Evolvability, population benefit, and the evolution of programmed aging in mammals

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Abstract

Programmed aging theories contend that evolved biological mechanisms purposely limit internally determined lifespans in mammals and are ultimately responsible for most instances of highly age-related diseases and conditions. Until recently the existence of programmed aging mechanisms was considered theoretically impossible because it directly conflicted with Darwin's survival-of-the-fittest evolutionary mechanics concept as widely taught and generally understood. However, subsequent discoveries especially in genetics have exposed issues with some details of Darwin's theory that affect the mechanics of the evolution process and strongly suggest that programmed aging mechanisms in humans and other mammals can and did evolve, and more generally that a trait that benefits a population can evolve even if like senescence it is adverse to individual members of the population. *Evolvability theories* contend that organisms can possess evolved design characteristics (traits) that affect their ability to evolve, and further that a trait that increases a population's ability to evolve (increases evolvability) can be acquired and retained even if it is adverse in traditional individual fitness terms. Programmed aging theories based on evolvability contend that internally limiting organism lifespan in a species-specific manner creates an evolvability advantage that resulted in the evolution and retention of senescence. This issue is critical to medical research because the different theories lead to dramatically different concepts regarding the nature of the biological mechanisms behind highly age-related diseases and conditions.

Keywords: Aging theory; senescence; medicine; gerontology; evolutionary mechanics theories

Introduction

There is very strong scientific agreement regarding most aspects of Darwin's evolution theory [1]: Evolution of Earth-life has taken place, current species are descended from earlier different species, evolution is a slow incremental process that has operated for billions of years, and in some form evolution is driven by natural selection or survival of the fittest. Darwin's evolutionary mechanics concepts regarding the nature of the evolution process explain the vast majority of biological observations concerning organism designs. However, one aspect that despite many decades of argument does not have agreement concerns the details of the evolutionary relationship between individual members of a species and populations of those individuals. In the vast majority of cases a trait that produced an individual advantage would also produce an advantage for a population of those individuals. However exceptions have been identified specifically including mammal senescence. Can an organism evolve an inherited design characteristic or trait that benefits a population at the expense of individual members of that population? Could organisms evolve aging programs, essentially suicide mechanisms, which purposely limit internally determined individual lifespan in order to obtain a population advantage? Darwin's evolutionary mechanics theory as currently widely taught is extremely individual-oriented and contends that the evolution process causes organisms to evolve traits that cause possessing individuals to have a higher probability of producing adult descendants.

However, since 1952 a series of more population-oriented concepts have appeared. Discoveries, especially in genetics, have exposed issues with details of Darwinian mechanics and strongly support the newer concepts.

This individual vs. population issue might appear to be a semi-trivial, arcane, and academic matter but has immense practical consequences for medical research because the two concepts logically lead to very different conclusions regarding the nature of human senescence and therefore the nature of the many highly age-related diseases and conditions such as cancer and heart disease.

Despite more than 150 years of effort theorists have been unable to produce an aging theory that plausibly explains mammal senescence observations while fully complying with Darwin's evolutionary mechanics concepts. In particular, why do biochemically similar species (e.g. mammals) have such different internally determined lifespans? Mammal lifespans vary over a range of more than 200 to 1 and fish lifespans vary over a range of more than 1300 to 1 [2]. Because longer-lived species "A" has a longer lifespan proving that it is possible, why didn't very similar shorter-lived mammal "B" also evolve a longer reproductive lifespan given that it obviously would convey a Darwinian advantage? These questions surfaced immediately after publication of *Origin* in 1859 [1b]. Consequently as summarized here, all modern theories of aging that provide plausible multi-species senescence explanations involve modifications to Darwin's mechanics concept that increase the importance of populations relative to individuals. This article describes how the need for evolvability, a property of a population, has caused the evolution of programmed aging in mammals and other organisms.

