Evolutionary Ecology Research, 2013, **15**: 527–543

Viscous populations evolve altruistic programmed ageing in ability conflict in a changing environment

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ABSTRACT

Questions: Is ageing evolutionarily adaptive? Can programmed ageing widely evolve as altruism in viscous populations (i.e. widely distributed populations with limited offspring dispersal) in a changing environment?

Features of model: The model is individual-based. The probabilities of survival and reproduction are determined by abilities, and abilities increase with both inherited abilities and age-related abilities, so the old can survive and reproduce even if they are genetically less adapted to the environment (termed 'ability conflict'). Inherited traits are determined by multiple independent loci; thus active ageing can enhance the local accumulation of adaptive inherited abilities in viscous populations.

Ranges of key variables: Dispersal varied from 0 (no dispersal) to 1 (global). The probability of environment-change during each calculation cycle varied from 0 to 1.

Conclusions: Altruistic ageing evolves in structured viscous biological populations with ability conflict in a changing environment to allow the survival of genetically fitter young progenies. To evolve altruistic ageing requires no more environmental change than does sex, suggesting that the generality of altruistic ageing should be no less than sex in viscous populations. If selfish mutants appear only at low rates, higher-level selection would be stabilized even if the environment changes slowly. More extrinsic death can decrease ageing rate (intrinsic death rate) to ensure the same expected lifespan in altruistic ageing, providing testable predictions against traditional ageing theories. My individual-based model also shows how traditional mathematical population genetics largely underestimated the prevalence of group selection.

Keywords: evolvability, genetic creativity, kin selection, longevity, population viscosity, senescence.

INTRODUCTION

Originally, evolutionists argued that ageing is an adaptation to each individual accumulating damage from small injuries during its lifetime, an adaptation that can 'make room for the young' (Weismann, 1889). However, most evolutionary theorists abandoned this group

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selection argument and came to regard ageing as mainly a non-adaptive consequence of the decreased power of natural selection at advanced age, so mutations that are deleterious only at old age accumulate in the population (Medawar, 1952). To counter the hypothesis of weak natural selection in this mutation accumulation theory, antagonistic pleiotropy theory suggests that genes deleterious only at old age can be fixed in the population if they are beneficial earlier in life (Williams, 1957; Hamilton, 1966; Bourke, 2007; Rose *et al.*, 2007; Kirkwood and Melov, 2011). Although antagonistic pleiotropy theory describes some adaptive life-history trade-offs, ageing itself is described as non-adaptive, and thus should not have conserved genetic mechanisms.

Increasing empirical evidence, however, shows that lots of age-related diseases have conserved genetic mechanisms to 'activate' them (Bowles, 2000a) without any apparent beneficial effect earlier in life (Linnane *et al.*, 1990; Mitteldorf, 2004; Khaidakov *et al.*, 2006; Brack *et al.*, 2007; Thum *et al.*, 2008; Goldsmith, 2010; Kenyon, 2010; Pishel *et al.*, 2012). Experimental support for the traditional ageing theories can also be explained by adaptive ageing theories (Mitteldorf, 2004, 2010; Goldsmith, 2010). More important, the traditional ageing theories predict that faster ageing evolves with higher extrinsic death rate, but guppies living in regions with higher predation actually have a slower ageing rate (and higher fecundity) (Reznick *et al.*, 2004).

Thus, some theorists return to Weismann (1889) and argue that ageing/programmed death can benefit the population or kin by making room for the young (Bowles, 1998; Skulachev, 2001; Goldsmith, 2004, 2008; Travis, 2004; Mitteldorf, 2006; Woodberry *et al.*, 2007; Mitteldorf and Pepper, 2009; Martins, 2011), especially in a changing environment where faster ageing can result in faster local evolution. However, these theories assume asexual reproduction and/or group selection and that makes many biologists sceptical about their validity or generality (Bourke, 2007). The assumption of asexual reproduction is used to argue against these theories (Bourke, 2007) because novel adaptive genes generated in faster ageing groups can be recombined into selfishly long-lived individuals in a sexual population. However, the assumption of asexual reproduction is not necessarily a problem for altruistic ageing because fitness can involve multiple genes, and it will be very difficult to recombine all the un-linked novel adaptive genes into a selfishly long-lived individual just by chance.

The rejection of group selection by most biologists is based on mathematical analyses from Price's equation (Price, 1970), evolutionarily stable strategy theory (Smith, 1976), and kin selection theory (Hamilton, 1964). Although powerful, these mathematical analyses ignored important factors in evolution that are extremely difficult to reduce to mathematical equations, because the mathematics has assumed the identity/similarity of individuals when counting individual/offspring/allele numbers or fitness, but the theory of evolution from the beginning stresses mutations, variations, and individual differences for natural selection to work on. Thus the way these mathematical analyses are constructed loses important information, such as exact individual genomic differences, and population–environment interactions in long-term evolution where novel adaptations differentially accumulate with time among different local groups. In addition, the Price equation ignores continuous (multiple) novel mutations, and thus does not apply to long-term evolution. Although population viscosity (i.e. limited offspring dispersal) has been proposed as a potential general kin/group selection mechanism for the evolution of altruism (Hamilton, 1964), existing models pursuing mathematical simplicity fail to show the evolution of altruism in viscous populations with constant carrying capacity because the benefit of additional offspring resulting from kin cooperation is exactly cancelled out by the cost of kin competition because offspring cannot be easily exported (Taylor, 1992; Wilson *et al.*, 1992).

