

Theories of Biological Aging

and

Implications for Public Health

Executive Summary

New: For a summary in article format see:

[An Introduction to Biological Aging Theory](#)

Or short ebook: **[Aging by Design](#)**

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Aging Theory Overview

- ***Why do we age?*** This question has baffled scientists for millennia. There is still substantial scientific disagreement regarding even the basic nature of aging.
- There are three main theories:
 - Simple Deterioration (wear and tear theories)
 - Non-programmed Aging (non-adaptive or passive aging)
 - Programmed Aging (also known as adaptive aging, active aging, or aging-by-design)
- Aging theories are important: Most people in developed countries die of age-related conditions such as cancer.
 - Understanding age-related diseases requires understanding aging.
 - Is anti-aging medicine (that generally delays aging) feasible or impossible?
 - Is anti-aging research foolish and wasteful or potentially vital to the future of medicine?
- Aging theories and evolution theories are critically interrelated.

Wear and Tear

Simple Deterioration Theories

- Aging is simply the accumulative result of fundamental and universal deteriorative processes such as oxidation, molecular damage, wear and tear, or accumulation of adverse byproducts. People age like machinery or exterior paint.
- Superficially provides good fit to human aging.
- Popular with general public, some physicians, and others primarily familiar with human aging.
- Compatible with traditional evolution theory.
- Ignores obvious maintenance and repair capability of living organisms: nails and hair grow, wounds heal, dead cells are replaced.
- Major problems with non-human species: Why would similar species have such different lifespans?
- Suggests contravening aging process is impossible because aging results from fundamental limitations.
- Little current scientific credibility.

Mammal Aging Observations

- Life spans of mammals vary over a 100:1 range.
 - Human ~80 years; Argentine desert mouse ~0.8 years
- Biochemistry of mammals is very similar.
- Deteriorative processes are biochemical in nature.
- Symptoms of aging and age-related diseases and conditions (cancer, heart disease, arthritis, etc.) are similar between mammals.
- No physical or chemical factor (such as body mass or metabolism) exists to generally explain gross life span differences (parrot and elephant have about the same life span; parrot and crow have very different life spans).
- Therefore life span must be part of or at least associated with the species-specific design of the particular species rather than a fundamental property of life. (There still could be some ultimate fundamental limitation.)
- Led to *evolutionary* theories of aging that attempt to explain why different species would have evolved different life spans.

Evolutionary Non-Programmed Theories

- Contend that the evolutionary benefit of longer life declines following reproductive maturity.
- Organisms consequently did not evolve and retain means for living longer.
- Provides much better fit to life span observations.
- Fails to match many other observations.
- Requires a modification to traditional evolutionary mechanics theory.
- Multiple incompatible proposals based on two different modifications to traditional theory.
- Better prospects for medical intervention in aging process: Aging is not the result of fundamental limitations.
- Most medical researchers currently favor one of these theories.

Evolutionary Programmed Theories

- Contend that organisms purposely limit their own life spans to obtain an evolutionary benefit. Aging is genetically programmed just as growth, reproductive maturity, and other biological events are programmed.
- Also based on age of reproductive maturity.
- Requires a diffuse-benefit modification to traditional mechanics theory.
- Explains the life span differences and provides a better match to many other observations.
- New discoveries increasingly favor programmed aging.
- Because aging is a biological function, medical alteration of that function is likely to be possible.

Very Brief History of Evolution Theory

- Darwin's theory of evolution (1859) had two parts:
 - **Species Origin:** Species are descended from other earlier species. Confirmed by overwhelming evidence. No *scientific* opposition.
 - **Evolutionary Mechanics Theory:** Describes process of evolution and defines organism design features that can result from that process. Involves mutations, natural variation, and natural selection (“survival of the fittest”). The traditional mechanics concept requires that evolved design characteristics benefit the ability of *individual* organisms to *survive* or *reproduce*. Some apparent discrepancies, all violations of the *individual benefit requirement*, were immediately noted and others surfaced later. However, the vast majority of observations conformed. Darwin and others suggested that the few apparently individually adverse discrepancies could be explained by some hidden individually beneficial effect that compensated for the adverse observation. *Traditional* evolutionary mechanics theory was virtually universally scientifically accepted until 1952 when *alternative mechanics theories* began to appear and is still taught in high school biology classes. Observed huge life span variation in otherwise similar species was one of the discrepancies originally noted.

Evolutionary Theories of Aging

- Aging in mammals was considered a complete mystery, an “unsolved problem of biology” until 1952 because of the life span observations.
- Because of the very species-specific nature of mammal aging, scientists turned to evolutionary mechanics in attempts to explain why similar species were observed to have vastly different life spans.
- *All* of the evolutionary explanations require modifications to traditional *survival* of the fittest evolutionary mechanics theory. There is *no* scientific agreement as to which, if any, of the modifications is valid. Endless academic argument now spanning more than 150 years has significantly inhibited aging research.