Evolvability and the Evolutionary Mechanics of Aging

Darwin's evolutionary mechanics concept assumes that the ability to evolve is a fixed inherent property of all living organisms. All wild organisms were capable of passing information concerning their designs to descendants (biological inheritance), were susceptible to mutations that would change that information and those designs, and were subject to competition and natural selection.

Evolvability theories (e.g. [3, 4]) suggest that *populations* of a species can possess differences in their ability to evolve (genetically adapt to changes in their external world) and that traits that increase the rate or comprehensiveness of such adaptation (increase evolvability) can be selected by the evolution process despite being adverse from the point-of-view of an individual organism. Aging theories based on evolvability [5, 6, 7] contend that a purposely limited lifespan increases evolvability in multiple ways and that mechanisms that cause such limitation have therefore been selected. In addition to providing explanations for observations concerning senescence, evolvability theories also provide explanations for other observations that are troublesome with regard to traditional Darwinian evolutionary mechanics such as sexual reproduction, apparently unnecessarily delayed reproductive maturity (especially in males), and certain animal behavioral traits such as animal altruism and individually-adverse mating behavior [3]. Evolvability theories are among a family of post-1952 theories to the effect that the evolution process is directed at survival and success of a population as opposed to individual survival and reproduction as emphasized by traditional Darwinian theory.

The evolution process is clearly population oriented. Whether a particular individual having a certain inherited phenotypic design lives longer and breeds more than another individual having a slightly different design is essentially a matter of luck or chance. What we can say is that individuals having a particular inherited design have a greater probability of surviving and reproducing than some other individuals possessing a different design. We can therefore consider that in evolutionary terms the life of an individual is a trial in the probability sense of the particular inherited design possessed by that individual. Does this design have a greater probability of producing adult descendants under wild conditions than some other design? Extending this concept, the rate at which the evolution process proceeds and the precision with which it can determine the answer to the above question depend on the rate at which the trials are conducted or the rate at which lives are lived, which we can simplify to read: *death rate*.

The evolution process is also performance oriented and measures how well a particular design performs in living longer and breeding more relative to some other design. Latent characteristics that do not affect performance cannot influence this aspect of the evolution process. Adult traits are not fully expressed in juveniles. Therefore deaths that occur in juveniles generally do not contribute to the evolution of adult traits. Consequently we can extend the previous paragraph to read that the evolution process is a function of *adult death rate*. Fig 1 describes the life of an organism in these terms.

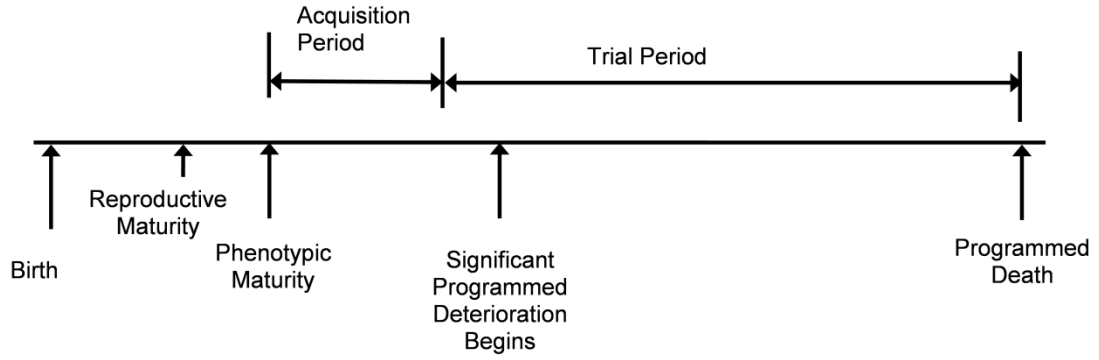

Fig.1. Organism Lifetime – Evolvability Concept

Adult death rate in turn is proportional to the size of the population and *inversely proportional to average lifetime* in addition to other species-specific factors. In order to optimize the evolution process organisms must live long enough to become mature adults and participate in a trial, but not too much longer! One might say that external causes of mortality under wild conditions would naturally limit lifetime and therefore remove the need for an internal senescence mechanism. However in such a non-senescing population some individuals would live very long lives and assuming population size was determined by external limitations many others would necessarily die as juveniles therefore reducing adult death rate. This problem would be more severe in more complex animals possessing a social structure or "pecking order." The "king of the hill" is less likely to die in combat or from starvation than other animals, and so, if lacking internal limitations on lifespan, could live a very long life and produce a very large number of descendants, reducing adult death rate, genetic diversity, variation, and evolvability.