These viscous population models, however, also imply that any additional benefit ignored by these models should be sufficient for the evolution of altruism. For example, altruism and ageing can evolve if population size is allowed to fluctuate to store temporarily the additional offspring resulting from kin cooperation (Mitteldorf and Wilson, 2000; Mitteldorf, 2006). More important, since these models only count offspring number (quantity) as fitness, they ignore the important fact that selection among progenies produced with mutation and sexual recombination in a changing environment will increase the average genetic quality of surviving progenies by eliminating the weaker progenies and helping to store the benefit of kin cooperation in the form of progeny quality, and that can be modelled only with individual-based models incorporating genetic information for each individual (emphasizing individual differences). These fitter progenies can invade other groups with inheritable long-term fitness. So, the generality of altruism has been severely underestimated in existing theories. Evidence from social insects also suggests that altruism evolves beyond the explanation of Hamilton's kin selection theory and inclusive fitness (Wilson, 2005; Gadagkar, 2011).

To explore the benefit of inheritable progeny quality in viscous populations and apply it to the evolution of altruistic ageing, I built individual-based computer-simulation models of viscous populations to show the evolution of programmed death (here called active/adaptive/altruistic ageing) without early-life benefit (i.e. without antagonistic pleiotropy). I base the models on assumptions that were not previously considered by adaptive models and were believed to be most adverse to the evolution of active ageing: sexual reproduction with possible selfish mutations (intra-group selfish mutants in adaptive groups are most adverse for altruism); constant carrying capacity (no room for additional individuals to store fitness); high cost of mutations; and relatively slow environmental change (against genetic creativity, which many call 'evolvability'). Individual-based models can more easily capture population structure, individual–individual interactions, individual–environment interactions, and genome structures in long-term evolution, each of which is important for altruistic ageing but typically ignored by pure mathematical models.

MODEL SUMMARY

The model has a number (N) of regions arranged in a circle. Each region can contain tens of diploid individuals, and offspring can be stochastically dispersed to other regions depending on parameters of dispersal probability and dispersal distance. Each individual in individual-based computer-simulation models contains individual-specific information that is independent of other individuals. In my model, groups do not split or become extinct as whole groups, and higher-level selection has to be based on individual-level selection. All individual traits are determined by multiple genes (binary numbers, with stochastic mutation and sexual recombination), and trait values are proportional to the proportion of 1s in these binary numbers. The multiple-gene nature of inherited abilities can make them difficult to segregate completely with their associated phenotypes (such as altruistic ageing) by chance during sex. Actual ability A of an individual is calculated from age a and inherited ability $A_{\mathbf{in}}$:

$$A = (a + 0.5)(A_{\mathbf{in}} - A_{\mathbf{min}} + \varepsilon)^{D}, \tag{1}$$

where $A_{\mathbf{min}}$ is the minimum inherited ability among all individuals in the same region, ε is a small positive number used to avoid A becoming 0 when all individuals have the same inherited ability, and D (ability distinctness, or selection strength) is a parameter used to set

the selection sensitivity to different values of inherited ability. When only individuals with the fittest phenotype can survive or reproduce, D equals infinity; otherwise, D can be as small as 0 for drift only. Individuals with larger A will proportionately compete more resources to survive and reproduce in a region. Thus continuous selection among progenies will lead to the accumulation of positive ability genes, which will be important for both short-term individual-level and long-term group-level competition. Individuals may die either because they (if any) have reached the end of their inherited maximum lifespans (L), or (mainly) because of failure in survival competition in a region with constant carrying capacity (individual selection). Both survival and sperm competition are stochastic with success probabilities proportional to resource acquired. Egg number is also proportional to resource acquired. I use the final evolved L compared to its initial value and its random walk under neutral evolution to determine whether active programmed death has evolved. During an environmental change, the binary site of ability genes that have evolved (without being reset) for the longest time is reset to 0 for all individuals to allow a novel ability gene to evolve.

I discuss the model in more detail in evolutionary-ecology.com/data/2825Appendix.pdf.

RESULTS

I chose parameter values close to the conditions of most animals (wide population distribution but limited offspring dispersal, some environmental change, heavy mutational costs, etc.) as the default parameters (2825Appendix.pdf, Table S1). Such parameter values improve our ability to understand the effects of different parameters on the evolution of altruistic ageing. I present a comprehensive exploration of the parameter space in a simpler model in the final subsection of the results. The default dispersal parameters are consistent with most terrestrial non-flying animals, as well as flying and aquatic animals that do not migrate continentally or globally. Parameters of environmental change and mutational costs are difficult to determine, but I will show that they were either set consistently to the requirements of the evolution of sex or else they were non-essential. The increase of actual abilities with age is also widely true for animals with body growth, learning and experience, and acquired immunities. I set sexual maturation age to 2 years (calculation cycles of reproduction, resource competition, death, and possible environmental change), although this did not qualitatively affect the results. The maximum L allowed is 100 years. The evolution of L without selection was a random walk around 50 ± 15 years (mean $\pm$ S.D.) across time.

Programmed death actively evolves in viscous populations with kin competition and group competition

L responded to dispersal conditions (Fig. 1). When dispersal distance dN/2 and dispersal probability p_d were both 0, different resource regions evolved independently and genes of longer L (72.2 ± 1.1 years) accumulated. When dispersal increased a little ($d = p_d = 0.04$) so that there existed both kin competition and group competition, L was 'attracted' from an initial value of 50 years to low levels with small standard deviation (17.5 ± 1.8 years), implying a benefit for low L. When dispersal was unrestricted ($d = p_d = 1$), L evolved to be very large (86.2 ± 5.8 years). Therefore, kin competition led individuals to have altruistically

