

The long-run moulding of senescence

David Bahry

Department of Biology, Carleton University, Ottawa, ON, Canada¹

E-mail: davidbah@buffalo.edu

Abstract. Senescence (ageing) evolves because natural selection cares less about late life than early life. Hamilton formalized this in terms of the sensitivities of the intrinsic rate of increase, a measure of fitness appropriate for density-independent age-structured populations, to small additive changes in mortality or fecundity rates; the framework can also be adjusted to alternative genetic and ecological assumptions. However, any age-specific force of selection is itself a function of the age-structured life history, meaning that as the life history evolves, the forces of selection evolve too; this raises the challenge of how to model evolution beyond the short term. This paper addresses long-run life history evolution by considering two simple evolutionary models, and for each, deriving equilibrium conditions that a life history must fulfill in order to no longer be evolving. The results shed further light on topics in the evolution of senescence, including high juvenile mortality and models predicting “catastrophic senescence.” A key conclusion is that the models have different, mutually exclusive equilibrium conditions, highlighting how the evolution of senescence depends not only on the forces of selection but also on the available genetic variation.

Keywords: Senescence; ageing; life-history evolution; biodemography; age structured populations; Hamilton’s forces of selection

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Senescence, or ageing, is an increase in risk of death as one gets older (Finch, 1991). Similarly, reproductive senescence is a decrease in the production of healthy offspring as one gets older. Not all species have senescence, but many do (Finch, 1991; Jones et al., 2014). The age-specific pattern of mortality and reproduction across the lifespan, senescent or not, is called an “age-structured life history.” Age-structured life histories are shown for a range of species in (Fig. 1), and the basic quantities are defined in (Table 1). Conveniently, these life history quantities can also be used to calculate measures of Darwinian fitness and fitness-related traits (Stearns, 1992).

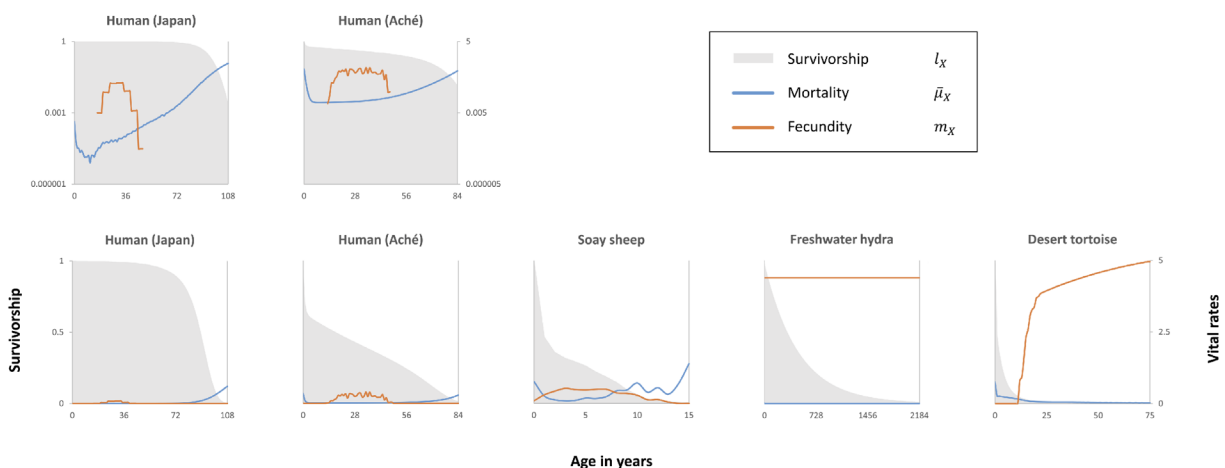


Figure 1. Age-structured life histories for a range of species. Humans and Soay sheep senesce; hydra do not senesce; desert tortoises negatively senesce. Modern Japanese adult mortality grows exponentially, which appears straight on a semilog plot; Aché hunter-gatherer mortality may include an age-independent component. Based on extended data of Jones et al. (2014).

¹ Present address: Department of Biological Sciences, University at Buffalo, Buffalo, NY, U.S.A.

Table 1. Basic age-structured life history quantities.

Continuous time		
x	Age	
l_x	Survival function	A newborn's probability of surviving to at least x .
b_x	Fecundity rate	A surviving individual's instantaneous rate of production of daughters at x .
$\mu_x = -l'_x/l_x$	Force of mortality	Instantaneous, age-specific death rate per capita; also called the hazard rate.
Discrete time		
X	Age-interval	
l_X	Survival function	A newborn's probability of surviving to at least the beginning of X .
m_X	Interval fecundity	A surviving individual's expected number of daughters produced during X .
$p_X = l_{X+1}/l_X$	Age-specific survival probability	Given survival to X , probability of surviving to $X + 1$.
$q_X = 1 - p_X$	Age-specific probability of death	Given survival to X , probability of dying before $X + 1$.
$\bar{\mu}_X = -\ln p_X$	Interval average force of mortality	Average force of mortality from X to $X + 1$, multiplied by interval length Δx .
For sexually reproducing species, this paper follows the convention of only counting female offspring (instead of counting sons and daughters as $\frac{1}{2}$ an offspring each); and for discrete-time, it assumes a birth-pulse population with a pre-birth census and age-intervals numbered from $X = 0$.		