Many other evolvability advantages of an internally limited lifespan have been identified, especially in more complex organisms such as mammals [3]. Example: An internally limited lifespan aids the evolution of traits such as intelligence or immunity that depend for their evolutionary value on the acquisition of something that accumulates during an organism's lifetime. Where intelligence is the genetically determined trait the selectable (fitness) trait is wisdom, essentially the product of intelligence and non-genetically acquired experience. In a non-senescent population less intelligent but older and more experienced animals would have a greater advantage than in a senescing case therefore detracting from the evolution of intelligence. The evolution of acquisition traits such as these would require a period to allow time for the accumulation of the acquired benefit to occur (Fig. 1). Some of us [3, 6] have further suggested that gradual senescence and multiparous reproduction such as seen in mammals enhances the evolution of acquisition traits (relative to acute suicide and semelparity) by gradually

compensating for the age-advantage that would otherwise exist and creating a "challenge effect," which increases the degree to which a life contributes to the evolution process.

Identified traits that contribute to evolvability (like senescence) are neutral or adverse in traditional fitness terms. Genetics discoveries have revealed many aspects of organism genomic design that have no known phenotypic effect but clearly do constrain the evolution process and affect evolvability [3].

Darwin suggested [1] that the evolution process was extremely incremental and took place in "tiny steps," an idea that has since been substantially confirmed (e.g.[3]). This suggests that the evolution process must be capable of distinguishing "tiny" differences in benefit, which in turn suggests that evolvability and statistics (precision) qualities associated with populations are essential to the evolution process.

The preceding analysis seems to suggest that larger organisms, necessarily having smaller populations and requiring a longer period to achieve maturity and therefore longer lifespans would evolve much more slowly than smaller organisms because of lower adult death rates. However a large number of evolvability traits such as described here greatly contribute to evolvability in complex organisms [3]. It is reasonable to conclude that in complex organisms, virtually all of an organism's ability to evolve is itself the result of evolved traits such as senescence, diploid reproductive schemes, and sexual reproduction.

Medawar's Modification

Darwin's evolutionary mechanics concept does not suggest that the evolutionary value of living longer and breeding more varies with age and therefore suggests that the force of evolution is toward a non-senescent state. This concept when coupled with the observation that senescence exists inevitably leads to the idea that aging is the result of a fundamental limitation such as a law of physics or chemistry that cannot be overcome by the evolution process. Entropy, oxidation, wear and tear, or other natural and universal causes of damage and dysfunction are often mentioned as the cause of senescence in aging theories based on unmodified Darwinian mechanics (e.g.[8]). Because nearly everyone receives training in Darwin's theory, this idea is still popular especially with those only concerned with human aging. However as suggested earlier, multi-species observations immediately exposed major issues: Why would a 50 kg dog be affected by some law of physics seven times as severely as a 50 kg human? What law of chemistry would cause a parrot to live six times longer than a crow? Eventually, species with no measurable senescence were discovered (e.g. [9]), somehow undeterred by laws of physics and chemistry! These issues eventually led to modern aging theories based on modifications to Darwin's mechanics.

