Chapter 6

‘Extrinsic mortality’ does not drive the evolution of senescence

M.J.Wensink, H. Caswell, A. Baudisch

Under revision with: American Naturalist

Abstract

The evolution of senescence is often explained by arguing that, in nature, few individuals survive to be old and that therefore it is evolutionarily unimportant what happens to organisms when they are old. A corollary to this explanation is that extrinsically imposed mortality, because it reduces the chance of living to be old, favors the evolution of senescence. These ideas, although incorrect, are widespread. We show that selection gradients are not proportional to survivorship, but to the stable age-distribution, and we highlight the difference. We also show that selection gradients decline with age even in the hypothetical case of zero mortality. We analyze age-independent perturbations of mortality, and show that they affect neither selection gradients nor the solution of optimal life history models. We propose correct verbal explanations of the reason that selection gradients decline with age, and discuss other relevant factors such as density effects and interaction mortality.

Introduction

The evolution of senescence is often explained by arguing that, in nature, only few individuals survive to be old and that therefore it is evolutionarily unimportant what happens to organisms when they are old. A corollary to this explanation is that extrinsically imposed mortality, because it reduces the chance of living to be old, favors the evolution of senescence.

Although both of these ideas have been refuted in the technical literature, they persist, and it is easy to find statements of them:

> "(...) The decline in the proportion of individuals remaining alive at progressively older ages, as a consequence of extrinsic mortality factors, provides sufficient explanation for the decline in the strength of selection with age" [1].

> "(...) the force of selection will show a monotonic decline (...), whether or not the organism experiences intrinsic ageing, being a consequence only of mortality" [2].

> "Extrinsic hazards (such as predation, infection and the physical environment) leave progressively fewer individuals alive, so that mutations affecting only older age classes experience a declining force of natural selection" [3].

Similar statements are found, e.g., in [4–7].

Thus, the claim is that since survivorship (the probability of survival from birth to a given age, $\ell(x)$ in life table notation) declines with age, it is relatively unimportant to evolution what happens to organisms when they are old. A natural consequence of this idea is that a steeper decline in survivorship should lead to higher rates of senescence, while a more gradual decline should lead to lower rates of senescence:

> "The central prediction of classic theory is that high extrinsic mortality leads to accelerated aging" [8].

In practice, it is difficult to define 'extrinsic mortality'. Intrinsic and extrinsic causes may interact to produce mortality, while only the latter are factors over which the organism has no control. Studies have compared populations with high and low levels of predation [e.g. 9], or compared populations with different habitats [e.g. 10] as ways to compare levels of extrinsic mortality. The level of internal control over the resulting mortality, however, may vary. Extrinsic mortality needs specification before its (evolutionary) effects can be discussed.

The issue that we wish to address, however, is not definitions of extrinsic mortality, but the role that extrinsic mortality has been ascribed in evolutionary theories of senescence in general. Selection gradients certainly decline with age, and that decline implies the relative unimportance of advanced ages, which does indeed facilitate the evolution of senescence. But declining survivorship does not drive the decline. We demonstrate

this by referring to Caswell's [11-13] decomposition of the selection gradients on mortality and fertility, by showing that selection gradients would decline even if mortality were zero at all ages (which is admittedly hypothetical, but proves the point), and by showing that selection gradients are not affected by the simplest representation of extrinsic mortality: age-independent mortality.

Once we have established that selection gradients decline, and why, we explore whether extrinsic mortality may affect the pattern of decline of the selection gradients, given some specific definitions of the term. Relevant findings in this respect are discussed.

Why senescence can evolve: selection gradients decline with age

The action of selection on a trait depends on how fitness changes in response to a change in that trait. This response is called the selection gradient.[1] It expresses by how much fitness changes if some trait changes, i.e. the sensitivity of fitness to changes in the trait.

Senescence can evolve because the selection gradients on mortality and fertility decline with age. The absolute value of these selection gradients goes down with age for all life histories.