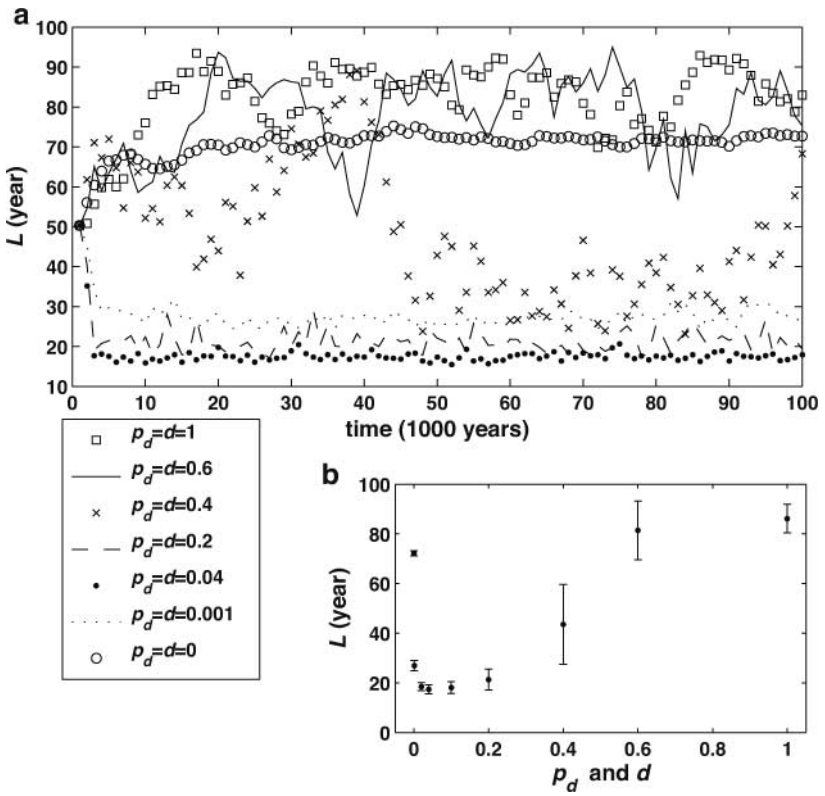

Fig. 1. Short inherited maximum lifespan (L) can actively evolve in viscous populations. dN/2 is the maximum distance offspring could be dispersed to (both sides), and p_d is dispersal probability. (a) Population average L actively and stably evolved to altruistically low levels from an initial value of about 50 years when kin competition (small dispersal) and group competition (non-zero dispersal) both existed. (b) More detailed response of the final evolved L (±S.D.) to the change of d and p_d, averaged from 100,000 to 300,000 years. The simulations were insensitive to initial values, so replicates were done by extension of time.

short L in interconnected viscous sub-populations. In accordance with L, more senescent deaths evolved when dispersal was neither 0 nor too large (2825Appendix.pdf, Fig. S1).

Programmed death evolves to overcome ability conflicts and increase genetic creativity in local populations in a changing environment

Environmental change was required for the evolution of active ageing (Fig. 2a), as it ensured the opportunity for the evolution of new ability genes. Similarly, setting inherited ability to a fixed value eliminated the evolution of active ageing. By default, the number of ability genes in a gamete was 31 for computational efficiency. This was a relatively small number, and all ability genes were quickly removed if the environment-changing rate was high, making novel adaptive ability genes no longer useful for long-term group competition (Fig. 2a). Individuals in the model with small-ability genome size were also very likely to have the same novel mutations, making the creation of genetically fitter progenies by sexual

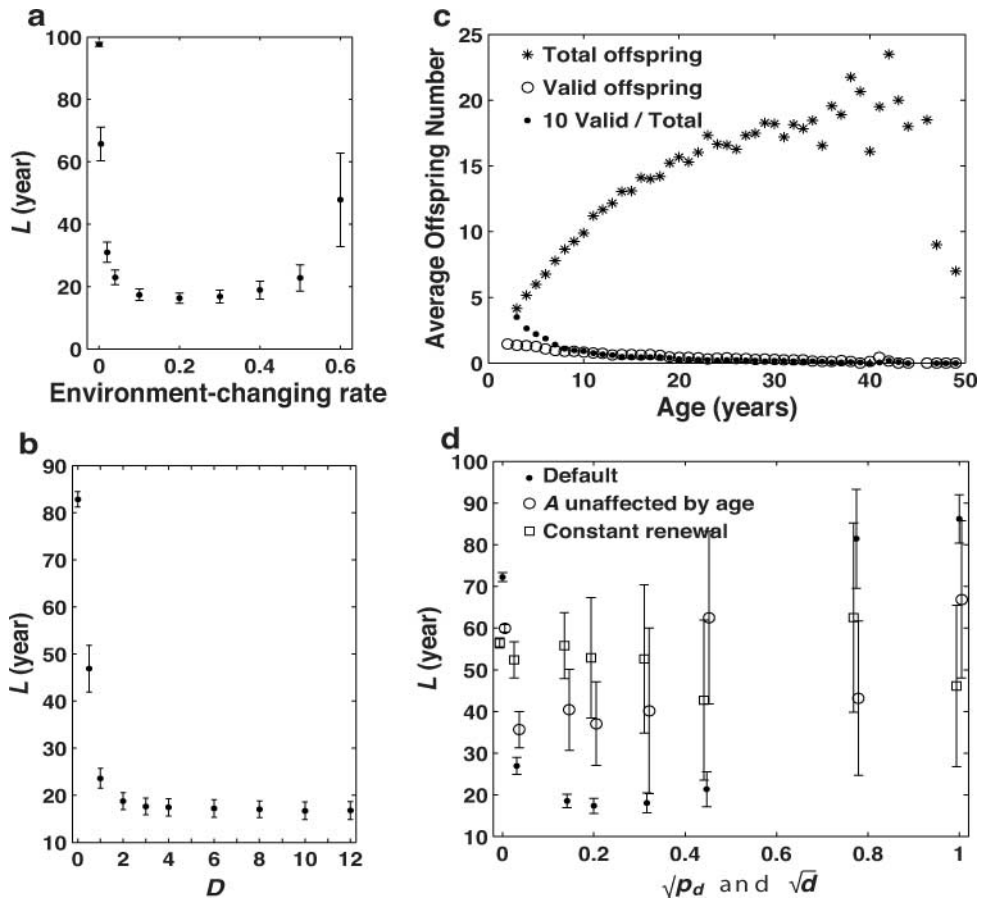

Fig. 2. Programmed ageing evolves to improve progeny inherited abilities in a changing environment under ability conflicts. (a) Environmental change was required for the evolution of short L. Environment-changing rate, the probability for environmental change to happen in a year. Extremely fast change of environment eliminated newly evolved ability genes so that they could no longer promote altruistic ageing. (b) Higher ability distinctness D (which measures selection efficiency) promoted the evolution of short L. (c) Old individuals' viable and reproductive (valid) offspring number continuously decreased with age (because of decreased inherited ability). (d) Little active ageing was observed when age did not contribute to actual ability A or A was recalculated every year according to inherited ability genes (constant renewal).