In 1952 Medawar proposed a modification [10] to Darwin's evolutionary mechanics concept to the effect that senescence, although adverse and ultimately catastrophic from an individual's viewpoint, has little effect on a wild population because of attrition due to external causes of mortality in the wild such as predators, severe environmental conditions, starvation, and infectious diseases. For any given size wild population, (even if non-senescent and not possessing internal limitations on lifetime), the size of an age-cohort decreases with age at a rate

proportional to the population-specific severity of external attrition and consequently the effectiveness of the evolution process decreases with age at a rate determined by the consequent size of the age-cohort. Trivial example: we can imagine that in a wild mouse population (even if non-senescent) few would survive beyond 3 years of age. Therefore there would be little *population* advantage from individuals having the internal capacity for living longer and little population-based evolutionary force toward evolving a longer lifespan. Modern programmed (adaptive) aging theories and modern non-programmed (non-adaptive) aging theories (e.g. mutation accumulation theory [10], antagonistic pleiotropy theory [11], and disposable soma theory [12]) are all based on Medawar's modification because these theories provide a much better match to the huge variety of internally determined lifespans seen in biochemically similar species than earlier theories based on unmodified Darwinian theory.

The reader will notice that Medawar's idea is a population concept based on logic very similar to the evolvability concepts discussed earlier. The effectiveness of the evolution process is affected by the size of an age-cohort, which is of course affected by the overall size of the population. For example, it is logically inconsistent to believe that the evolution of increased longevity is limited by the size of the cohort that would benefit but simultaneously believe that a mutation in a single individual would immediately affect the evolution process. Wouldn't the force of evolution toward selection of the mutation be proportional to the size of the cohort possessing the mutation? If you believe Medawar's concept you logically also believe that organism populations can possess characteristics like population size and adult death rate from external causes that alter their ability to evolve. Similarly, species-specific internal characteristics such as age-at-puberty and other reproductive traits would clearly alter adult death rate and a species' need for a particular lifespan.

Medawar's modification led to a family of modern non-programmed aging theories (e.g. [10, 11, 12]) to the effect that the evolution process causes each species to evolve a particular *minimum* lifespan, i.e. the internal capacity for living and reproducing for a species-specific period. Following that period, natural deteriorative processes such as wear-and-tear, random (stochastic) mutations, and the ever-popular entropy (now unopposed by the evolution process) might cause senescence. No one denies the existence of natural deteriorative processes and these theories provided a better match to the multi-species observations.

Subsequent to Medawar's modification, in 1957 Williams introduced a now widely accepted objection to the effect [11] that observed fitness deterioration from mammal senescence occurs at too early an age to have a negligible effect on a wild mammal population and that therefore senescence must convey a compensating population benefit that acted to prevent the evolution of a longer lifespan and later appearance of significant fitness deterioration in any particular species. Studies of wild mammal populations (e.g. [13]) provided confirmation of this idea by showing that adult death rates increased with age and that therefore senescence caused at least some population disadvantage. Evolvability-based theories of aging contend that increased evolvability is the compensating benefit of senescence! Note also that because of acquisition traits in animals, we would expect animal adult death rates to decline with age if senescence was not producing a population disadvantage. Modern non-programmed theories [10, 11, 12] have difficulties in producing plausible explanations for the evolutionary benefit of senescence [3, 14].

This has resulted in multiple non-programmed theories and no strong consensus supporting any particular theory.

Digital Genetics and the Evolution of Local Variation

Darwin specified that "natural" variation in inherited characteristics was essential to the evolution process. Without variation there would be no way for an organism to have more inherited fitness than other members of its species and therefore nothing for natural selection to select. "Local" means that the variation would need to exist between individuals that could plausibly compete or otherwise interact with each other. Darwin assumed that variation was an inherent "natural" property of wild organisms: All organisms have the ability to transfer information concerning their designs to their descendants and all were susceptible to mutations that would change that information in their descendants.

In addition, Darwin reasonably assumed that the information transfer process was *analog* in nature and such information transfer schemes inherently produce variation. In analog schemes variation always occurs and the size of an instance of variation is inversely proportional to frequency of occurrence. Larger deviations are progressively less likely than smaller deviations, a behavior that at least superficially matched observed organism variations such as those between mammal parents and their immediate descendants.