The mathematics are as follows. Darwinian fitness is given by r [14-17], the unique real root of the Euler-Lotka equation [18]:

$$\int_0^\infty e^{-rx}\ell(x)m(x)dx = 1 \tag{6.1}$$

Here, $m(x)$ is the reproductive rate at age x, while $\ell(x)$ denotes survivorship up to age x, which is a function of the mortality rate $\mu(x)$:

$$\ell(x) = e^{-\int_0^x \mu(t)dt} \tag{6.2}$$

The differential of r is

$$\delta r = \int_0^\infty \left[H^*(a)\delta m(a) + H^\dagger(a)\delta\mu(a)\right] da \tag{6.3}$$

where

$$H^*(a) = \frac{1}{T}e^{-ra}\ell(a) \tag{6.4}$$

$$H^\dagger(a) = -\frac{1}{T}\int_a^\infty e^{-rx}\ell(x)m(x)dx \tag{6.5}$$

[1] In earlier literature, terms like 'force of selection' [e.g. 19] or 'selection pressure' [e.g. 44] were used for this quantity. Analogies to forces, or pressures, however, obscure the nature of the term as the slope, or gradient, of fitness as a function of the trait. The term was carefully defined by Lande [15] and Arnold and Wade [45], and is fundamental to quantitative genetics. It also appears in the formalism of the canonical equation of Adaptive Dynamics [e.g. 46].

with

$$T = \int_0^\infty x e^{-rx} \ell(x) m(x) dx \tag{6.6}$$

$H^*(a)$ and $H^\dagger(a)$ are the selection gradients on age-specific fecundity and mortality respectively, discovered by Hamilton [19]. Together with the description of some biological perturbation $dm(a)$ and $d\mu(a)$, the selection gradients describe how fitness changes, i.e. dr (see [20,21] for discussion and application). The absolute values of (6.4) and (6.5) decline with age for all life histories[2]

Declining selection gradients with age reduce the evolutionary disadvantage of late-life deterioration, i.e. senescence [22]. Senescence may evolve because over age, selection becomes progressively inept to counterbalance the accumulation of deleterious mutations [17,22], or because selection may favor early-life benefits that are correlated with negative effects at later ages [22-24]. It should be noted that declining selection gradients are a necessary but not a sufficient condition for the evolution of senescence, and that selection gradients are only part of a complete description of evolutionary change (equation (6.3), [20]). The response to the selection gradients depends on the genetic (co)variance structure of the traits involved [e.g. 15].

Why the selection gradient declines with age

To understand what determines the selection gradients, it is helpful to decompose Hamilton's indicators into well-known demographic quantities within the framework of stable population theory [24], to consider the case when mortality is zero for all ages, and to evaluate the result of an age-independent perturbation of mortality.

Survivorship versus the stable age-distribution

Let $v(a)$ be the reproductive value, which expresses the value of the expected reproductive output of an organism given that it is alive and of age a:

$$v(a) = \frac{e^{ra}}{\ell(a)} \int_a^\infty e^{-rx} \ell(x) m(x) dx \tag{6.7}$$

Let $c(a)$ be the stable age-distribution, which gives the proportional composition of the population by age:

$$c(a) = \frac{e^{-ra} \ell(a)}{\int_0^\infty e^{-rx} \ell(x) dx} \tag{6.8}$$

[2]One special exception must be mentioned. Unlike the gradient on mortality, the selection gradient on fertility can *increase* with age in a declining population. If r is sufficiently negative relative to survival probability [47-49], the stable age distribution, and thus the selection gradient on fertility, will increase with age. It is unlikely that a population would persist in such a negative growth phase for long enough for evolution to act. However, Mertz [47] suggested that the delayed onset of reproduction in the California condor (*Gymnogyps californianus*) might reflect millenia of population decline from a distribution over all of North America to the species current restricted range in central California. Caswell [49] proposed that selection gradients while declining could be important for nonequilibrium populations.