One widely-cited pattern of senescent mortality, especially in humans, is the “Gompertz model,” in which the force of mortality μ_x grows exponentially with age in adulthood; in adult humans, μ_x doubles with about every eight years of age (Finch, 1991). Juvenile mortality begins higher, falling to a minimum around maturity. Humans have long post-reproductive lifespans, which may be an adaptation to our extended parental and even grandparental care (Hawkes et al., 1998; Lee, 2003). In very late life, mortality rates may decelerate or even plateau; such late-life mortality deceleration and mortality plateaus have been observed in fruit flies and medflies, and have also been suggested for humans (Vaupel, 1997; Barbi et al., 2018). An extension of the Gompertz model is the “Gompertz-Makeham model,” which adds a constant age-independent mortality component to the age-dependent exponential mortality component (Finch, 1991).

Forces of selection

Senescence evolves because late life matters less to natural selection than early life (Rose, 1991). This insight was developed by Haldane (1941), Medawar (1946; 1952), and Williams (1957), and formalized by Hamilton (1966). An example from Haldane makes the insight intuitive: Huntington’s disease, a fatal inherited neurodegenerative disorder, can nevertheless persist in the population, because it tends to only strike in middle age, after the mutation’s bearer has likely already reproduced and the mutation already been passed on. Medawar and Williams then developed the insight into two overlapping theories of the evolution of senescence: the “mutation accumulation” theory, under which senescence evolves due to alleles that are neutral early in life and harmful late in life, and the “antagonistic pleiotropy” theory, under which it evolves due to alleles that are *beneficial* early in life and harmful late in life. Some later theories, bridging the gap between evolutionary theory and proximate biology, can be seen as versions

Box I. Life history evolution

The basic age-structured life history quantities can be used to define fitness-related quantities, illustrated here for discrete time.

Density-independence (r selection) vs. population stationarity (R selection)

Density-independent populations, if real, would grow exponentially forever at rate r ; if different lineages within a population have different r , the highest r lineage is favoured by selection. All real populations are density-dependent. One common way to model selection with density-dependence is in stationary populations, held at constant size by a factor such as early-juvenile mortality; in such populations then lifetime reproductive output R can be used as a measure of fitness. Note that the stationarity constraint requires that population average $\bar{R} = 1$, so absolute fitness will generally also be frequency-dependent.

Stable age distribution

For most life histories, a population eventually converges to a stable age distribution where the age classes remain in equal ratios to each other and the population grows at rate r . Relative abundance in the stable age distribution, compared to newborns, is

$$c_X = e^{-rX} l_X$$

R from the life history

Lifetime reproductive output is a newborn's sum of the expected reproductive outputs at each age, each of which is the product of fecundity at that age and the probability of the newborn surviving to that age:

$$R = \sum_{X=0}^{\infty} l_X m_X$$

r from the Euler-Lotka equation

If you divide a cohort of newborns into groups according to the ages of their mothers, then add them back together, you get back the whole cohort. If a population is in stable age distribution, then the fraction of newborns to mothers aged X is $e^{-rX} l_X m_X$, and this truism becomes the Euler-Lotka equation; plugging in the age-specific survivorship and fecundity schedules allows you to calculate the value of r that makes the equation true (its root):

$$1 = \sum_{X=0}^{\infty} e^{-rX} l_X m_X$$

Reproductive value and residual reproductive value

Age-specific individual reproductive value measures expected future reproductive output from age X , with farther-future offspring discounted according to population growth:

$$V_X = \sum_{Y=X}^{\infty} e^{-r(Y-X)} \frac{l_Y}{l_X} m_Y$$

In stationary populations there is no discounting term, and reproductive value is identical to expected future reproductive output: $V_X = \sum_{Y=X}^{\infty} \frac{l_Y}{l_X} m_Y$. Reproductive value also measures the expected remaining contribution to the ancestry of future generations, relative to a newborn; newborn reproductive value is $V_X = 1$. Reproductive value can also be partitioned into current reproduction and residual reproductive value, $V_X = m_X + RRV_X$.

Stage structure

A stage-structured population projection matrix is a grid of numbers, with columns and rows corresponding to life cycle stages, and entry a_{ij} representing the per-individual contribution from stage i to stage j per time step. The relative abundance vector and the reproductive value vector are eigenvectors of the matrix; the life history's fitness is often defined as its an eigenvalue $\lambda = e^r$.

of antagonistic pleiotropy. The “disposable soma” theory says that senescence is cellular or molecular damage, which can build up due to selection for optimal resource allocation favouring fast growth or reproduction over perfect maintenance and repair (Kirkwood, 1977).

