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Review of Shefferson, Jones, and Salguero-Gómez (Eds.), *The Evolution of Senescence in the Tree of Life* (Cambridge: Cambridge University Press, 2017)

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As Yeats lamented, growing "old and grey and full of sleep, and nodding by the fire" awaits the best of us, a fortunate consequence of our evolved longevity. But how inevitable is the deterioration of our bodies with age, and what determines whether such decay will be swift or prolonged? Darwin himself had very little to say about why we age and senesce. It was Weisman, Fisher, Medawar, Haldane, Williams, and Hamilton who laid the foundation for an evolutionary understanding of senescence. Whereas aging describes the mere passage of time, senescence is usually defined as age-related decreases in survivorship and/or fertility; presumably these declines come with physiological impairment as well. Stated as such, the evolution of a fitness-decreasing late life stage is puzzling. The key insight was that the force of natural selection declines with age, even in an immortal population. From this starting point came the triad of classical evolutionary theories devised to explain aging. Mutations with harmful effects expressed at late ages when selection is weak can accumulate over generations by drift ("mutation accumulation"), and more so if such mutations carry benefits at early ages ("antagonistic pleiotropy"). A related idea is that when germ line and soma are separate, the high-level investments necessary to maintain the body indefinitely will never be favored because reproduction is a more profitable way to spend limited resources and maximize fitness ("disposable soma"). Those three classic theories suggest how to think about patterns of senescence. The problem is that now, with longitudinal data on many species, some findings do not fit the classical framework. Hamilton famously proclaimed that senescence should be found "even in the farthest reaches of almost any bizarre universe" (1996), yet numerous plant and fungus species show no evidence of age-related declines in vital rates. Evidence also supports negligible or *negative* senescence at late ages in some species, wherein survival rates increase with age. Humans are also a strange beast, with a long postreproductive lifespan even under poor

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conditions, and show even further improvements in longevity over the past two centuries.

Biologists Richard Shefferson, Owen Jones, and Roberto Salguero-Gómez invited 49 researchers from 14 countries to review new findings and perspectives, with the ambitious goal of "develop[ing] a unifying theory of the evolution of and escape from senescence" across the tree of life. Most contributors are biologists aiming to build a broader biodemography and to infuse related fields with new insights of the past two decades. The evolution of aging is a key area of life history theory, and much of the progress in biodemography is likely unfamiliar to evolutionary anthropologists, whose main interest in this area often lies with explaining human postreproductive lifespan or slow growth in primates. An informed understanding of aging in nonhumans is critical; it guards us against favoring convenient, familiar explanations with little relevance beyond a single species. An appreciation for any traits deemed exaggerated or unique among humans requires us to understand why other species might lack those same traits.

The book highlights the latest research on birds, bees, numerous mammals, hydra, herbs and other plants, trees, yeast, botryllids, and fungi. It is organized into 20 chapters divided into five sections: Theory, Animals, Plants, Microbes, and the Tree of Life. Instead of going methodically from chapter to chapter, I highlight selected savory bits from the book. First, I mention morsels on the theoretical side that have been floating around over the past two decades but have yet to be appreciated by a broader audience, including evolution-minded social scientists.

The very notion that the force of selection declines with age, declining to zero once reproduction ceases—thereby leading to the conclusion that senescence is inevitable everywhere—is a classical notion derived by W. D. Hamilton in 1966. That result, however, is derived from one particular way of examining changes in fitness with respect to an age-specific mutation in a vital rate. Annette Baudisch famously showed how different ways of operationalizing the "force of selection" concept can lead to different expectations of what should happen at late ages. The case for negligible or negative senescence whereby mortality risk can level or even decline at late ages is no longer just a theoretical possibility. Robust evidence for it now exists among numerous plants, fungi, bony fish, reptiles, and unicellular organisms that grow indeterminately (i.e., grow bigger with age, whereby fertility either remains constant or increases with size). The evidence is described and summarized in several of the chapters.

Another departure from traditional Hamiltonian forces of selection comes from the recognition that nonreproductives can nonetheless impact fitness through helping behavior, or as described more generally, "transfers." These can reflect provisioning and protection of juveniles, facilitating marriage (in humans), or any other skill or activity that affects kin fertility or mortality. In social species with intergenerational transfers, the force of selection after physiological menopause may indeed be non-zero. This could apply not just to humans, but also to several species of toothed whales (Ellis et al. 2018). Several authors (e.g., Oskar Burger; Alan Cohen; Lucas and Keller) acknowledge the need to modify Hamiltonian forces of selection to accommodate transfers, but it is remarkable that such an exercise has not yet been done. Doing so could be an example of when starting from humans helps illuminate broader relationships between sociality, complex foraging, and long life in other mammals.