recombination inefficient. However, by allocating 310 ability genes in a gamete, strong altruistic ageing ($L = 13.8 \pm 1.4$ years) evolved for the default parameters, and evolved L decreased even with the fastest allowed environment-changing rate of 1 (default 0.1) (to 10.4 ± 1.2 years).

Higher ability distinctness D (selection efficiency/strength) should increase the importance of inherited abilities, and could promote altruistic ageing (Fig. 2b). An example of ability distinctness of a trait is running speed and survival. Individuals that can run slightly faster may have a much greater chance of survival than others if they are chased and preyed upon by carnivores (high ability distinctness). However, if those same individuals are easily

preyed upon by eagles (extremely fast) or snakes (stealthy), running faster will probably make little difference (low ability distinctness) unless they still have a fair chance to escape after being targeted. An ability distinctness of 1 was sufficient for obvious altruistic ageing to evolve (Fig. 2b), suggesting that altruistic ageing does not require extremely high selection efficiency.

Active intrinsic death requires old individuals to have strong actual abilities to survive extrinsic death even though they are genetically inferior to their progenies. This condition is termed 'ability conflict' and is achieved by the contribution of age (acquired ability) to A. With ability conflicts, old individuals had fewer viable and reproductive offspring even though their total offspring increased with age (Fig. 2c). Active ageing could not evolve if actual ability was not affected by age or was constantly renewed by germ-line inherited ability (Fig. 2d). The reason for that result is that intrinsic active death is no longer necessary where there are no ability conflicts, and the poorly adapted old individuals can be eliminated by extrinsic death from local survival competition.

Dynamically, altruistically shorter L could be stochastically generated in a few, although not many, local regions and then spread to other regions because of its association with higher inherited ability (http://evolutionary-ecology.com/data/2825Video.avi). Eventually, the population achieved equilibrium when the random generation and selected spreading of short L were cancelled out by the invasion of selfish variants. Any factor affecting this equilibrium should also affect L.

The evolution of programmed death does not require more environmental change than does sex

The evolution of active ageing requires environmental change. But how quickly does that change have to occur? To answer this, I incorporated the evolution of sexual reproduction, which also requires environmental change, as a control. The model was modified by adding another trait, the probability of infant sexual development. Infants could either develop into sexually reproducing individuals or develop into asexual individuals [which do not pay the two-fold cost of sex (Otto and Lenormand, 2002)]. When environment-change rate increased above a certain level so that sex probability evolved above 0.5, active ageing also evolved in viscous populations (Fig. 3). So, the evolution of active ageing does not require more environmental change than the evolution of sex does. The evolution of sex requires genetic diversity, which also forms the basis for the increase of offspring genetic fitness after selection and promotes the evolution of altruistic ageing. Thus, the generality of sex also suggests the generality of altruistic ageing. Comparing Figs. 2a and 3b, we see that the evolved altruistic L was lower given the possibility of asexuality, which suggests that sex itself reduces altruistic ageing and increases L. However, sex suggests the existence of environmental change, which promotes altruistic ageing.

Slower (or biased) mutation rates of genes for ageing and larger population ranges promote programmed ageing by higher-level selection

Traditional theories often assumed arbitrary mutations and argued that higher-level selection is too slow to be common in biology. However, both mutation rate and manner are important. The emergence of selfish mutants also takes time and their predominance in

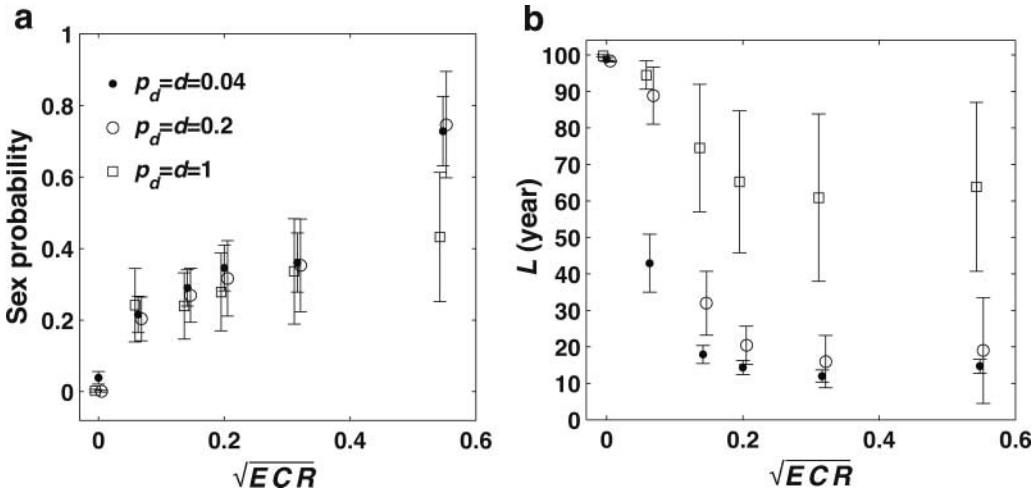

Fig. 3. Altruistic ageing does not require more environmental change to evolve than sex does. (a) The evolution and maintenance of sexual reproduction required a relatively high environment-changing rate (ECR). (b) Altruistically short L had already evolved under such a rate of environmental change in viscous populations.

the population is not necessarily faster than higher-level selection. It is unreasonable to assume a selfish mutant whenever there is a possibility of such. In fact, a slower mutation rate of L genes could evolve to promote the evolution of limited L (Fig. 4a,b).