The “hyperfunction theory” says that senescence is due to the continuation of developmental processes past their point of usefulness (Blagosklonny, 2009). Both theories say that natural selection is favouring an early benefit at the price of a later-life mortality cost.

Hamilton’s formalism (1966) defined the “force of natural selection” on a scalar trait as the sensitivity of a suitable fitness measure to small additive changes in that trait. This can be thought of as the partial derivative on the right-hand-side of the approximation (Bahry, 2022a):

$$\Delta \text{fitness} \approx \Delta \text{trait} \cdot \frac{\partial \text{fitness}}{\partial \text{trait}} \quad (1)$$

Thus a mutation’s fitness effect depends both on its affect on the trait and on the sensitivity of fitness to such effects. To flesh this out, however, we have to specify the fitness measure and the trait. Hamilton assumed density-independent populations in stable age distribution, with the intrinsic rate of increase r as fitness (for stationary populations, held at constant size by a factor such as density dependent newborn mortality, lifetime reproductive output R would be fitness, albeit in a subtle sense since the stationarity constraint requires population average $\bar{R} = 1$). He then considered mutations subtracting from interval-average force of mortality $\bar{\mu}_X$ or adding to interval fecundity m_X for some age-interval X (as opposed to, for instance, multiplying $\bar{\mu}_X$ or m_X). Thus the relevant fitness sensitivities Hamilton sought are $-\partial r / \partial \bar{\mu}_X$ and $\partial r / \partial m_X$. The formulae he found for these, by differentiating the Euler-Lotka equation, must be decreasing functions of X , as can be seen by giving them intuitive, semi-verbal demographic translations:

$$-\frac{\partial r}{\partial \bar{\mu}_X} = \frac{\text{Fraction of newborns with mothers } X + 1 \text{ or older}}{T} \quad (2a)$$

$$\frac{\partial r}{\partial m_X} = \frac{\text{Relative abundance of age class } X}{T} \quad (2b)$$

where T is generation length, defined as the mean age of mothers, and newborns have relative abundance = 1. For mortality selection, of course the higher X is, the fewer mothers can be older than that (but with no mothers younger than the age of maturity anyway). For fecundity selection, for most populations there must be fewer individuals at older ages, both because individuals die off, and because in a growing population there were (say) fewer born last year than this year. A minor exception is that for fecundity selection, equation (2b) can grow with age in rapidly-shrinking populations, which can have more individuals at older ages; but such populations tend to go extinct without having become the ancestors of today’s species anyway,

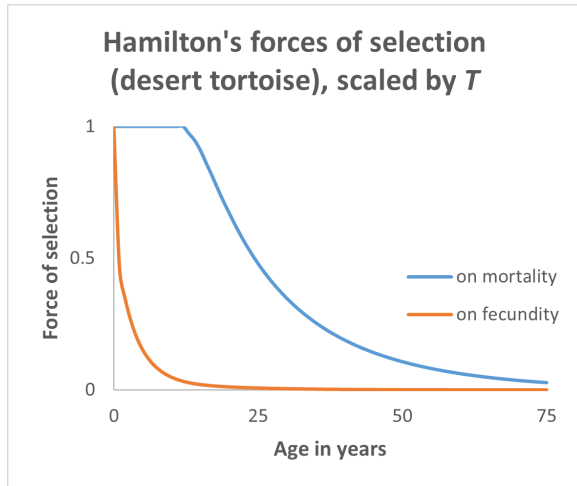


Figure 2. Hamilton's forces of selection, illustrated for the desert tortoise. Selection on mortality is constant until maturity then falls, selection on fecundity begins falls from birth. Hamilton's forces of selection fall with age even though the tortoises are negatively senescing.

and so are of little relevance (Charlesworth, 1980, p. 225). Thus Hamilton's forces of selection vindicated the intuition of Haldane, Medawar, and Williams, while making it more precise. His force of selection on mortality is constant until maturity and then falls with age; his force of selection on fecundity starts to decrease with age from birth (Fig. 2). His formalism also clarified existing theoretical issues, such as correcting a previous suggestion of Fisher that age-specific reproductive value V_x was the force of selection (Charlesworth, 2000); and improved the generation of testable predictions, such as

clarifying the conditions under which increased “extrinsic” mortality risk such as predation is or isn't expected to also weaken selection against “intrinsic” senescent mortality (Abrams, 2004; Williams et al., 2006; Kozłowski et al., 2020). In short, despite the limitations we will discuss presently, Hamilton's formalism is a triumph of evolutionary biology and a cornerstone of life history evolution (Fabian and Flatt, 2011; 2012).

