensating benefit could be between negligible and small.

Extraneous societal factors tend to confuse evolution and aging science to a very unusual degree. One example: Unlike any other field of science, evolution has been under continuous attack from religionists since 1859. *Creationists* attack the species descendency theory and contend that all of the species were created simultaneously in the relatively recent past. *Intelligent Design* proponents attack the mechanics theory and contend that the evolution process cannot be explained without invoking the supernatural. This is not a trivial problem for bioscience. A Harris poll in 2005 indicated that 54 percent of Americans do not believe in species descendency much less any scientific mechanics theory.

Most people who are only casually familiar with evolution theory have never heard that apparent observational discrepancies with traditional theory exist, that there is consequently significant scientific uncertainty and dissent regarding evolutionary mechanics, or that multiple alternative mechanics theories have been developed. Most people who believe in evolution therefore consider the traditional concept of evolutionary mechanics to be as certain as the fact of evolution. However, since the 1950s when

currently widely respected traditional aging theories originated, our collective scientific certainty in the traditional mechanics theory has dramatically declined. At any scientific venue in which relatively open discussion of evolutionary mechanics occurs, one can now expect to see group selectionists, small-group selectionists, kin selectionists, gene-oriented selectionists, and evolvability proponents in addition to, of course, traditional Darwinists, including "neo"-Darwinists, and "modern" (1942) synthesis proponents. Every advance in genetics adds complexity that potentially affects evolutionary mechanics. There is a growing sentiment that *nobody* really understands the finer details of evolutionary mechanics. All three alternatives may have some validity and between them they propose explanations for all of the observed discrepancies. This is a familiar phenomenon in science: the more you know, the more you realize you don't know.

Thus, we now have two scientific factions. The traditional faction believes in the absolute truth of traditional (circa 1945) evolutionary mechanics and proposes conforming explanations for the apparently conflicting observations including mammal aging. For the traditionalists, the discrepancies are annoying anomalies to be deprecated, discounted, or even disregarded in the face of the overwhelmingly greater number of conforming observations, not to mention 150 years of tradition and intuitively obvious mechanism.

The reformist faction believes that at least some adjustment to traditional mechanics theory is necessitated by the combined impact of all of the observed discrepancies, and endeavors to find such adjustments with corresponding explanations for the conflicting observations including mammal aging. For this faction, the discrepancies are very important. Study of the discrepancies is the key to advancing understanding of evolutionary mechanics and dependent processes such as aging. The obvious metaphor is the difference between *Newtonian physics* (also highly traditional, intuitive, and explaining 99+ percent of observations) and *relativistic physics* (extremely counter-intuitive). However, physics is hard science and does not have to deal with the extraneous factors.

It is reminiscent of religion. In one form or another, this argument has been going on for 150 years and might continue indefinitely. It is unusual for a member of either faction to change sides.

Proponents of the older traditional mechanics theories tend to be older themselves and therefore higher on the academic food chain. It is difficult to publish a paper or obtain a grant based on, say, evolvability theory, if your editor or boss is a neo-Darwinist!

Note that the traditional mechanics view is the diametric antithesis of Intelligent Design. Where ID holds that it is impossible to *ever* understand the evolutionary process in purely scientific terms, the traditionalists believe that it is impossible that their particular *current* scientific understanding of the process is less than perfect and complete. Both groups use the word "impossible" a lot. Either view inhibits further study and is therefore self-fulfilling. ID proponents presumably think that scientific study of the evolution process is futile and heretical, while traditionalists presumably consider further inquiry foolish,

wasteful, and divisive. To the extent that either group controls research funding, there will be no advance in our understanding of evolutionary processes.

There is little doubt that the existence of creationism and ID has historically and presently acted to push science toward the opposite extreme. Any indication of uncertainty or disagreement by scientists gives aid and comfort to the enemy. This encourages a sort of scientific "emperor has no clothes" phenomenon in which science pretends, for public consumption, that no problems and no scientific dissent with traditional mechanics exist. Imagine the quandary faced by editors of a high-school biology textbook or other educational publication covering evolution: Do they include discussion of the scientific issues and disagreements while simultaneously attempting to avoid including ID and creationism? Or do they, in the interest of solidarity and "fairness," exclude *all* of the problems, disagreements and alternative mechanics theories, thus perpetuating public ignorance of the situation?

The interminable academic wrangling regarding the precise evolutionary definition of the word "benefit" would have little practical significance except for potentially major public health implications. In the last century, developed countries have been very successful in preventing and treating infectious diseases that formerly severely limited average human life span. Now, most of the more intractable diseases are highly associated with aging. For example, in the U.S. (2005 CDC data) the chance of dying of cancer between the ages of 5 and 14 is very slight (0.25 percent) while the chance of dying from cancer between the ages of 75 and 84 is very large (12.8 percent). About 75 percent of all deaths in the U.S. now result from age-related conditions. It is clearly not possible to really understand cancer or other massively age-related condition without understanding aging.