Finally, let b be the birth rate:

$$b = \left[\int_0^\infty e^{-rx}\ell(x)dx\right]^{-1} \tag{6.9}$$

With T as in equation (6.6), Hamilton's indicators of selection pressure can be decomposed as follows[11,13]:

$$H^*(a) = \frac{c(a)}{bT} \tag{6.10}$$

$$H^\dagger(a) = \frac{-c(a)v(a)}{bT} \tag{6.11}$$

Of both indicators, the denominator is just a scalar. The numerator of each indicator consists of the proportional abundance of organisms in some age class, $c(a)$, and the value of its expected reproductive output in the subsequent age-class. In case of reproduction, the 'subsequent' age-class is age zero, in which the value of the expected reproductive output is one ($v(0) = 1$, since equation (6.1) holds). Hence equation (6.10). In case of survival, the value in the next age-class is $v(a)$. Hence equation (6.11). Because $H^\dagger$ refers to mortality rather than survival, $H^\dagger$ is negative.

The decomposition above clarifies why the suggestion that "potential contributions to fitness by individuals of a given age must be weighted by the probability of surviving up to that point" [26] is incorrect. Rather, it must be weighed by the proportional abundance of organisms of some age, i.e. the stable age-distribution $c(a)$ (equation (6.8)).

Survivorship and the proportional abundance of organisms in each age class are not the same. Survivorship at age a is the proportion of a cohort that dies after age a. Survivorship is a function of mortality only (equation (6.2)); no organisms are added to the population that is considered (a cohort). The stable age-distribution on the other hand is a function not only of mortality, but also of reproduction, because organisms are added to the population that is considered. In age-classified models, newborns are zero-year-olds, which next become one-year-olds while more zero-year-olds are born, and so forth. In this way, reproduction affects the distribution of the population over age-classes. The term e^{-rx} in the stable age-distribution (equation (6.8)) models this effect.

Why would impact on individual fitness (H^* and $H^\dagger$) be a function of the population growth rate r through e^{-rx}? The answer lies in the use of r as a measure of fitness. Although fitness is an attribute of individuals, high fitness results in a growing population that descends from the focal organism. It is this "population growth rate of the individual" that r refers to if it is used as a measure of fitness [27]. Reproduction adds zero-year-olds to that population. As a result, the proportion of that population that is of high ages is reduced, as modeled by e^{-rx} in equation (6.8), so that an event at higher ages is experienced by a reduced proportion of the population. This mechanism also causes the decrease in the proportion of older test tubes in Medawar's [22] famous thought experiment, and not, as Medawar thought, extrinsic mortality. The survivorship function does not model this phenomenon.

Although evolutionary impact is proportional to the stable age-distribution, survivorship is part of the formal description of the stable age-distribution. To understand fully why the selection gradients decline with age, we now consider the case in which mortality is zero for all ages, and evaluate what happens if mortality is perturbed in an age-independent way.

If mortality is zero for all ages

Consider the extreme case of zero mortality at all ages. Then survivorship remains constant at 100% and does not decline with age:

$$\ell(a)\,|_{\mu=0} \;=\; 1 \qquad \text{for all } a \tag{6.12}$$

The stable age-distribution, in contrast, still changes with age and becomes:

$$c(a)\,|_{\mu=0} \;=\; \frac{e^{-ra}}{\int_0^\infty e^{-rx}dx} \tag{6.13}$$

As long as there is some reproduction, r is necessarily greater than zero, which makes $c(a)$ a declining function of age. Since births add zero-year-olds to the population, this age-class will always be the largest compared to progressively older ages. The stable age-distribution declines with age as a result.

Hamilton's selection gradients for the case of zero mortality yield:

$$H^*(a)\,|_{\mu=0} \;=\; \frac{e^{-ra}}{T} \tag{6.14}$$

$$H^\dagger(a)\,\big|_{\mu=0} \;=\; -\frac{1}{T}\int_a^\infty e^{-rx}m(x)dx \tag{6.15}$$

Again, $r > 0$ given that there is some reproduction, so $H^*(a)$ and $H^\dagger(a)$ decline with age even if survivorship does not.