Alternatives to Hamilton's ecological and genetic assumptions can be chosen, such as stationary populations with R as fitness (e.g. Dańko et al., 2018), or mutations subtracting from log mortality $\ln \bar{\mu}_x$ or adding to log fecundity $\ln m_x$ (multiplying mortality $\bar{\mu}_x$ or fecundity m_x) (Baudisch, 2005; 2008). Fitness sensitivities corresponding to some of these combinations of assumptions are given in (Table 2). Some of these, such as Baudisch's “proportional hazards” sensitivity (in contrast to Hamilton's “additive hazards” sensitivity), can increase with age under some circumstances, though the proportional-hazards assumption alone does not necessarily lead to the evolution of non-senescence or negative senescence, since the conditions for it to rise with age include that mortality must already be senescent (Bahry, 2022a). It is also possible to model “stage-structured life histories,” using population matrices (van Groenendael et al., 1988). Unlike age-intervals, life cycle stages (e.g. polyp vs. medusa) need not all have the same duration; later-life stages can matter more to selection if they last longer and mutations affect entire stages (Bahry, 2022a). Stage structure may play a role in the evolution of non-senescence and negative senescence (Roper et al., 2021; Bahry, 2022a; Roper and Salguero-Gómez, 2022).

Table 2. Fitness sensitivities under four pairs of assumptions.

	Density independence (r as fitness)	Population stationarity (R as fitness)
Genes add to $-\bar{\mu}_X$ (i.e. multiply p_X)	$-\frac{\partial r}{\partial \bar{\mu}_X} = \frac{\sum_{Y=X+1}^{\infty} e^{-rY} l_Y m_Y}{T}$	$-\frac{\partial R}{\partial \bar{\mu}_X} = \sum_{Y=X+1}^{\infty} l_Y m_Y$
Genes add to m_X	$\frac{\partial r}{\partial m_X} = \frac{e^{-rX} l_X}{T}$ (Hamilton, 1966)	$\frac{\partial R}{\partial m_X} = l_X$ (Dańko et al., 2018; cf. Charnov, 1993, p. 129)
Genes multiply $-\bar{\mu}_X$	$-\frac{\partial r}{\partial \ln \bar{\mu}_X} = \bar{\mu}_X \left(-\frac{\partial r}{\partial \bar{\mu}_X} \right)$	$-\frac{\partial R}{\partial \ln \bar{\mu}_X} = \bar{\mu}_X \left(-\frac{\partial R}{\partial \bar{\mu}_X} \right)$
Genes multiply m_X	$\frac{\partial r}{\partial \ln m_X} = m_X \left(\frac{\partial r}{\partial m_X} \right)$ (Baudisch, 2005; 2008)	$\frac{\partial R}{\partial \ln m_X} = m_X \left(\frac{\partial R}{\partial m_X} \right)$ (This paper; Bahry, 2022b)

The top-row sensitivities cannot rise with age (except for Hamilton's fecundity indicator, in rapidly-shrinking populations). The bottom-row sensitivities can rise with age under some conditions.

Tools of economic demography have also been used to incorporate intergenerational resource transfers into Hamilton's model for species with parental and grandparental care (Lee, 2003).

A more complicated issue is when and whether Hamilton's approach is appropriate for sexually-reproducing Mendelian populations. To be sure, it is possible to measure age-specific mortality and fecundity rates associated with a genotype, for instance Aa , substitute them into the Euler-Lotka equation, and derive an associated intrinsic rate of increase r ; but the problem is that with sex, the rate of production of daughters *by* Aa mothers need not equal the rate of birth *of* Aa daughters, raising uncertainty about whether r is a good guide to genotype fitness (Charlesworth, 1970). This question has been investigated by Charlesworth (1980); he found that it's not perfect, but it does work as an approximation, especially when selection is weak or there are no complications like sex differences or non-random mating (Charlesworth, 2000).

A challenge for the "forces of selection" framework in general is that fitness sensitivities are themselves functions of the life history: as a life history evolves, the forces of selection evolve too (Tuljapurkar, 2013). This makes it challenging to predict how an age-structured life history

Table 3. Equilibrium conditions for two models.

Log mortality mutation-accumulation model	Log mortality cost-of-reproduction model
$\mu_x = \frac{\Phi}{c_x V_x}$	$\mu_x = \frac{\theta}{V_x}$
$\Phi \approx \mu_0$ and $\theta \approx \mu_0$ when the models' premises apply to all ages including newborns; if newborn mortality is somehow special, for instance a function of maternal control rather than newborn state, it may be acceptable to let them be adjustable parameters.	

should evolve in the long term—or to understand the life histories of species around us, which presumably got that way by evolving for a long time. One option is to simulate evolution over many generations (Charlesworth, 2001). For instance, this has been used to study a model of late-life mortality deceleration; a difficulty is determining how long to run it, and whether its state is transient or at equilibrium (Mueller et al., 2011). An alternative, used in this paper, is to assume a simple, analytically tractable model of the evolutionary process; assume that life histories eventually approach an evolutionary equilibrium; and seek any simple conditions that a life history must fulfill to satisfy the equilibrium assumption that it is no longer evolving.

In this paper I consider two simple evolutionary models and derive their equilibrium conditions (Table 3). First, I also give intermediate theoretical results that were used to derive the equilibrium conditions or support the framework. Proofs and details are found in the MSc thesis on which this paper is based (Bahry, 2022b), and may later be included as a supplement. It should be noted that I do not prove whether any equilibria that exist are stable or unstable.