The model of Fig. 4 differs from the model of Fig. 1 by having lifespan genes with mutation coolness r so that the mutation rate of L genes is 100^{2r-1} times (ranging from 0.01 to 100) that of other genes. Smaller r could enhance selection at higher levels by protecting altruistic groups from selfish invasion for a longer period of time, allowing them to accumulate larger inter-group differences, and by reducing the chance for selfish mutations to occur simultaneously in different regions. If dispersal increases, making selection for low r and L less efficient, r and L could still be selected to low levels if more resource regions existed (Fig. 4c). A large number of resource regions can reduce the probability that all regions become occupied by selfish individuals and thus can also enhance selection at higher levels. When I allowed only 20% L mutations to increase L while the other 80% decreased L (by default, L mutations had an equal chance to increase and decrease L), L also decreased consistently to low levels (7.1 ± 0.6 years) from the model of Fig. 1. Biased mutation could happen if immortality requires perfect functions/sequences in some genes, since it would be easier for mutations to make a sequence imperfect rather than perfect (only individual selection promotes perfection).

To further illustrate higher-level selection, I allowed dispersal probability p_d and the level of dispersal distance d to change independently (Fig. 4d) in the model of Fig. 1. A small value of either of them was sufficient for the evolution of active ageing. Active ageing could evolve even if all offspring were dispersed, as long as they were dispersed only to nearby regions. This result also strongly supports the generality of altruistic ageing; it can evolve even if genes can flow freely among nearby regions.

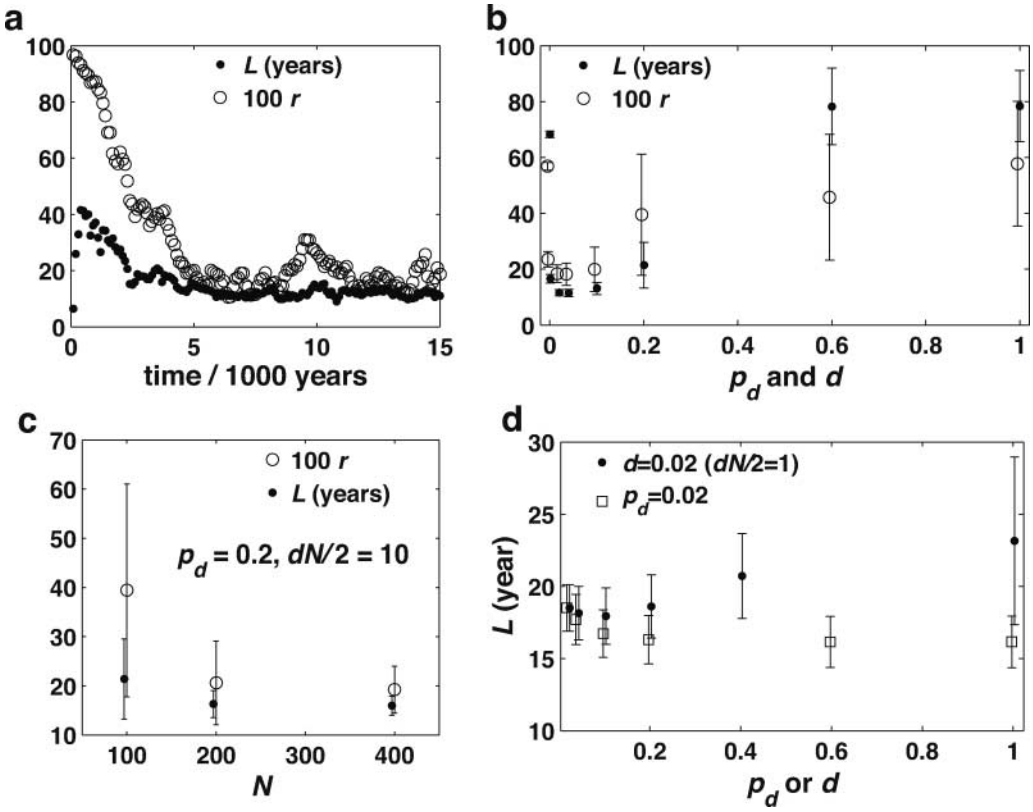

Fig. 4. Evolved low mutation rate of ageing genes and wide population distribution can promote altruistic ageing by higher-level selection. (a) The evolution began with mutation coolness (r) near 1 so that lifespan genes mutated $100^{2r-1} = 100$ times as fast as other genes, so selfish invasions became more frequent and individuals gave up altruistic ageing. However, r was quickly selected to low levels and promoted the evolution of short L. (b) r evolved to low levels only in viscous populations where altruistic ageing could evolve. (c) A large number (N) of resource regions (i.e. a wide population distribution) restored low levels of r and L when dispersal became less favourable for altruistic ageing. (d) A low level of p_d or d alone could result in altruistic ageing. The default value of N was 100.

Higher extrinsic death rate decreases ageing rate under altruistic ageing

I tested the effect of death rate on the evolution of L. I imposed an additional random death at a certain rate on each individual each year before survival competition (Fig. 5). In accordance with the traditional theory, higher death rate reduced selection forces at old ages and decreased L when conditions did not favour altruism. However, when dispersal ($d = p_d = 0.04$) and environmental change favoured a short L, high death rate actually increased L. This happened because old individuals were actively dying, so higher extrinsic death rate reduced the need for active intrinsic death, as seen in guppies (Reznick *et al.*, 2004). So, the relationship between death rate and L depends on the degree of altruistic ageing. If altruistic ageing is general, higher random death rate should decrease ageing rate instead of increasing it.