Medawar's Evolutionary Hypothesis

- Peter Medawar (1952) proposed that age measured relative to age of first reproductive capability was a factor in the evolution process. Adverse effects (e.g. aging) that occurred well beyond reproductive maturity would have relatively little or no impact on the organism's ability to reproduce and propagate its design relative to the same effects occurring at a younger age. Subsequent theorists Williams, Kirkwood, and others suggested that aging might be a side effect of some design feature that created individual benefit in younger animals.
- Explains observed loose relationship between life span and age of reproductive maturity and wide disparity of mammal life spans.
- Assists both programmed and non-programmed evolutionary theories because a minor benefit of aging (at younger ages) could offset the catastrophic adverse effects (at older ages).

Diffuse Benefit Theories

- Diffuse benefit evolutionary mechanics theories were developed beginning in 1962 in efforts to explain observations of apparently individually adverse or neutral organism design characteristics including:
 - Altruism (individually adverse behavior) in animals
 - Biological suicide (salmon, octopus, marsupial mouse, many plants and animals that die after reproducing rather than from gradual aging)
 - Sexual reproduction
 - Some mating rituals
 - Excessive reproductive maturity age in some animals, especially males (reproductive limitation)
 - Many aspects of inheritance (genetic) systems
- Aging in mammals was *not* the impetus behind development of diffuse theories.

Diffuse Benefit Theories

- Diffuse benefit theories contend that organism design characteristics that provide benefits to groups or enhance the evolution process can evolve despite some degree of individual survival or reproductive disadvantage.
- Group selection theory (1962), Kin selection theory (1965), Selfish gene theory (1975), Evolvability theories (1995+).
- Relatively recent discoveries in genetics add to issues with traditional mechanics.
- Growing agreement that traditional mechanics theory is inadequate.
- Multiple diffuse theories provide support for programmed aging by trading the relatively small (or zero per Medawar) disadvantage of aging for a diffuse benefit of a limited life span.

Benefits of Life Span Limitation

- A number of plausible group or evolvability benefits of a design-limited life span have been proposed:
 - Aids evolution process by shifting resources to younger, more evolved members of population (Weismann 1882)
 - Reduces possibility of extinction by overpopulation (Mitteldorf)
 - Aids evolution process by challenging older individuals (Schulachev)
 - Aids evolution, especially of features like intelligence and immunity (Goldsmith)
 - Prevents domination of the gene pool by a few older individuals
 - Etc., etc.
- Main choice is between diffuse benefit based programmed theories and better match to observational evidence, non-programmed theories based on earlier modifications to traditional theory and poorer match, or simple deterioration theories based on traditional evolutionary mechanics theory and terrible match.

Evolvability and Aging

- Traditional Darwinian mechanics assumes all organisms have the same capacity for evolution. However, developments in genetics suggest complex (sexually reproducing) organisms have evolved improvements in their ability to evolve (adapt to their environments).
- Evolvability issues are relatively new (~1995) and may eventually result in major changes in the way we think about evolution.
- All the apparent conflicts between traditional theory and observations have evolvability explanations.
- Aging-by-design and biological suicide have multiple evolvability benefits.

Non-Aging Species

- Some species have been identified that apparently do not age or have *negligible senescence*. Older individuals do not appear to be weaker, less agile, less reproductive, more susceptible to disease, or otherwise less fit than younger animals. (Ages of some wild animals can be determined by annual marks in scales or bones similar to tree rings.)
- Determining the maximum age a long-lived animal can achieve is generally not possible because the vast majority of deaths are caused by external causes and very old individuals are very rare. Some species with age of oldest recorded specimen:
 - **Rougeye Rockfish** **205 Years**
 - **Lake Sturgeon** **152 Years**
 - **Aldabra Tortise** **152 Years**
 - **Koi** **226 Years**
 - **Bowhead Whale** **211 Years**
- Non-aging species tend to defeat simple deterioration theories and suggest dramatically longer human life spans are possible.

Progeria and Werner Syndrome

- Hutchinson-Guilford Progeria, a very rare human genetic disease, accelerates many symptoms of aging including atherosclerotic heart disease. Victims usually die by age 13.
- Werner syndrome, another genetic disease, involves acceleration of most symptoms of aging including baldness, hair and skin conditions, heart disease, calcification of blood vessels, some cancers, cataracts, arthritis, diabetes, etc. Victims usually die by age 50.
- These conditions suggest aging is centrally controlled such that a single genetic defect could result in proportionally accelerating all of the expressed symptoms. Central control suggests aging-by-design. Non-programmed theories contend that aging is the result of many deficiencies that *independently* evolved.

Caloric Restriction

- Rats fed a calorie restricted (CR) but nutritious diet live about 50% longer than rats fed “normal” diet. Rats on the restricted diet are more active and generally appear and act “younger”. Similar results for diverse species.
- If we accept that species are designed to have a species-specific life span, the CR effect has a plausible benefit: Temporary increase in life span would help a group survive a famine.
- CR is a problem for non-programmed theories because reduction in food supply nominally reduces energy available for maintenance and repair, increasing deterioration.
- Efforts are in place to explore biochemical differences, (hormone levels, etc.) between normal and restricted animals.
- Efforts also underway to develop a “mimetic” that would simulate the biochemical effect of caloric restriction without restricting calories.
- CR suggests an active aging mechanism that can sense the CR condition and adjust life span in response.