Intermediate theoretical results

This section gives three intermediate theoretical results. The first two were used in deriving the models' equilibrium conditions; the third defends the coherence of the proportional-hazards assumption, and its corresponding fitness sensitivities, from previous criticisms.

Selection on mutations with multiplicative effects in stationary populations

Hamilton assumed density independence (r as fitness) and mutations additive on mortality $\bar{\mu}_x$ or fecundity m_x . Authors including Danko et al. have modified the ecological assumption to consider stationary populations, maintained at constant size by density dependence (R as fitness); and Baudisch modified the genetic assumption, considering mutations for instance multiplying $\bar{\mu}_x$ or m_x . We can also combine these alternative assumptions. Baudisch did not

show her full derivation, but it is general, following from basic rules of calculus. For any fitness measure W and any trait ϕ :

$$\frac{\partial W}{\partial \ln \phi} = \phi \left(\frac{\partial W}{\partial \phi} \right) \quad (3)$$

Plugging in $W = R$, as well as $\phi = \bar{\mu}_x$ or $\phi = m_x$, lets us complete Table 2, relating Danko et al.'s forces to the forces of selection on multiplicative genetic effects in stationary populations. Like Baudisch's proportional-effects forces, these can also rise with age in some circumstances.

Residual reproductive value as the ratio of Hamilton's forces

Age-specific reproductive value V_x is approximately expected future reproductive output at age x , but with farther-future offspring “discounted” according to population growth (since a daughter born sooner can begin producing granddaughters sooner, a fitness benefit in growing populations; in stationary populations, there is no discount factor). For discrete time, we can partition this into current reproduction plus “residual reproductive value” $V_x = m_x + RRV_x$; of course, if we consider very short intervals with very low per-interval fecundity, then $RRV_x \approx V_x$. The reproductive value of a newborn is $V_x = 1$; this becomes intuitive when we learn that reproductive value is also equivalent to an individual's relative expected contribution to the ancestry of future generations, *compared* to that of a newborn.

Interestingly, residual reproductive value can also be written as the ratio of Hamilton's mortality force of selection to his fecundity force of selection:

$$RRV_x = \frac{-\partial r / \partial \bar{\mu}_x}{\partial r / \partial m_x} \quad (4)$$

The analogous relationship also holds in stationary populations, where residual reproductive value (with no discounting) is the ratio of Dańko et al.'s forces. Intuitively, I view these results as saying that residual reproductive value measures the relative importance to your own fitness of remaining alive at age X , versus accelerating the production of newborn clones of yourself.

Population genetics for mutations with multiplicative effects

When Baudisch proposed her alternative fitness sensitivities, these were criticized by Mueller et al. (2011, appendix), on two grounds. First, the proportional-hazards sensitivity apparently made false predictions about a simulation result, compared to Hamilton's additive-hazards sensitivity. Second, Charlesworth had derived population genetic equations for the spread of

an allele with an age-specific mortality or fecundity effect in sexually-reproducing Mendelian populations, and these equations contained terms for Hamilton's forces (Charlesworth, 1980, eqn. 5.6 and 5.12); no such equations had yet been found that featured Baudisch's sensitivities.

This debate has since been resolved, in correspondence between myself, Baudisch, and Mueller, to the satisfaction of both sides (Baudisch, Mueller, pers. comm.). Charlesworth's derivation of the population-genetic equations was general, and can be adapted to other traits and other parameterizations. Where ρ_i is the frequency of allele i , and $\alpha_\phi = \rho_a(\phi_{Aa} - \phi_{aa}) + \rho_A(\phi_{AA} - \phi_{Aa})$ is the average effect of substituting allele A for allele a on any trait ϕ , the initial change in frequency per unit time of a rare mutant allele A is:

$$\Delta\rho_A \approx \rho_a\rho_A\alpha_\phi\left(\frac{\partial r}{\partial\phi}\bigg|_{aa}\right) \quad (5)$$

with the sensitivity evaluated for the initial population, homogeneous for aa ; multiplying both sides by generation length T_{aa} gives the frequency change per generation rather than per unit time. Substituting $\phi = -\bar{\mu}_X$ or $\phi = -m_X$, using Hamilton's additive-effects assumption, and multiplying by generation length yields Charlesworth's equations. Instead substituting $\phi = -\ln \bar{\mu}_X$ or $\phi = \ln m_X$ yields the equations for multiplicative effects on mortality and fecundity:

$$T_{aa}\Delta\rho_A \approx \rho_a\rho_A\alpha_{\ln \bar{\mu}_X}\left(-\frac{\partial r}{\partial \ln \bar{\mu}_X}\bigg|_{aa}\right) \quad (6a)$$

$$T_{aa}\Delta\rho_A \approx \rho_a\rho_A\alpha_{\ln m_X}\left(\frac{\partial r}{\partial \ln m_X}\bigg|_{aa}\right) \quad (6b)$$

These are the equations that Mueller et al. (2011) desired. They are approximately equal to Charlesworth's equations, for mutations of small effect.