If mortality changes in an age-independent way

It is frequently claimed that an evolutionary effect of additional extrinsic mortality is that it exacerbates senescence. However, it has been shown that this is not true if extrinsic mortality is independent of age: in this case it has no effect on the (pattern of decline in the) selection gradients [28,29]. A unit increase in an age-independent mortality term leads, per definition, to a unit decrease of the population growth rate. While such extrinsic mortality reduces survivorship at older ages, thus reducing the abundance of this age class in the overall population, the reduced population growth rate means that fewer organisms will be present in lower age classes too, canceling the effect of reduced survivorship on the stable age-distribution or the reproductive value. The selection gradients are therefore essentially insensitive to age-independent mortality.

Imposing an age-independent extrinsic mortality is equivalent to disregarding part of the population. Nothing except for the population size, implying a greater role for stochasticity, would be different if partitions of a population are considered rather than the population as a whole:

> "Imagine that we take a population with a huge number of individuals into a sufficiently large laboratory such that there is no density dependence. We allow the population to reach a stable equilibrium with respect to age-structure and gene frequencies. Now we take that population and apply extra mortality by removing half the individuals at random, regardless of age. After this extrinsic mortality event, absolutely nothing will have changed that can affect selection: the environment, reproductive output of survivors, age-distribution, phenotypes, and gene frequencies all stay the same" [30].

The mathematics, in line with the results of Abrams [28] and Caswell [29], are as follows. Survivorship (equation (6.2)) can be written as the product of two exponentials, one that contains a constant that represents the age-independent extrinsic mortality γ, and one that contains all age-dependent mortality terms, $\mu_0(x)$:

$$\ell(x) = e^{-\gamma x} e^{-\int_0^x \mu_0(t)dt} \tag{6.16}$$

Plugging this expression in the Euler-Lotka equation and merging e^{-rx} with $e^{-\gamma x}$ yields

$$\int_0^\infty e^{-(r+\gamma)x} e^{-\int_0^x \mu_0(t)dt} m(x)dx = 1 \tag{6.17}$$

For any specified pattern of reproduction $m(x)$ and age-dependent mortality $\mu_0(x)$ there exists one and only one real $r+\gamma$ that satisfies equation (6.17). This implies, r being the dependent variable, that:

$$\frac{\partial r}{\partial \gamma} = -1 \tag{6.18}$$

As a result, the outcome is invariant under a change in γ wherever survivorship and e^{-rx} appear together. This is true for the stable age-distribution $c(a)$, reproductive value $v(a)$, generation time T and the birth rate b, i.e. for all components of Hamilton's indicators of selection pressure (see decompositions (6.10) and (6.11)). Thus, Hamilton's selection gradients as a whole are insensitive to γ:

$$\frac{\partial H^*(a)}{\partial \gamma} = 0 \tag{6.19}$$

$$\frac{\partial H^\dagger(a)}{\partial \gamma} = 0 \tag{6.20}$$

Survivorship declines more steeply with age if γ is increased; the selection gradients do not.

In this section we have demonstrated three points: 1. The selection gradients at each age are proportional to the stable age-distribution at that age, not to survivorship (equations (6.10) and (6.11)). The stable age-distribution is quite distinct from survivorship, and we have highlighted the difference. 2. Even if survivorship did not decline with age ($\mu = 0$), the stable age-distribution and the selection gradients would still go down with age. 3. An age-independent perturbation of mortality does not affect any of the components of the selection gradients, even though it clearly does affect survivorship. These three things combined unequivocally demonstrate that declining survivorship does not drive the age-related decline in the selection gradients.

A correct verbal expression of the basic reason for the decline of the selection gradients with age could be as follows. If an organism is older, it has accumulated more reproduction during its past life course than when it was young. Current events do not change past reproduction. The offspring that have been produced started life as zero-year-olds that contribute to a population that descents from the focal organism. A progressively smaller proportion of that population is affected by anything that affects only the old. Since past contributions to fitness can only go up with age, the selection gradients can only go down with age.