However, subsequent genetics discoveries [15] have revealed that the biological information transfer process is actually *digital* in nature and is accomplished by the sequences in which four bases appear in long DNA molecules. Digital information transfer does not inherently produce structured variation as described above but most often produces either exact duplicates or gross unstructured "errors" [3]. In complex organisms the observed variation in a population is actually almost entirely the result of very complex and obviously evolved mechanisms that handle the digital data such as genes, chromosomes, meiosis, unequal crossover, diploid genomic organization, and sexual reproduction.

Because variation is produced by evolved traits and variation is essential to the evolution process we can consider traits that produce variation to be evolvability traits. Like other evolvability traits they are adverse in terms of traditional Darwinian fitness. For example if we consider a population that is well adapted to its external world there would exist an optimum organism design for that population. Any deviation from that design would represent a reduction in fitness. Therefore the most fit population with the largest probability of avoiding extinction under given external conditions would be one in which there existed no variation and therefore no evolvability and no capability for adapting to changes in its external world. More variation would result in more evolvability but less average fitness. Variation is a property of a population.

Note that variation can be affected by evolved behavioral traits in animals. An animal that had a behavioral trait that caused it to seek mates that were different from itself or remotely located would produce more variation. A trait that caused an animal to prefer mating locally or with close relatives would decrease variation.

The digital nature of inheritance imposes other attributes and limitations that are common to any digital information scheme [3]. Examples: ***Quantizing*** – The precision with which an organism design parameter can be uniquely specified depends on the number of symbols (in this case in sequences of the genomic symbols A, C, G, T) that are used to communicate that parameter. Genetically specifying an attribute that requires precision such as the internal anatomical nature of eyes and ears requires a different genomic design than simpler anatomic structures in order to deliver the required precision. ***Language*** - A digital scheme requires that both ends of a data communication possess, in advance, information regarding the meaning arbitrarily assigned to particular digital sequences. E.g. the CAT codon means Histidine and not Lysine.

These aspects of digital genomic design greatly complicate the evolution process and also suggest that, in totality, the evolution process is much more time-consuming than previously thought. In addition to mutations and natural selection, many other evolutionary processes are involved that operate over vastly different time-scales [3].

Relationship between Mutations and Natural Selection

Darwin's mechanics as generally understood can be summarized as follows: A mutation occasionally occurs that changes the inheritable phenotypic design of a single organism. If such a mutation subsequently causes possessing individuals to produce more adult descendants than competing non-possessing individuals it propagates in a population. Natural selection individually evaluates each mutation. This "one mutation at a time" concept essentially precludes the existence of programmed aging, or any other evolved trait that limits an individual's ability to produce adult descendants such as animal altruism, delayed puberty, mating behaviors that limit individual reproduction, or even sexual reproduction. Darwin knew that a single mutation could cause major adverse effects but considered that only minor changes could potentially cause a beneficial effect.

However, recent genetics discoveries have revealed that the medically normal (healthy) human population contains at least ninety-seven million individual genetic differences (e.g. *single nucleotide polymorphisms* or *SNPs*), each of which nominally originally occurred in a different individual at a different time and place [16]. As SNP is defined, each allele of a SNP appears in at least 1 percent of the population. Further, the phenotypic effect of any one polymorphism is generally minor. The observed phenotypic differences between diploid individuals result from combining SNP alleles to produce a particular set. A tall individual could be the result of combining hundreds or even thousands of preexisting SNP alleles where each has a minor positive effect on height. In a diploid organism a single individual can possess substantial genetic diversity resulting from differences between its two sets of genetic data. This is a major evolvability advantage over haploid reproduction: If some event decimates a population it can recover into one having substantial variation. In a diploid case a single pair of parents can produce descendants having diverse phenotypes obviously increasing local variation.