Regarding the apparent simulation result, Mueller has kindly reviewed his records, and uncovered that the result was due to a typo in the simulation setup: the survival function l_X was intended to be calculated from exponentially-decreasing age-specific survival probability p_X , but was accidentally set up as exponentially-decreasing l_X (implying constant mortality $\bar{\mu}_X$; when the corrected simulation is run, there is no conflict (Mueller, pers. comm; Bahry, 2022b, appendix). Indeed, considering the concept of a fitness sensitivity in light of eqn. (1) reveals that Hamilton's model and Baudisch's model cannot make different predictions for the same stipulated mutation; any mortality mutation's fitness effect can always be partitioned in either way (e.g. a change from $\bar{\mu}_X = 1$ to $\bar{\mu}_X = 2$ can be described either as "plus 1" or as "double").

Rather, the additive-hazards assumption and proportional-hazards assumptions define different equivalence classes of mutations: mutations with “the same” additive effect, vs. ones with “the same” multiplicative effect. Whether it is more appropriate to describe mutations as additive hazards or as proportional hazards depends on convenience, which depends on how mutations empirically turn out to behave under a range of circumstances. For instance, if mutations tend to arise at the same rate for the same proportional effect size across age-classes, then it is more apt to consider mutations as proportional hazards than as additive hazards.

Hamilton’s additive-hazards assumption was a reasonable one. Additive effects on $\bar{\mu}_x$ are equivalent to multiplicative effects on survival probability p_x (since $p_x = e^{-\bar{\mu}_x}$); and multiplicative effects on survival probability occur when mortality risks are independent (e.g., if the probability of avoiding a heart attack *and* a lion attack is the product of the probabilities of avoiding each individually). Nevertheless, this does not guarantee its truth; and Baudisch cites evidence that mutations may indeed be proportional hazards (Baudisch, 2008, pp. 24–26).

Equilibrium conditions for two models

Here I consider two simple evolutionary models, and derive their equilibrium conditions (Table 3). One is a mutation-accumulation model with no pleiotropy; the second is a model optimizing reproductive effort given a same-age log-mortality cost of fecundity. A key finding is that the models’ equilibrium conditions are *mutually-exclusive*, highlighting how senescence evolution depends not only on forces of selection, but also on the available genetic variation.

A mutation-accumulation model

This is a model of mutation-selection balance, assuming no pleiotropy. For every age class, mutations arise with age-limited effects on mortality that age, with every age subject to the same mutation rate and with the same distribution of mutational effect sizes (under a specified parameterization). At any given age, mortality is pushed up by mutation pressure, and pushed down by natural selection: at equilibrium, the forces of mutation and selection cancel out. But if mutations push mortality up with the same force at each age, then for this to be canceled out by selection at each age, the force of selection must also be the same at each age. Thus, the intuition for this model is that at equilibrium, we must have, for the relevant force of selection:

$$\frac{\partial \text{fitness}}{\partial \text{trait}} = \varphi \quad (7)$$

where $\varphi = \text{constant}$. If mutations are additive hazards, there is no non-extinction equilibrium: the relevant sensitivity is Hamilton's additive-hazards force of selection on $\bar{\mu}_X$ (or its stationary-populations analogue), which must decrease with age. If mutations are instead proportional hazards, the equilibrium condition becomes that Baudisch's proportional hazards sensitivity $-\partial r / \partial \ln \bar{\mu}_X$ (or its stationary populations analogue) be constant with age. Rearranging this, including rescaling the constant by generation length, yields the equilibrium condition:

$$\bar{\mu}_X = \frac{\Phi}{c_X \cdot RRV_X} \quad (8)$$

where $\Phi = \text{constant}$ and c_X is relative abundance in the stable age distribution. If “all ages” includes newborns, then $\Phi \approx \bar{\mu}_0$ (since newborns have $c_X = 1$ and $V_X = 1$, and $RRV_X \approx V_X$). However, if we assume newborn mortality is special (e.g. subject more to parental control than to their own state), it may be acceptable to treat Φ as a parameter. In the continuous-time limit of infinitely short intervals with infinitely low per-interval fecundity, this condition becomes:

$$\mu_x = \frac{\Phi}{c_x V_x} \quad (9)$$

Interestingly, this condition, together with the lack of equilibrium under additive hazards, may reverse-engineer a result of Williams and Taylor (1987), as will be discussed in the final section. Note also that $c_X RRV_X$ is another way to write the numerator of Hamilton's mortality force of selection, which must decrease with age; therefore this model necessarily predicts senescence.

Similar mutation-accumulation models can also be constructed, and their equilibrium conditions derived, for evolution of fecundity: for instance, if mutations are additive on $\ln m_X$, then at equilibrium $c_X m_X$ must be constant with respect to X . Since evolutionary changes to fecundity also affect selection on mortality, and evolutionary changes to mortality also affect selection on fecundity, it is also worth investigating whether life histories can be in “general equilibrium” for mortality and fecundity rates simultaneously, under various combinations of genetic and ecological assumptions; for a preliminary discussion of this, see (Bahry, 2022b).