An equivalent verbal intuition is given by Flatt and Promislow [31]:

> "If the effects of [a] mutation are confined to some late age, individuals carrying the mutation will likely have already passed it on to their offspring by the time it is expressed, and natural selection will be relatively ineffective in eliminating it."

These verbal explanations are straightforward and in line with evolutionary theory.

Optimization models

Our considerations so far have focused on changes of fitness (dr): selection gradients indicate how fitness would respond if some trait value were changed. Evolutionary theory uses this to predict changes in the traits, given patterns of genetic variance and covariance [15]. An alternative approach is optimization: given mechanistic considerations, what strategy maximizes fitness? For example, in the disposable soma theory it is posited that organisms allocate their resources, for instance energy, between the competing demands of reproduction and somatic maintenance [24,32,33]. There are two places to invest: 1. keep your own entity going. 2. create more copies of your entity. Resources invested in one function cannot be invested in the other. Depending on the return on each investment, some allocation strategy will maximize fitness, i.e. be optimal. Proposed models of such trade-offs (reviewed in [33]) apply direct optimization rather than relying on selection gradients, although the trade-offs certainly can be modeled in terms of selection gradients [12,20].

If an investment is made in either the organism itself or in its offspring, and both die of purely extrinsic mortality at the same rate, then nothing is gained by making one allocation rather than the other. Alternatives are equally bad, no organism does better

than the other, so no evolutionary response to natural selection may be expected. As a result, optimality is not affected by age-independent mortality. Additional information is necessary to decide what is optimal, such as how mortality would increase over age if an organism were to forego somatic maintenance. This intuition is formalized below, in line with earlier results [35-37].

Trade-offs between or within the mortality and fecundity functions are subject to some lower level parameter θ that is optimized so as to maximize r. In addition to θ, r depends on the age-independent mortality γ, which is independent of θ. Given relationship (6.18), which is a general result of the Euler-Lotka equation (equation (6.1)), it follows that

$$r(\theta,\gamma) = r(\theta,0) - \gamma \tag{6.21}$$

As a result of this independence, it holds that

$$\frac{dr(\theta,\gamma)}{d\theta} = \frac{dr(\theta,0)}{d\theta} \tag{6.22}$$

Thus, if $\hat{\theta}$ satisfies the optimality condition

$$dr = \left.\frac{\partial r(\theta,0)}{d\theta}\right|_{\theta=\hat{\theta}} = 0 \tag{6.23}$$

it also satisfies the optimality condition

$$dr = \left.\frac{\partial r(\theta,\gamma)}{d\theta}\right|_{\theta=\hat{\theta}} = 0 \tag{6.24}$$

The optimal value of θ is thus independent of (a change in) age-independent mortality γ.

Discussion

The ghost of extrinsic mortality continues to haunt the evolutionary theory of senescence. It does so in two ways. First, as the quotes in the introduction exemplify, it is still widely believed that extrinsic mortality causes senescence, because it reduces the chances of survival to advanced ages. If few organisms survive to old age, it is argued, old ages are less evolutionarily important. This idea is admittedly intuitive, but wrong, and leads to a second error: the idea that higher extrinsic mortality should lead to a higher rate of senescence.

As we show, evolutionary impact is not proportional to survivorship, but to the proportion of the population that is of some age, i.e. the stable age-distribution. We have demonstrated the differences between these quantities and shown that selection gradients would decline with age even in the hypothetical case of zero mortality at all ages. We have shown that the decline in survivorship that results from age-independent mortality does not affect the selection gradients.

Our analysis holds for r as a measure of fitness, within the context of stable population theory. However, the basic reason why state- and age-independent mortality should

not matter to evolution is much more general, and unrelated to the choice of the measure of fitness: If mortality is purely extrinsic and age-independent, no strategy will allow the organism to avoid this mortality.