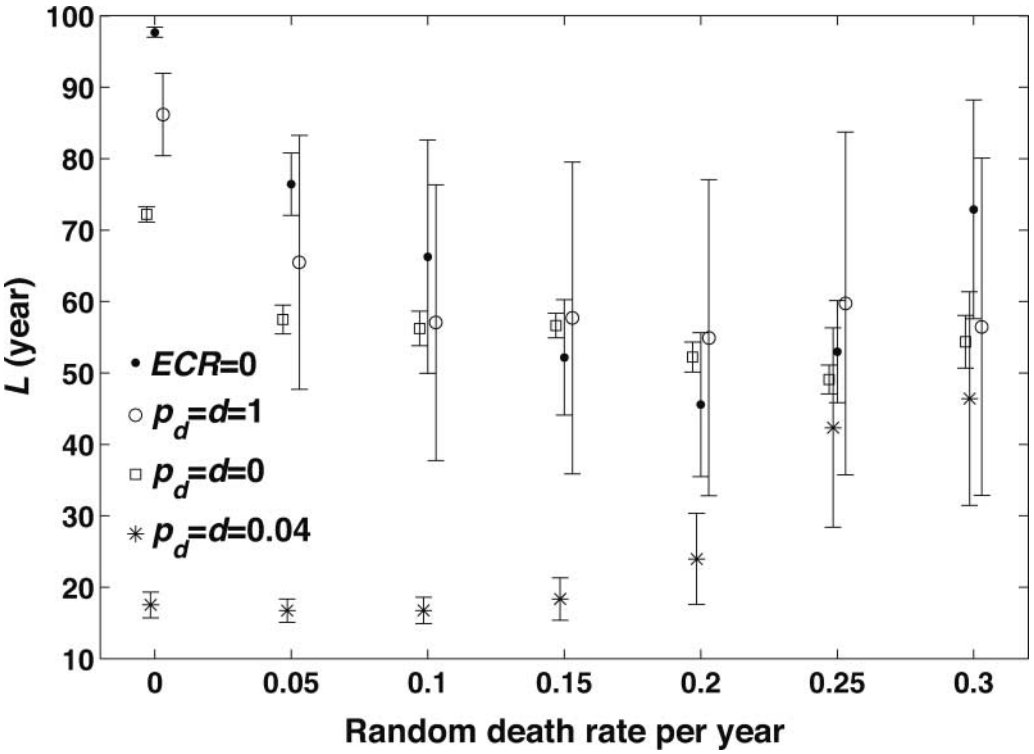

Fig. 5. Extrinsic death decreases non-altruistic inherited maximum lifespan (L) but also increases altruistic L. All individuals were subjected to random death every year with random death rate values displayed along the x-axis. Whether the environment-changing rate $ECR = 0$, or $p_d = d = 0$ or $p_d = d = 1$, the model always evolved non-altruistic (long) L. But if $p_d = d = 0.04$, the model evolved altruistic short L for death rate < 0.20 and non-altruistic long L for death rate ≥ 0.25.

The parameter spaces that evolved altruistic ageing

To further understand how altruistic ageing could evolve, it would be helpful to identify the parameter spaces where altruistic ageing could evolve. To achieve this, the model needed to be simplified to comprehensively simulate different parameter combinations and to show the key determinants of altruistic ageing.

To simplify the model, I set carrying capacity (final local survival each year) to 1, thus reducing regions to virtual points. I set dispersal probability to an even distribution within the dispersal distance. I set ability distinctness D to 1 to achieve completely linear selection on inherited abilities. I assumed no mutational costs and used mutation rate as a parameter instead of an evolvable trait. Individuals reproduced every calculation cycle to avoid the use of maturation age (i.e. setting it to 1). I set the maximum possible value of L to 40 years; thus a random walk of L would be around $L = 20$ years.

After these simplifications, only five parameters remained: the number of resource regions/points (N); dispersal distance; environment-changing rate (ECR); mutation rate ($MutRt$); and resource at each region/point (Q_T). I used three or four values spanning at least two orders of magnitude for each parameter and I simulated all their possible

Table 1. Parameter combinations where short inherited maximum lifespan (L <17) evolved

Variables	*MutRt*	*Dispersal*	*N*	*ECR*	Q_T	*L* (S.D.)
Possible values	3.3×10^{-5} 0.001 0.033 1	0 Adjacent Global	4 40 400	0 0.01 0.1 1	1 10 100	0 ~ 40
1	3.3×10^{-5}	Adjacent	400	0.01	100	2.77 (0.4)
2	3.3×10^{-5}	Adjacent	400	0.1	100	2.83 (0.5)
3	3.3×10^{-5}	Adjacent	400	1	100	2.95 (0.3)
4	0.001	Adjacent	400	0.1	10	3.10 (0.6)
5	0.001	Adjacent	400	0.1	100	4.00 (0.8)
6	0.001	Adjacent	400	1	100	5.30 (1.3)
7	0.033	Adjacent	400	0.1	10	10.6 (1.9)
8	0.033	Adjacent	400	0.1	1	12.6 (1.5)
9	0.033	Adjacent	40	0.1	10	14.6 (8.8)
10	0.001	Adjacent	40	1	100	15.9 (11.6)
11	0.001	Adjacent	400	0.01	1	16.1 (3.3)

combinations (Table 1). Small changes of the parameters did not qualitatively affect the results since the results showed continuity with the change of parameters. I used values at the last two-thirds of the calculation time. I made calculation times long enough (600,000 to 100 million years) so that the absolute values of Spearman's rho (rank correlation) between the values of L and time were smaller than 0.1. I used an evolved average L smaller than 17 years as the cut-off value for altruistic ageing.