A reproductive-effort model

This reproductive-effort model assumes that whatever the life history, and whatever trade-offs have already occurred, the following trade is always available: an evolving lineage always has

the option to additively increase its fecundity m_x at the expense of proportionally increasing its mortality $\bar{\mu}_x$ at the same age-interval X , with the price always the same:

$$\frac{\partial m_x}{\partial \ln \bar{\mu}_x} = \theta \quad (10)$$

where θ is constant. For any age, equilibrium is where the cost of further-increased mortality balances the benefit of increased fecundity: for density-independence,

$$\Delta m_x \left(\frac{\partial r}{\partial m_x} \right) = \Delta \ln \bar{\mu}_x \left(-\frac{\partial r}{\partial \ln \bar{\mu}_x} \right) \quad (11)$$

A life history is in equilibrium when mortality and fecundity are in equilibrium at every age. Rearranging eqn. (11) (or its stationary-populations analogue) and substituting yields:

$$\bar{\mu}_x = \frac{\theta}{RRV_x} \quad (12)$$

Again, if “all ages” includes newborns then $\theta = \bar{\mu}_0$, but if newborns are somehow special then θ may be a parameter. In the continuous-time limit, this equilibrium condition becomes:

$$\mu_x = \frac{\theta}{V_x} \quad (13)$$

Interestingly, this result provides potential support for Fisher’s (1930) hunch that the seeming inverse curves of human mortality and reproductive value was meaningful, without requiring his fallacious explanation (Fisher, 1930; cf. Hamilton, 1966; Charlesworth, 2000).

Discussion

In this section I discuss the relevance or irrelevance of the models to interesting features of age-structured life histories, in theoretical models and in nature; and then remark on their value despite their simplicity and potential unrealism.

Catastrophic senescence in mutation-accumulation models

As mentioned, the equilibrium condition for the mutation-accumulation model appears to reverse-engineer a previous result from Williams and Taylor (1987). We concluded that in this model, when mutations are proportional hazards, at equilibrium mortality is inverse to $c_x V_x$, but when mutations are additive hazards there is no non-extinction equilibrium. Williams and Taylor concluded that when mutations are proportional hazards, at equilibrium mortality is

inverse to $l_x V_x$, but when mutations are additive hazards, the population evolves semelparity (a single “big bang” reproductive period followed by death). However, they did not make explicit their assumptions about mutation rates or the presence or absence of pleiotropy. I suspect that the present model may in fact be equivalent to theirs: in stationary populations, $c_x V_x = l_x V_x$, and the model is otherwise simple and clear enough to have been independently considered. If so, then I suggest that their conclusion of semelparity was in error, since no semelparous life history would be in equilibrium either; I suspect the only true outcome would be extinction.

Other theoretical models of mutation accumulation have also predicted “catastrophic senescence,” whereby evolutionary increases in late-life mortality also erode selection against still further increases in mortality (Partridge and Barton, 1993; Wachter et al., 2013), argued to eventually lead to a “bacterial limit” of short life (Tuljapurkar, 2013). These models also tend to assume additive hazards. I suspect that my mutation-accumulation model is also analogous to theirs, and that the erosion of selection against mortality is due to such models having no equilibrium with additive hazards. I suspect that these authors also may have erred, in that the “bacterial limit” may not be an equilibrium either, with only extinction being an equilibrium.

Thus, the present mutation-accumulation model corroborates previous findings that there is no mutation-accumulation equilibrium with additive hazards, but that there can be equilibria with proportional hazards. However, compared to other models, the present model makes it intuitive *why* this should be so. For this model to lead to equilibrium under additive hazards, Hamilton’s mortality sensitivity would need to be constant with age—but it can’t be.

High juvenile mortality

The mutation-accumulation model, even with additive hazards, always predicts mortality to be constant until maturity and then rise, since at equilibrium mortality is inverse to Hamilton’s mortality sensitivity (which is constant until maturity and then falls). Therefore the mutation-accumulation model can’t explain juvenile mortality starting off high then falling to maturity.

In contrast, the reproductive-effort model predicts that juvenile mortality *must* start off higher and then decrease towards maturity. This is because at equilibrium, mortality is inverse to reproductive value; and reproductive value *always* increases towards maturity, as you survive the mortality risks of the juvenile period and get closer to beginning reproduction. However, note that the model does not make at all transparent by what process the equilibrium might be reached, if it even is reached—for instance, whether selection achieves it by pushing early-

juvenile mortality up, by pushing late-juvenile mortality down, or by shaping the entire rest of the life history until the equilibrium itself shifts to meet the existing juvenile mortality curve.