Stress Effects

- Various forms of stress apparently delay aging. Exercise is widely accepted as delaying many manifestations of aging.
- Programmed aging proponents suggest this effect was selected by the evolution process because it aids in group survival in a manner similar to CR: A population under heavy predation or environmental stress could increase its chance of avoiding extinction by increasing life span to compensate for mortality caused by external pressure.
- Stress effects are a problem for non-programmed theories: Stress nominally increases deterioration.

Aging Genes

- Several investigators report discovery of *aging genes* that cause aging and do not appear to have any other function. Disabling these genes in nematode worm, mice, and other organisms has resulted in life span increases of as much as a *factor of ten* (Kenyon, et al).
- Aging caused by these genes is reported to involve complex signaling via hormones, and also in some cases involves sensing of external signals.
- Genes that cause aging and have no other purpose are incompatible with passive and simple deterioration theories. An aging mechanism involving signaling and hormones is consistent with the programmed aging theories.
- Non-programmed aging proponents suggest the aging genes must have a hidden individually beneficial purpose but none has been identified.

Octopus Suicide

- The octopus suicide mechanism (Wodinsky 1977) involves behaviors. Females stop eating and die of starvation after reproducing. Experiments in which optical organs were removed inhibited this behavior.
- Demonstrates a complex suicide mechanism that communicates with the nervous system on both input (sense) side and output (implementation) side.
- Is human aging a subtler version of the octopus life span management system as some active proponents believe?
- Do octopi have some undiscovered individually beneficial need for biological suicide not possessed by *any* gradually aging organism as some passive aging proponents believe?

Potential Anti-Aging Agents and Protocols

- Some agents or behaviors appear to beneficially affect two or more major manifestations of aging:
 - Statins are useful in heart disease and also appear to have an anti-cancer effect.
 - Aspirin appears to beneficially affect several symptoms of aging.
 - Caloric restriction is generally beneficial.
 - Exercise apparently delays incidence of many aging symptoms. Some studies suggest exercise is more important to life span than even obesity.
 - Resveratrol, a constituent of red wine and grape skins has been found to extend life span in animal studies and may beneficially affect heart disease, cancer, and diabetes. A fish experiment (Valenzano et al 2006) increased life span 56 percent.

Implications for Medicine

- We cannot really understand cancer or other massively age-dependent disease without understanding aging.
- The major medical question is whether there exist potentially treatable (medically alterable) factors that are common to two or more major manifestations of aging.
- Simple deterioration and passive theories suggest there is no treatable common factor – continues existing main-line medical thinking.
- Programmed theories suggest existence of controlling mechanisms (signaling, sensing, etc.) that are common to multiple symptoms and therefore existence of treatable common factors. Direct observational evidence supports this (progeria, caloric restriction, aging genes, etc.)

Conclusion

- Aging theory has been treated as an academic issue. However it is increasingly clear that our approach to age-related diseases could be dramatically affected by our understanding of the aging process and that therefore aging theory has become a major public health issue. Efforts should therefore be expended to definitively resolve the theory issues and develop research funding policy based on the results.

Attitudes about Aging

We conducted a general public survey via the Internet. Some results:

- Views about anti-aging treatments:
 - Meaningful treatments are impossible or very distant future possibility: 80%
 - Treatment of fundamental cause of aging possible in near term: 13%
 - Effective anti-aging medications are already available such as HGH: 7%
- What causes aging:
 - Answers seemed relatively evenly split between offered choices including “we are designed to age”, wear-out theory, accumulation of damage theory.
- Morality of Anti-Aging Efforts:
 - No issue: 43%
 - Somewhat concerned: 35%
 - We should not try to extend normal life span: 22%
- Attitudes obviously affect public funding and career choice decisions relative to anti-aging research.

See web site for complete survey results

Additional Information

- [*Ageing by Design: How New Thinking on Ageing Will Change Your Life*](#) General-interest book on history and current status of ageing theories – free PDF, 49 pages. Available on [Kindle](#). **New in 2011.**
- <http://www.programmed-ageing.org/> Comprehensive information on ageing theories.
- [*An Introduction to Biological Ageing Theory*](#) Overview in article format. **New in 2011.**
- <http://www.azinet.com/ageing/> Additional detail and links to many online resources on ageing.
- [*Evolution Controversies and the Theory of Ageing*](#) – General interest article.
- [*The Case for Programmed Ageing*](#) – Russian Chemical Journal special issue on programmed vs non-programmed ageing.
- Book: [*The Evolution of Ageing*](#), ISBN: 0-9788709-0-5, Oct 2006, 2nd Edition 200 pages
[Electronic version](#) (free PDF)
- Journal article: *Ageing, Evolvability, and the Individual Benefit Requirement; Medical Implications of Theory Controversies*, Journal of Theoretical Biology [DOI:10.1016/j.jtbi.2008.02.035](#) 2008
- Journal Article: [*Biological Ageing: Active and Passive Mechanisms Compared*](#), Journal of Bioscience Hypotheses 12/2008 DOI: 10.1016/j.bihy.2008.12.002