The difficulty is that the two evolutionary mechanics positions lead directly to very different concepts regarding the mechanisms of aging, which in turn lead to very different research directions. If aging is indeed the manifestation of an evolved biological life span regulation function that serves a necessary evolutionary purpose, we can infer that its mechanisms are similar to those of other biological functions. We can suppose that the aging mechanism involves coordination of various tissues and systems via hormone signaling. We can suppose that the mechanism has means for sensing local or temporary conditions and tailoring the aging function to those conditions. These sorts of characteristics are common to most biological functions and match observations. Examples: Hormone signaling, sense functions, and nervous system participation are known to exist in some organism life span regulation systems such as that of the octopus. Such a complex life span regulation system in mammals would explain why aging is counter-intuitively slowed by caloric restriction or exercise and would also explain why progeria and Werner syndrome, which are single-gene human genetic diseases, simultaneously accelerate many different symptoms of aging. Aging genes discovered in various organisms that appear to limit life span without other purpose would also fit. Researchers looking into programmed aging mechanisms would logically look for signaling, hormones, genes, control mechanisms, possible nervous system and sense functions, etc.

Aging theories based on traditional mechanics theory are much more limited in complexity and scope and therefore have difficulty in explaining the complex observations. Most proponents of traditional aging theories therefore cite compatibility with traditional evolutionary mechanics as their *only* rationale for believing in non-programmed aging as opposed to programmed aging (see Reading). Researchers following the traditional theories tend to look at actual deterioration mechanisms such as oxidation, telomere shortening, and other molecular damage as opposed to, in addition, looking for a higher-level life span regulation mechanism. The approaches are very different.

Aging is ***still*** an unsolved problem of biology. What can be done to finally resolve this 150-year-old dilemma? Perhaps a scientific jury, staffed by recognized scientists who are not members of either faction, could hear testimony and collect evidence provided by the two factions and deliver a verdict. Perhaps the government should set up a major project similar to the Human Genome Project to finally determine why we age. The U.S. government spends $30 billion dollars per year on medical research. Is it not time to spend a few of those dollars to resolve the fundamental nature of aging? Millions of aging baby-boomers want to know that their government is effectively pursuing research into age-related diseases and conditions!

Theodore C. Goldsmith August 18, 2009 Rev 10/21/09
tgoldsmith@azinet.com

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Additional Reading:

The traditional aging theory view:

From their Scientific American article *No Truth to the Fountain of Youth* (2004):

> *"The way evolution works makes it impossible for us to possess genes that are specifically designed to cause physiological decline with age or to control how long we live."* Olshansky, Hayflick, and Carnes (Republished 2008)

Medawar, P.B. 1952. *An Unsolved Problem of Biology*. London: H.K. Lewis. Paper developing the evolutionary relationship between life span and age at sexual maturity. Medawar also suggested that aging was the result of myriad accumulated genetic defects that persisted in mammal genomes because they had negligible effect on fitness. This is the *mutation accumulation theory* of aging.

Kirkwood, T.B.L. *Evolution of aging*. 1977. *Nature*, **270**: 301–304. Paper proposes aging occurs because of a tradeoff between using energy resources to maintain and repair an organism and using the energy for reproduction – based on Medawar's concept. This is the *disposable soma theory* of aging.

Williams, G. *Pleiotropy, natural selection, and the evolution of senescence.* 1957. *Evolution*, **11**: 398–411. Paper proposing that aging is an unavoidable side-effect of unknown beneficial functions – also based on Medawar's concept. This is the *antagonistic pleiotropy* theory of aging.

More on programmed (adaptive) aging:

Azinet site on aging (contains links to many resources): http://www.azinet.com/aging/

Journal articles and book on evolution and aging theory by Theodore Goldsmith:

The Evolution of Aging 2nd ed. 2006. ISBN 978870905 Book explores logical flaws in the traditional theories of aging, post-1950 developments in evolution theory and observational evidence that support programmed aging, and discusses an *evolvability theory* of aging.

The case for programmed aging, 2009*, Russian Chemical Journal Special Issue on Programmed vs Non-Programmed Aging* (in publication). This article is part of a special issue contrasting programmed and non-programmed aging theories to be published in 2009.

Aging, evolvability, and the individual benefit requirement, 2008, *Journal of Theoretical Biology.* doi:10.1016/j.jtbi.2008.02.035 -- discusses an evolvability theory of aging.

Mammal aging: active and passive mechanisms and their medical implications, 2009, *Journal of Bioscience Hypotheses.* doi:10.1016/j.bihy.2008.12.002 -- discusses empirical evidence favoring programmed aging.

Other journal articles on programmed (adaptive) aging:

Mitteldorf, J. *Aging selected for its own sake*. 2004. Evolutionary Ecology Research, 6: 1–17

Apfeld, J. and Kenyon, C. *Regulation of lifespan by sensory perception in Caenorhabditis elegans.* 1999. *Nature*, **402**: 804–809. PMID: 10617200

Hsin, H. and Kenyon, C. 1999. *Signals from the reproductive system regulate the lifespan of C. elegans.* 1999. *Nature*, **399**: 362–366. PMID: 10360574

Skulachev, V.P. *Aging is a specific biological function rather than the result of a disorder in complex living systems: biochemical evidence in support of Weismann's hypothesis*. 1997. *Biochemistry* (Moscow), **62**: 1191–1195. PMID: 9467841

Wodinsky, J. *Hormonal Inhibition of Feeding and Death in Octopus: Control by Optic Gland Secretion*. 1977. *Science* Vol. 198. no. 4320, pp. 948 – 951. DOI: 10.1126/science.198.4320.948 PMID: 17787564