Regardless, the reproductive-effort model potentially revives an influential hunch from Fisher (1930). Fisher was impressed by the fact that in humans, mortality falls to maturity and then rises, while reproductive value rises to maturity and then falls; he suggested that this was “probably not without significance,” as well as suggesting that this was because reproductive value measured age-specific importance to natural selection. Hamilton (1966) noted the fallacy of equating reproductive value with the force of selection; he also suggested that his forces of selection, neither of which rises from birth to maturity, cannot explain high juvenile mortality, and instead suggested an alternative kin-selection based “sibling replacement” theory. It is thus interesting to find a trade-off model, combined with Hamilton’s framework and its extensions, that can not only explain but require high juvenile mortality after all.

Senescence, non-senescence, and negative senescence

The mutation-accumulation model with proportional hazards always predicts that mortality be constant until the age of maturity and then rise with age. This model is incompatible with non- or negative senescence. The reproductive-effort model, in contrast, is compatible with all three kinds of life history. Species with decreasing reproductive value will senesce; species with constant reproductive value will be non-senescent; species with increasing reproductive value will be negatively senescent. Thus, interestingly, this model does not strictly predict senescence, though it does constrain the predicted shapes of senescent mortality and fecundity curves.

Late-life mortality plateaus

The mutation-accumulation model cannot explain late-life mortality plateaus. Either mortality keeps rising with age (as Hamilton’s mortality sensitivity keeps falling), or it becomes infinite (as reproduction ends and Hamilton’s mortality sensitivity hits zero). The reproductive effort model, in contrast, does seem compatible with late-life mortality plateaus, though not actively predicting them. If after a late age mortality and fecundity are constant, reproductive value will by definition also be constant—which is also what the equilibrium condition requires it to be.

Post-reproductive lifespan

Neither of the present models, as described here, can explain post-reproductive lifespan. Both require mortality at equilibrium to be inverse to a term with reproductive value in the product;

as reproduction ends and reproductive value falls to zero, mortality must rise to infinity. It may be possible to *redefine* reproductive value for species with extended parental or grandparental care, since these do help you contribute more descendants to future generations through your children or grandchildren, and include it in the models; but I have not attempted this. Still, the models may contribute some amount to our understanding of post-reproductive lifespan. Lee (2003) derived a fitness sensitivity for mortality which included both an effect due to death ending fertility, and an effect due to death ending resource transfers. He then compared his model to Hamilton's model, as predictors of human hunter-gather life history data, implying that his and Hamilton's model each predicted mortality to be inverse to the relevant sensitivity. However, he did not explicitly derive this as an equilibrium condition. This suggests that Lee's model, or at least his empirical comparison, may be implicitly assuming proportional hazards.

Are the models realistic?

I have no confidence in the realism of the present mutation-accumulation model. It seems to have very stringent conditions: equal mutation pressure at all ages countered by equal selection at all ages. I do not know how the model can or should be refined in complex situations where mutation accumulation and antagonistic pleiotropy are both acting, for instance. Additionally, it seems unable to explain prominent life history phenomena such as high juvenile mortality.

I am more open to the realism of the reproductive-effort model: its conditions are less stringent, requiring only that whatever else happens, the proposed trade-off is always available. As well, it more easily fits the diversity of life histories, including senescing, non-senescing, and negatively-senescing ones. Its strictest prediction—high juvenile mortality that decreases until maturity—is a prominent phenomenon whose explanation has been debated. The mechanistic basis of the log-mortality cost of fecundity is uncertain (perhaps it involves allocating resources between reproduction, vs. increasing redundancy of vulnerable components?); but if mortality mutations are arguably proportional hazards, as has already been argued by others, then it is not a huge leap to suppose trade-offs may also involve proportional hazards.

Mutually-exclusive equilibrium conditions

The two models' equilibrium conditions are different: in the mutation accumulation model, at equilibrium mortality μ_x is inverse to $c_x V_x$; in the reproductive-effort model, at equilibrium

mortality μ_x is inverse to V_x . Since c_x cannot be constant with age (an age distribution cannot be flat from zero to infinity), these two models' equilibrium conditions are mutually-exclusive.

Conclusion

This paper reviewed the evolutionary theory of senescence, including Hamilton's model and its extensions; and then extended it further, to understand how life histories evolve in the long run, by considering two simple evolutionary models and finding their equilibrium conditions. The models were discussed in relation to widely-discussed features of life histories, including negative senescence and high juvenile mortality; the models' level of realism was also discussed.

Regardless of their realism or unrealism, the models remain useful for three reasons. First: they offer proof of principle that aspects of the long-run evolution of age-structured life histories *can* be studied analytically, not only with simulations, at least in some cases. Second: they clarify some existing discussions in the evolution of senescence, such as whether and why catastrophic senescence evolves in mutation accumulation models that use additive-hazards, and whether any model based on the forces of selection can explain high juvenile mortality.

Third, perhaps most importantly, the mutual-exclusivity of the equilibrium conditions is itself a key result. No life history can simultaneously be in equilibrium with respect to *both* models' evolutionary processes. This highlights how deeply the evolution of age-structured life histories depend on the nature of the available genetic variation. It is not just a factor deciding how quickly an equilibrium can be evolved—it is a factor affecting the shape of the equilibria.

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