Another updated theoretical claim is "Williams's hypothesis." In 1957 George Williams predicted that higher mortality should always select for earlier and faster senescence because of the diminished shadow of the future. This idea has inspired much empirical study with mixed support, depending on whether it was investigated in the lab or the field, and within species or across species. A few nuanced modifications described in several chapters help amend this simple prediction in ways that could benefit future study. Hal Caswell, a mathematical biologist who popularized and improved matrix population models, and Esther Shyu show that an increase in mortality has no effect on the force of selection when mortality affects all ages equally (i.e., as is commonly argued when defining extrinsic mortality as age-independent). Caswell and Shyu add nuance to the Williams argument by considering when the effects of density-dependent mortality in a population differ by age group. If additional mortality affects mortality more at later ages, then more rapid senescence can evolve, but when mortality is more affected at early ages, reduced senescence can result.

Andrew Furness and David Reznick further discuss the role of density dependence, and introduce "condition dependence" as another important complicating factor in the Williams hypothesis. Your physical condition can affect whether or not you succumb to a predator or other environmental hazard; selection can act to delay senescence in any such trait that affects the likelihood of experiencing this risk. The strange but true prediction is that high levels of condition-dependent mortality should delay senescence in certain traits, but not in others. A recent elegant artificial selection experiment in the nematode *Caenorhabditis remanei* cleverly confirms how condition-dependence can lead to longer lifespan (Chen and Maklakov 2012). Further work along these lines that considers how mortality affects individuals may help reconcile the conflicting findings rife in this literature.

The lone chapter on humans, by Burger, may be the most familiar (and engaging) to evolutionary anthropologists. He reminds us that the doubling of life expectancy between human hunter-gatherers and chimpanzees is overshadowed by the tripling of life expectancy between that in contemporary industrialized countries and hunter-gatherers. Infrastructural changes over the past several hundred years have resulted in massive improvements in survival at all ages, yet does this decline in mortality mean that we are now biologically younger than our age-matched ancestors? It is a complicated question for a variety of reasons, and there is not yet a definitive answer. Burger argues with convincing evidence that neither the Williams hypothesis nor the traditional Hamiltonian forces of selection help us understand how senescence has changed over the course of human history. For example, the Hamiltonian force of selection varies minimally among human populations that vary widely in mortality.

Much of the gain in knowledge for students of human biology will come from the many spectacular descriptions of aging in diverse species. The chapter on social insects by Lucas and Keller explores how cooperative breeding in eusocial species such as honeybees and certain ants leads to large longevity differences between the queen and worker castes. Workers are like the colony's soma, and the queen its germ line. Queens often have both high fecundity and longer life than workers or solitary queens, in seeming contrast to expectations based on high costs of reproduction. But fed and cared for by workers, social queens may not experience typical trade-offs, analogous to human females who are actively supported by family and group members. The egg yolk protein vitellogenin is linked to longer life in honeybees, possibly through its

antioxidant and immune effects and interactions, but not so in other social insects. In some cases, differences in the ability to mount immune responses, or resist heat stress and oxidative stress, can help explain mortality differences between castes.

Species with "modular" bodies contain genetically identical clonal parts that either remain attached or can become independent. These include the many plants, fungi, hydra, and other critters described in multiple chapters. What is striking about this body structure is that all cells are totipotent (i.e., no clear distinction between germ and soma), so these species possess the potential to "escape" senescence. Many of them grow indeterminately, such as a ten-ton "humongous fungus" estimated to be 1500 years old, and a 6000-ton aspen tree stand estimated to be 80,000 years old. Yet even some fungi do senesce, as explained by Marc Maas and colleagues, such as saprophytic and coprophilic fungi that grow on spatially or temporally restricted substrates (in this case, dung). Caloric restriction without malnutrition, known to delay senescence in rodents and rhesus monkeys, also extends life and delays reproduction in fungi. A number of mechanisms have been proposed to explain this phenomenon, but in fungi, caloric restriction seems to help maintain mtDNA integrity.