Selection gradients decline with age because reproduction accumulated up to a given age, which is unaffected by events after that age, contributes to the population and reduces the fraction of the population that is affected by events at higher ages. Since past reproduction can only go up with age, the selection gradients can only go down with age.

Our analysis of age-independent mortality shows that extrinsic mortality *per se* has no effect on the evolution of senescence. Age-dependent mortality, and age-dependent density effects, by contrast, can have such effects [28,29].

Abrams [28] suggested that extrinsic mortality could affect the rate of senescence through age-dependent density effects, even if the mortality is the same for organisms of any age and state. This occurs when organisms of different age respond differently to population density. He concluded that, depending on the age dependence of the density effects, anything is possible [28]; no universal evolutionary result, such as promotion of senescence, can be expected from an increase in extrinsic mortality.

In the case of density-independent models, Caswell [29] suggested from preliminary results that extrinsic mortality focused on young individuals would reduce the evolution of senescence, while extrinsic mortality focused on old individuals would increase the evolution of senescence. Indeed, a role for extrinsic factors in some death event does not exclude a role for intrinsic factors in the same event [38,39]. In fact, it is hard to think of mortality that is determined exclusively extrinsically. For instance, predation certainly needs an extrinsic factor, the predator, but it also needs an intrinsic factor, the prey. What about abiotic factors, such as being hit by lighting? Surely, few forms of life may reasonably be expected to withstand a 30kA lightning discharge. But even if vulnerability is independent of age, exposure may not be, because behavioral patterns will determine which individuals are in locations with high probability of lightning strikes. These behavioral factors may well vary with age, leading to age-dependence of the interaction mortality.

What would be the evolutionary consequences of changing an extrinsic cause (of all the causes that are required to cause the death event), for instance the density of predators? The general answer is that depending on the interactions, anything goes[29]. Natural selection will tend to shift life histories so as to avoid spending time in vulnerable states, depending on the costs and the alternatives [39]. For instance, experiments have shown that if only adults are subject to 'extrinsic mortality', a higher rate of senescence can evolve [8,40]. In this case, organisms can increase reproduction at a cost to survival, so that resources are concentrated in organisms of less vulnerable state. On the other hand, if weaker organisms are targeted by predators, it is evolutionary beneficial to remain a strong and vigilant adult, and 'extrinsic mortality' will work counter-senescence (a possible explanation for the findings of Reznick et al. [9]). Notice that such age-dependent density effects are only feasible if organisms of different ages have different physiological states, for otherwise there is no good reason why extrinsic factors would affect organisms in an age-dependent way: age-specificity can only exist if it is in fact (hidden) state-specificity [41].

The arguments laid out in this paper have theoretical and practical consequences. Empirical research has shown little support for the "central prediction" of the evolutionary theory of senescence [8] that a higher level of extrinsic mortality (predators, environment, laboratory) should lead to a higher rate of senescence [9,26]. A number of authors have concluded that hence there is a need for a more involved theory of senescence, in which mortality is state dependent, and/or in which density effects play a prominent role [8,9,26]. Given the results derived in this paper, it becomes clear why there is little support for the central prediction. It is not that this prediction happens not to predict biological reality; life history theory simply makes no such prediction. After decades of theoretical work, we are still challenged to develop theory that provides more than an incidental match with the data. Our results corroborate the need for theory that is more involved; it may include combinations of age- and stage-specific mortality [42], density effects, and/or interaction mortality. Such a theory should involve mechanisms of senescence, as evolutionary pressures alone are only half the story [20,43].

Conclusion

1. Selection gradients on mortality and fertility decline with age because accumulated reproduction from earlier ages, that remains unaffected by later events, contributes to the population, reducing the share of the population that is subject to any events specific for higher ages.
2. The age-related decline of selection gradients can be explained without reference to mortality.
3. An age-independent change in mortality does not affect the selection gradients.
4. Since it is unlikely that purely extrinsically determined mortality even exists, (supposed) causes of mortality and their (supposed) interactions must be specified before any conclusions about evolutionary effects of the mortality can be drawn.
5. The evolutionary response to age-dependent mortality and/or age-dependent density regulation depends on how different age groups are affected; no general statement can be made about how density effects and interaction mortality mold the evolution of age-patterns.
6. There is need for more involved theory that includes not only density effects and age-dependent mortality, but also an account of the mechanisms and their interaction with the environment that shape the evolution of senescence.