It is unlikely that any single change to a complex organism's phenotypic design would be beneficial. For example, suppose we assume more speed would help an antelope. Longer legs might help with speed. However, a longer leg bone would actually be adverse unless accompanied by bigger leg muscles, changes in other bones, better joints, and a long list of other

complementing changes each of which would be adverse by itself. Darwin assumed that therefore evolution was extremely incremental in nature.

The Evolution of Diploid Organisms and Evolvability

It is widely accepted that diploid sexually reproducing organisms evolved from haploid organisms despite the fact that sexual reproduction is massively adverse in traditional fitness terms relative to asexual reproduction and haploid inheritance schemes [3]. Example: In sexual reproduction reproductive effectiveness is nominally reduced by a factor of two because of the relative reproductive uselessness of males. This is one of the proofs that evolvability can trade off against traditional individual fitness.

In addition, it is common for a mutation (i.e. cause of a new SNP) to have little or no phenotypic effect unless the organism possesses the new SNP allele in both of its genomes. This has the effect of substantially aiding the propagation of mutations that have a minor adverse effect on fitness while suppressing propagation of mutations that have a beneficial effect on fitness, another reason that diploid reproduction is unlikely to have evolved if the Darwinian concepts were correct. Note that this effect aids the propagation of slightly adverse mutations that can later be recombined to produce a net beneficial effect as described in the antelope example.

Genetic Linkage

Genetics discoveries have revealed many ways in which a trait could be genetically linked to other traits in ways that would affect the evolution process [3]. Mutational changes are not random but are severely restrained by the particular genomic design possessed by a diploid species. In 1957 Williams suggested [11] that a particular form of genetic linkage, *antagonistic pleiotropy*, could cause an individually beneficial trait to be linked to an adverse trait (in this case senescence) in such a way as to impede the evolutionary rejection of senescence because doing so would also eliminate the beneficial effect and cause a net disadvantage. He suggested that this effect would explain the existence of senescence despite his simultaneous contention that senescence, per se, was somewhat adverse to populations. Subsequently, many other sources of genomic linkage have been identified [3] having vastly different time scales. That is, the difficulty and therefore the evolutionary time required to produce the genomic changes necessary to accomplish the needed beneficial change without also causing linked adverse changes varies greatly depending on the particular linking mechanism.

Example: It is now known [17] that because of the nature of meiosis and unequal crossover that traits that are affected by genes on the same chromosome are genetically linked and that the strength of the linkage is determined by the genomic distance between the genes.

Example: The evolution of a new hormone having evolutionary value requires the existence of a complex mechanism including new genes for producing the hormone and determining when to produce the hormone. However, producing the hormone creates no value unless there also exist receptors for that hormone in the proper tissues and systems that then cause a useful effect. Consequently the genetic changes required to change the amount of some hormone are

essentially trivial compared to those required for a functionally new protein. This sort of "chicken and egg" problem can plausibly take longer to solve than the time a mammal species has existed. Indeed inter-species genomic comparisons suggest that genes are widely conserved between mammal species [17]. One famous consequence: humans can and did use porcine insulin.

Other Population-Oriented Evolutionary Mechanics Theories

Beginning in 1962 a series of additional evolutionary mechanics theories appeared (e.g. group selection [18], kin selection [19], and small group selection [20]) to the effect that a population benefit (that increased the probability that a population would avoid extinction or produce descendant species) could offset individual disadvantage and allow the evolution of a trait that like senescence produced an individual disadvantage. These theories were originally developed in efforts to explain observations other than senescence (like animal altruism) that also conflicted with traditional theory. Eventually they were extended to include programmed aging theories based on population benefits other than evolvability (e.g. [21, 22]). Note that genetic linkage (above) describes how an individually-adverse trait could be retained long enough for a population benefit to be obtained and thus provides a solution for the future vs. present problem (below).