Plants can have complex life cycles, including modular growth, and thus definitions matter in determining whether and how plants senesce (e.g., "whole-plant" vs. tissue-specific senescence). Four chapters highlight features of plant life history to reflect on different aspects of senescence. An interesting chapter on the semelparous (monocarp) thale cress by Liana Burghardt and Jessica Metcalf highlights the role of flowering time as an important determinant of growth, seed dispersal, and post-flowering mortality, and how all are affected by environmental factors (e.g., seasonality). Evidence suggests that senescence (i.e., how quickly resources shift from survival to seeds after the onset of reproduction) itself may be plastic under conditions of year-to-year environmental variability. Iteroparous plant species (polycarps) show mixed evidence of senescence, as described by Johan Dahlgren and Deborah Roach, partly because of confounding age and size given indeterminate growth, and because few demographic studies of long-lived species exist. Many plants also demonstrate density-dependent effects whereby sedentism allows older, established plants to outcompete younger ones, which can then reduce selection against senescence at high densities. Prolonged dormancy, whereby perennial plants produce no biomass above-ground but thrive underground, can affect vital rates in various ways, as lucidly modeled by Jennifer Gremer and colleagues. Their results suggest that dormancy acts to "reboot" physiological processes related to senescence, irrespective of the plant's prior history. Retrogression, or shrinkage, also challenges conventional views because it could reflect senescence itself or instead act as a form of rejuvenation.

Large herbivores and primates are the mammals most well-studied longitudinally. Jean-Michel Gaillard and colleagues highlight that increases in mortality with age have been observed in a growing number of mammals, from moose and buffalo to woodrats and Colombian ground squirrels. Reproductive senescence has also been observed from brown bears and elk to meerkats and Barbary macaques. The numbers of examples have been steadily increasing over the past four decades with longer periods of field study (Nussey et al. 2013). Anthropologists will appreciate that mortality does not increase exponentially from the age of reproductive maturity, as mathematician Benjamin Gompertz had posed in his Law of Mortality in 1825—not just among humans, but among many species. Mortality instead appears to be relatively flat after

maturity for a period of years and then increases exponentially. This and other chapters suggest that data are now good enough, and new metrics have been devised, to help facilitate comparative analyses. For example, a recent study indicated that captive populations of large ungulates show slower rates of senescence than their wild counterparts (Lemaître et al. 2013). Little is yet known, however, about how environmental and social factors affect senescence rates between, and especially within, mammalian species.

The last section is a single chapter by Salguero-Gómez and Jones comparing lifespans across 571 animal and plant species, with the hope of understanding key drivers of the magnitude of variation in how long individuals live. Their results show a suite of life history traits associated with adult life span. Slow-growing species reproducing serially (iteroparous) senesce more slowly, and plants senesce more slowly than animals overall—perhaps not surprising, but consistent with the notion that life history trade-offs affecting the pace of life impact most species in fairly predictable ways.

As might be expected for an ambitious book attempting to explain variability in aging across the tree of life, reconciling wild vs. captive, laboratory vs. field, and ultimate vs. proximate, the obvious complaints include inconsistent coverage for different species, a few chapters relying heavily on specialist jargon, and only one chapter on humans and minimal attention to primates. The target audience is a bit unclear, though there is something for everyone. Placing evolutionary theory front and center may be new territory for researchers focused on more proximate aspects of cellular and physiological aging. Gerontologists, anthropologists, and demographers will benefit from thinking beyond humans. The book is too advanced for most undergraduates but could be used for graduate-level courses on aging or life-history theory. More figures and boxes with definitions of important concepts would have helped make the volume more reader-friendly. There is relatively little referencing of other chapters, and much redundancy. At times it reads more like a collection of papers than an edited volume. On the plus side, each chapter can be read as stand-alone without the reader getting lost. However, it is unfortunate that greater coherence and synergy is lacking.

One consequence of this lack of coherence is the Rashomon effect whereby different authors sometimes hold contradictory views on similar concepts, findings, and even definitions. Are the three evolutionary theories sufficiently well supported to explain much of aging in the wild, or do the theories themselves require modification, or only in certain species (e.g., where germ and somatic lines are separate). Authors seem to disagree on what exactly the state of the field is, and what is needed to move forward. Unfortunately, such disagreements represent real schisms in the field (which is itself many fields!). Still, more attempt at synthesis for the somewhat naive reader would be welcome. For example, one definition of senescence invokes deterioration in *intrinsic* physiological processes. According to this definition, the only way to properly study aging is under ideal conditions whereby all *extrinsic* mortality sources are removed. This would require lab-based studies of short-lived model organisms or, among humans, limiting studies to urban industrialized populations in which most mortality occurs in late adulthood (e.g., in the United States in 2014, >94% of deaths occurred after age 50). The study of aging "in the wild" is viewed by these researchers as misguided since those deaths are due to both intrinsic and extrinsic causes (which cannot be controlled for). This view is stated explicitly by Michael Rose and colleagues