Acknowledgments

HC acknowledges financial support from ERC Advanced Grant 322989, NSF Grants DEB-1145017 and DEB-1257545, and the Alexander von Humboldt Foundation.

References

1. Monaghan, P., Charmantier, A., Nussey, D.H. and R.E. Ricklefs (2008) The evolutionary ecology of senescence. Functional Ecology 22:371-378.

2. Kirkwood, T.B.L. and S. Melov (2011) On the programmed/non-programmed nature of ageing within the life history. Current Biology 21:R701-R707.

3. Regan, J.C. and L. Partridge (2013) Gender and longevity: Why do men die earlier than women? Comparative and experimental evidence. Best Practice & Research Clinical Endocrinology & Metabolism 27:467-479.

4. Gems, D., and L. Partridge (2013) Genetics of longevity in model organisms: debates and paradigm shifts. Annual Review of Physiology 75:25.1-25.24.

5. Fabian, D. and T. Flatt (2011) The evolution of aging. Nature Education Knowledge 2:9.

6. Fabian, D. and T. Flatt. (2012) Life history evolution. Nature Education Knowledge 3:24.

7. Vijg, J. and J. Campisi (2008) Puzzles, promises and a cure for ageing. Nature 454:1065-1071.

8. Chen, H. and A.A. Maklakov (2012) Longer life span evolves under high rates of condition-dependent mortality. Current Biology 22:2140-2143.

9. Reznick, D.N., Bryant M.J., Roff, D., Ghalambor, C.K. and D.E. Ghalambor (2004) Effect of extrinsic mortality on the evolution of senescence in guppies. Nature 431:1095-1099.

10. Austad, S.N. (1993) Retarded senescence in an insular population of Virginia opossums (*Didelphis virginiana*). Journal of Zoology 229:695-708.

11. Caswell, H. (1978) A general formula for the sensitivity of population growth rate to changes in life history parameters. Theoretical Population Biology 14:215-230.

12. Caswell, H. (2001) Matrix population models. Construction, Analysis, and Interpretation. Sinauer, Sunderland, MA, USA.

13. Caswell, H. (2010) Reproductive value, the stable stage distribution, and the sensitivity of the population growth rate to changes in vital rates, Demographic Research 23:531-548.

14. Fisher, R.A. (1930) The fundamental theorem of natural selection. Pages 25-30 *in* The Genetical Theory of Natural Selection. Clarendon Press, Oxford, UK. (Reprinted and revised, 1958. New York: Dover).

15. Lande, L. (1982) A quantitative genetic theory of life history evolution. Ecology 63:607-615.

16. Metz, J.A.J., Nisbet, R.M. and S.A.H. Geritz (1992) How should we define 'fitness' for general ecological scenarios? TREE 7:198-202.

17. Charlesworth, B. (1994) Evolution in age-structured populations, second edn. Cambridge University Press, Cambridge, UK.

18. Lotka, A. (1924) Elements of Mathematical Biology. Reprinted 1956 by Dover Publications Inc., New York, USA.

19. Hamilton, W.D. (1966) The moulding of senescence by natural selection. Journal of Theoretical Biology 12:12-45.

20. Wensink, M.J., Wrycza, T.F. and A. Baudisch (2014) No senescence despite declining selection pressure: Hamilton's result in broader perspective. Journal of Theoretical Biology 347:176-181.

21. Arthur, W.B. (1984) The analysis of linkages in demographic theory. Demography 21:109-128.

22. Medawar, P.B. (1952) An unsolved problem of biology. Pages 3-24 *in* Uniqueness of the individual, Lewis, London, UK.