Objections to Evolvability Theories and Programmed Aging

Many bioscientists have taken the position that programmed aging obviously, grossly, and even diametrically violates Darwin's individual-oriented survival-of-the-fittest concept and can therefore be summarily dismissed as ridiculous and "impossible" without any further investigation, current literature review, science rationale, or counter-argument (e.g. [23]). Some have equated programmed aging to popular but scientifically ridiculous concepts concerning evolution such as Creationism and Intelligent Design. Indeed Darwin's concept is widely taught as the *only* science-based evolutionary mechanics concept. Fundamental limitation theories of aging are still popular despite gross conflicts with multi-species observations. Many social and academic forces act to perpetuate this situation [3].

In 1882 Weismann proposed [7] what was essentially an evolvability-based programmed aging theory. This idea (like Darwin's) predated the entire science of genetics, was almost universally dismissed because of the Darwinian mechanics conflict, and today is cited by some critics as evidence that programmed aging is an early but long-discredited and obsolete idea.

These critics are taking what is essentially a philosophical (as opposed to science-based) position to the effect that any deviation from Darwin's mechanics is, by definition, incorrect regardless of current evidence or logic. This position can be expected in people who are very aware of Darwin's ideas but not as familiar with modern genetics discoveries or their impact on evolutionary mechanics and dependent aging theories. However, as summarized here genetics discoveries and other developments (some quite recent) have disproved multiple details of Darwin's mechanics that are key to the evolution of senescence. These include Darwinian concepts regarding the nature of evolvability, the nature of variation, the analog (vs. digital) nature of biological inheritance, the random nature of mutations, the "one mutation at a time"

concept, and the individual vs. population nature of evolution. In general, it is now obvious that as so often happens in science the evolution process is grossly more complex than originally thought. Darwin's theory was based on very detailed *phenotypic* comparisons between individuals and species. Our ability to perform similarly detailed *genomic* comparisons is in its infancy. Details of biological inheritance mechanisms clearly affect evolutionary mechanics theories and few consider that we are even near to completely understanding biological inheritance.

With regard to modern science-based opposition, there has been no scientific disagreement with the idea that a hypothetical trait could benefit populations at the expense of individuals, nor to the idea that limiting individual lifespan could benefit a population, nor to the idea that limiting lifespan benefits evolvability, nor to the idea that increasing evolvability benefits populations. Nor has there been objection to any specific proposed evolvability benefit of a limited lifespan such as summarized here. Further, even fierce proponents of modern non-programmed aging theories who have attempted science-based counter-arguments (e.g. [24, 25]) no longer claim that programmed aging is "impossible" but only that it is less likely than *their particular* non-programmed theory.

Since the more recent population-benefit theories first appeared in 1962, the primary objection has been what might be termed the "present vs. future" or "short-term vs. long-term" issue. This sort of analysis attempts to show that a mutational change that produces a long-term benefit (e.g. reduced probability that a population will become extinct) cannot propagate if it also produces a short-term disadvantage (e.g. reduced probability that a possessing individual will produce adult descendants). In brief, they accept Medawar's modification but reject all of the later population-oriented theories. This sort of logic is a version of the individual-oriented "one mutation at a time" concept that has been disproved (for diploid organisms), is also inconsistent with Medawar's modification as described earlier, and also ignores the evolutionary effects of genetics discoveries. This issue has resulted in multiple versions of "group selection" theories that differ regarding the size of the group and therefore the magnitude of the short-term vs. long-term issue. There are now kin selection theories [19], small-group theories [20], etc. In this connection some critics have suggested that evolvability benefits a species and therefore evolvability theories can be dismissed as versions of "species-level" group selection, widely seen as the least feasible version. However, evolvability benefits the evolution process [3] and therefore applies regardless of what size group or what time-scale is considered. In addition, as mentioned earlier, genetic linkage arguments suggest that even species-level group selection is feasible [3]. The short-term vs. long-term issue depends on one's concept regarding the "term" associated with the evolution process itself. Genetics discoveries have revealed that various evolutionary processes operate on a time-scale that is long even by comparison to the time any mammal species has existed [3].

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