in their chapter summarizing their research program based on "Hamiltonian demography," and by Bilinski and Zadrag-Tecza in their chapter on the use of yeast as a model species to study senescence. One problem with these views is that most, if not all, causes of death do not fit neatly into these discrete categories: predators are more likely to kill the weak and infirm (infants and old), pathogens are fatal among those with underdeveloped immunity, and even lightning may be more likely to strike the vulnerable and bold. Other chapter authors agree that "intrinsic" and "extrinsic" may be loose, heuristic terms. Several authors (e.g., Burger on humans; Burghardt and Metcalf on plants) emphasize the importance of environmental context and the need to better understand aging in naturalistic environments to both document and quantify the relevant selection pressures. Indeed, little is known about the natural ecology of many model species, yet some authors don't seem to think that's a problem. So how does one reconcile such disparate views?

What else would I liked to have read about in this volume? Old age remains the most important risk factor for most major causes of human death today, such as heart disease, cancer, and stroke. Regardless of the suite of causes, mortality creeps up exponentially with age; more researchers are beginning to believe that trying to cure diseases one at a time is less effective than delaying biological aging processes directly. The National Institutes of Health/National Institute on Aging (with its Division of Aging Biology and trans-NIH Geroscience interest group launched in 2012) has even made the biology of aging processes a key target to prevent or slow progression of disease and disability. Yet the physiology of aging has been studied for decades with relatively little direct application of evolutionary insight. While ultimate- and proximate-level explanations are certainly compatible and complementary, examples of harnessing evolutionary theory to help improve understanding of how the organic machinery works to accomplish different functions across ages or life stages are hard to find. In a historical overview, Thomas Kirkwood describes how his ideas about the optimal level of somatic maintenance, a critical part of the disposable soma idea, were inspired by a recognition that physiological mechanisms affect cellular integrity. He considered the effects of oxidative and other damage to macro-molecules such as DNA and proteins, and metabolic costs of a variety of cellular repair mechanisms. His approach was highly influential in its attempt to link whole-organism aging with cellular mechanisms in an optimality framework and has since led to interesting follow-up work (e.g., Davison et al. 2014). Unfortunately, much of the literature on physiological aging since Kirkwood's work in the 1970s has not been informed by evolutionary theory. Vast literatures exist on cellular and molecular processes of aging and on inflammation, immunosenescence, and telomere attrition; allostatic load and stress adaptations; protein stasis; epigenetic maintenance; and other processes related to aging. Bridging the gap between the cogs in the living machine and whole-body organism is key. Tomasz Bilinski and Renata Zadrag-Tecza mention how beliefs about universal mechanisms of aging led to the use of simple experimental model organisms (such as yeast) but argue that the utility of these simple models for understanding the physiology of aging in complex organisms is questionable. As they state, similar survival curves do not require similar physiological mechanisms.

Many more researchers focus on these aging-related processes, and the lucrative quest of developing omniscient biomarkers, than on modeling the evolution of senescence. For example, the industry of studying "allostatic load" and "physiological

dysregulation" has been useful for describing age-related changes in physical state, and being predictive of death (a search of these joint terms on Google Scholar reveals 10,700 hits). But to what extent are patterns by-products of adaptive processes, or evidence of evolutionary mismatch, maladaptation, or nonadaptive developmental constraints? To genuinely bridge fields and reach a broader audience, greater effort is needed to link the evolutionary models to proximate-level processes. Alan Cohen, who has helped develop new statistical indices of biological aging using multiple biomarkers, briefly addresses this in his chapter. Others' coverage of proximate mechanisms is uneven. Yet we live in a time when healthspan is as much a target as lifespan. New drugs ("senolytics") are claiming to extend life and delay onset of multiple diseases by eliminating senescent cells (Xu et al. 2018). Why do certain cells senesce rather than die, given the health problems they may cause? This is a clear example where consideration of evolutionary trade-offs is needed. Benefits for development early in life, and those related to avoiding cancer (Childs et al. 2014), are likely possibilities, but many similar questions will continue to arise as we attempt to set new goals for extending life and improving well-being.

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