Generally, population viscosity was required for the evolution of altruistic ageing, i.e. altruistic ageing evolved where population range (N) was large and dispersal was neither 0 nor global. Altruistic ageing was still possible even though the other three parameters changed over at least two orders of magnitude, suggesting the robustness of altruistic ageing.

Mutation rate could change over three orders of magnitude without determining whether altruistic ageing could evolve. But smaller mutation rates stabilized stronger altruistic ageing. However, when mutation rate was below 3.3×10^{-5}, the occurrence and spread of longevity and ability mutations could easily become independent, and altruistic ageing could evolve only if resource in each region/reproduction rate was high (which speeds up the occurrence and accumulation of novel ability genes). High mutation rate diminished altruistic ageing, because higher-level selection cannot work when selfish mutants easily arise everywhere.

Altruistic ageing requires environmental change. However, its effect on altruistic ageing depended on mutation rate. When mutation rate was low, contrary to popular belief, slower environmental change actually promoted altruistic ageing, because it provided more time for the rare novel ability genes to remain adaptive in higher-level selection. Thus, slow environmental change is not necessarily a problem for the evolution of altruistic ageing as long as mutation rate is low. Since the model had only a small number of sites (31 sites) for ability genes, environmental change created opportunity for novel ability genes by removing older ones (though not always true in nature). So, if it occurred too fast for different regions

to maintain variability, it diminished altruistic ageing. On the other hand, at higher mutation rates (0.001 or 0.033), altruistic ageing became weaker with slow environmental change (0.01), since the sites for ability genes could easily be filled and few novel ability mutations could co-occur with selfish mutations.

The effect of resources in each region/point depended on other factors; by itself, it did not strongly affect altruistic ageing. At low mutation rate, more resource (thus more reproduction) promoted altruistic ageing because it accelerated the local accumulation rate of novel ability genes more than that of long-lived selfish mutations (a longevity mutation does not affect fitness in earlier life but an ability mutation does). However, by the same mechanism, it diminished altruistic ageing at higher mutation rate (half of the mutations were beneficial) coupled with slow environmental change (because ability sites could easily be filled).

So, the regional co-occurrence of novel ability genes at the rise and spread of selfish mutations is the key for the evolution of altruistic ageing and is required for understanding the complexity of the above factors.

DISCUSSION

I built individual-based models to study the evolution of programmed death (i.e. ageing) and longevity in sexual populations with selfish mutations, heavy costs of beneficial mutations, and constant carrying capacity. For simplicity, I did not consider age-associated gradual fitness decline in these models. Nor was model longevity associated with antagonistic pleiotropy.

Originally, sexual reproduction with selfish mutations, costly beneficial mutations, and constant carrying capacity were believed to work against the evolution of active ageing, and few of them were included in previous models of active ageing. However, I have demonstrated here that active ageing can evolve even if these conditions are present as long as the species has limited offspring dispersal, a wide distribution, and faces an environment that keeps changing, thus driving ability conflicts between generations. Limited offspring dispersal maintains kinship and altruism among local individuals. The demand for high creativity and evolutionary responsiveness to keep up with environmental changes drives the selection of programmed ageing. Although old individuals tend to have superior survival abilities associated with age if they lack ageing and active death, their inherited abilities tend to be inferior (ability conflicts), because variation and natural selection among progenies increase the average fitness of survived progenies. Active ageing can evolve even when high cost of mutations is introduced to work against the improvement of progenies (2825Appendix.pdf, Fig. S2), as 'excessive' reproduction and selection enable local populations to tolerate the costs of lethal and detrimental mutations. Increasing the importance of inherited abilities in survival and reproduction also increases the rate of ageing. For the evolution of active ageing, the environment is not required to change any faster than it must for sex to evolve. Lower mutation rate of ageing mechanisms can evolve to reduce the generation rate of selfish mutations and to promote and stabilize the evolution of active ageing, and this also decreases the requirement for fast environmental change. More resource regions (larger population distribution) can similarly promote active ageing by preventing selfishness from winning in all local regions. Higher extrinsic death rate can decrease the rate of ageing (intrinsic death) if conditions allow altruistic/active ageing to evolve and if extrinsic

death has low ability distinctness (i.e. more random for different individuals and capable of eliminating strong old individuals).

The model and improvement of population genetics

The success of altruism through stronger ability genes is based on a mechanism known as genetic hitchhiking or genetic drift (Barton, 2000), although traditional hitchhiking requires the neutral/harmful gene to be directly linked to the beneficial gene in sexual populations, which is not the case here, as I assumed no genetic linkages at all. It works because both ageing and abilities involve multiple genes, so they are much harder to separate by chance than just two genes. It will take many generations for the progenies from selfishly long-lived groups to gain all the novel adaptive genes from altruistic groups by sexual recombination. However, without competitive inherited abilities, these progenies can hardly survive and reproduce for so many generations once they come into competition with altruistic strong individuals (slower ageing is of no help if one cannot survive to an old age).

Slower generation rate of selfish mutants can evolve to promote altruistic ageing. Because of mutation, Hamilton's rule of kin selection does not apply. For example, if there are no mutations, individuals in a population will eventually become identical because of selection and genetic drift. However, if mutation rate is high, even 'identical twins' cannot be viewed as relatives. This is why mutation rate of altruistic genes (and population range), which is not considered in kin selection theory, is so important for the evolution of altruistic ageing. The key to understanding the evolution of altruism is the maintenance of altruism against selfish variants in the population dynamics of the stochastic emergence of altruism, the spreading of altruism by higher-level selection, and the invasion by selfish variants. Kin selection based on Hamilton relatedness is only a specific means for individuals in un-mutated lineages to defend against selfish invaders from mutated lineages.