23. Williams, G.C. (1957) Pleiotropy, natural selection, and the evolution of senescence. Evolution 11:398-411.

24. Kirkwood, T.B.L. (1977) Evolution of ageing. Nature 270:301-304.

25. Preston, S., Heuveline, P. and M. Guillot (2001) Demography. Blackwell, Oxford, UK.

26. Williams, P.D., Day, T., Fletcher, Q. and L. Rowe (2006) The shaping of senescence in the wild. Trends in Ecology and Evolution. 21:458-463.

27. McGraw, J.B. and H. Caswell (1996) Estimation of individual fitness from life-history data. The American Naturalist 147:47-64.

28. Abrams, P.A. (1993) Does increased mortality favor the evolution of more rapid senescence? Evolution 47:877-887.

29. Caswell, H. (2007) Extrinsic mortality and the evolution of senescence. Trends in Ecology and Evolution 22:173-174.

30. Moorad, J.A. and D.E.L. Promislow (2010) Evolution: aging up a tree? Current Biology 20:R406-R408.

31. Flatt, T. and D.E.L. Promislow (2007) Still pondering an age-old question. Science 318:1255-1256.

32. Kirkwood, T.B.L. and R. Holliday (1979) The evolution of ageing and longevity. Proceedings of the Royal Society London B 205:531-546.

33. Kirkwood, T.B.L. and M. Rose (1991) Evolution of senescence: late survival sacrificed for reproduction. Philosophical Transactions of the Royal Society London, B 332:15-24.

34. Baudisch, A. (2012) Birds do it, bees do it, we do it: Contributions of theoretical modelling to understanding the shape of ageing across the tree of life. Gerontology 58:481-489.

35. Gadgil, M. and W.H. Bossert (1970) Life historical consequences of natural selection. The American Naturalist 104:1-24.

36. Taylor, H.M., Gourley, R.S., Lawrence, C.E. and R.S. Kaplan (1974) Natural selection of life history tributes: an analytical approach. Theoretical Population Biology 5:104-122.

37. Law, R. (1979) Optimal life histories under age-specific predation. The American Naturalist 114:399-417.

38. Wensink, M.J., Westendorp, R.G.J. and A. Baudisch (2014) The causal pie model: an epidemiological method applied to evolutionary biology and ecology. Ecology and Evolution 4:1924-1930.

39. Williams, P.D. and T. Day (2003) Antagonistic pleiotropy, mortality source interactions, and the evolutionary theory of senescence. Evolution 57:1478-1488.

40. Stearns, S.C., Ackermann, M., Doebeli, M. and M. Kaiser (2000) Experimental evolution of aging, growth, and reproduction in fruit flies. Proceedings of the National Academy of Sciences of the USA 97:3309-3313.

41. Wensink, M.J. (2013) Age-specificity and the evolution of senescence - a discussion. Biogerontology 14:99-105.

42. Caswell, H. and R. Salguero-Gómez (2013) Age, stage and senescence in plants. Journal of Ecology 101:585-595.

43. Baudisch, A. and J.W. Vaupel (2012) Getting to the root of aging. Science 338:618-619.

44. Emlen, J.M. (1970) Age specificity and ecological theory. Ecology 51:588-601.

45. Arnold, S.J. and M.J. Wade (1984) On the measurement of natural and sexual selection: theory. Evolution 38:709-719.

46. Doebeli, M. (2011) Adaptive Diversification. Princeton University Press, Princeton, New Jersey, USA.

47. Mertz, D.B. (1971) Life history phenomena in increasing and decreasing populations. Pages 361-400 *in* G.P. Patil, E.C. Pielou, and W.E. Waters, eds. Spatial ecology, volume 2: Sampling and monitoring biological populations and population dynamics. Pennsylvania State University Press.

48. Caswell, H. and A. Hastings (1980) Fecundity, developmental time, and population growth rate: an analytical solution. Theoretical Population Biology 17:71-79.

49. Caswell, H. (1982) Life history theory and the equilibrium status of populations. American Naturalist 120:317-339.