Higher-level selection is often argued to be too slow to be common for altruistic evolution. However, this claim is also based on unjustified assumptions of selfish mutations. It ignores that the generation rate of selfish mutants also takes time and it is not necessarily faster than the accumulation of adaptive genes. By assuming that lifespan genes and ability genes had the same mutation rate and number of loci, the present model showed that altruistic ageing could stably evolve. Slower mutation rate of altruistic genes could also evolve to promote higher-level selection and altruism. If mutations were more likely to decrease than increase longevity, higher-level selection and altruistic ageing could also be more predominant. So, even if the generation rate of novel adaptations is slow and the young are sometimes genetically no better than the old, altruistic ageing can still evolve, because the generation rate of selfish mutants is also limited. Besides, fitness is multi-dimensional in the complex ecological interactions but longevity is only one factor. Genes affecting longevity is generally conceived to be encoded by only a small proportion of the genome. This also promotes the evolution of altruistic ageing by promoting the faster overall occurrence of novel ability genes than that of selfish mutations.

How altruistic ageing theories explain empirical evidence better than the theory of mutation accumulation and antagonistic pleiotropy

In the natural world, most animal species have limited offspring dispersal but wide distribution, so kin group selection and altruistically limited lifespan are the usual predicted

cases in my model. Species that suffer less or no kin competition usually have longer inherited maximum lifespan (IML). For example, as birds and bats can fly (Crow, 1997; Arnheim and Calabrese, 2009), they usually live in a wider range of areas and thus suffer less kin competition than terrestrial non-flying mammals, and they usually have longer lifespan than terrestrial non-flying mammals with the same body size and similar life cycle. An alternative explanation from the traditional ageing theory of extrinsic mortality (Medawar, 1952) is that flight enables animals to escape predators and leaves more older individuals alive to promote the evolution of longer lifespan (Drake *et al.*, 1998; Dytham and Travis, 2006; Arnheim and Calabrese, 2009). Although the present study does not exclude the effect of extremely high death rate on IML evolution if conditions favour longer lifespan, it shows that higher extrinsic random death rate can also result in longer IML if altruism can evolve. This complementarity between extrinsic and intrinsic death rates has been observed in natural guppy populations (Reznick *et al.*, 2004). Some counterarguments based on highly unrelated species, such as comparing porcupines and elephants with some short-lived mammals, may be irrelevant, because the long lifespan of porcupines and elephants may simply be because of their life-history differences (such as slower sexual maturation and yearly reproduction) compared with short-lived animals, rather than because of their good protection from predators.

Animals living individually in vast oceans (and maybe hunting different prey at different ages), such as sea turtles (other turtles usually have much shorter lifespans) and some fishes (Vaupel *et al.*, 2004), or corals (Vaupel *et al.*, 2004) and most plants that do not move freely but disperse offspring relatively far away, are all species that suffer little kin competition and thus have long lifespan and negligible senescence. The immortal hydras (Solomon *et al.*, 2002) also suffer little kin competition, as their adhesive lifestyle is similar to that of plants; their constant tissue renewal (Martinez, 1998) may also imply that they do not have obvious ability conflicts between young and elder ages.

Most longevity villages in humans are found in nearly isolated mountain areas (Poulain *et al.*, 2004) such as Bama in China or islands (e.g. Okinawa in Japan) where higher-level selection does not exist. The longevity of residents in Rugao County in China may possibly evolve from the other extreme condition of kin competition, as the county is not isolated but characterized by many immigrations throughout its history and dense population [it is the most populated agricultural area in China (Government of Rugao County, 2001)], and thus low level of relatedness and kin competition. Evidence from birds is similar: generally, island birds live longer than mainland birds, and colonial birds live longer than solitary birds (Arnheim and Calabrese, 2009).

Alleged experimental support (Sinclair, 2005; Charmantier *et al.*, 2006; Rose *et al.*, 2007) for the antagonistic pleiotropy theory does not solely support this theory either. For example, experiments on caloric restriction and life-history 'trade-offs' are also consistent with adaptive ageing theories. The main point of adaptive ageing is to avoid competition with and leave resource to genetically fitter progenies, so individuals should have enough offspring before ageing to ensure the existence of fitter progenies to inherit their resource. On the other hand, adaptive/active ageing itself means that individuals should not live to too old an age, i.e. individuals should have an optimized number of offspring given a certain degree of altruism. Thus, of course, when food is restricted and reproduction rate has to be reduced, individuals should live longer.

The proposition in the theory of mutation accumulation that there are too few old individuals in natural populations to allow the evolution of active ageing is a false assumption. The theory often gives examples of highly preyed upon species with high

mortality rate, but does not mention carnivores or even top predators that also show obvious senescence. Bowles (2000b) clearly pointed out that natural immortal populations can be old-dominated because of stronger acquired abilities of the old. There is sufficient evidence that survival and fecundity decrease with old age in natural populations (Ricklefs, 1998, 2008; Loison *et al.*, 1999; Bonduriansky and Brassil, 2002; Libertini, 2008; Nussey *et al.*, 2009). So, ageing does exist in natural populations, and the alleged non-existence of very old individuals in natural populations may simply be because of active ageing itself.

CONCLUSION

This paper strongly supports an adaptive theory that ageing and age-related diseases are actively evolved altruistic characteristics. It is possible this altruism can evolve in most animal species with wide distribution but limited offspring dispersal. I predict that species with less random death and stronger selection should have a stronger active ageing mechanism (relative to their wild life history such as sexual maturation age and reproduction rate). I also predict that the molecular mechanism of ageing and age-related diseases should lie in mechanisms where it is difficult for selfish mutants to arise or spread, such as sequence imperfection of genes involved in DNA repair, DNA replication, cell cycle control and other body maintenance [longevity gene sequences of short-lived species should evolve more imperfections and some have been found (Semeiks and Grishin, 2012) to diverge further from long-lived species such as humans], as it is much easier to mutate from than to a perfect sequence because of entropic reasons.

ACKNOWLEDGEMENTS

I thank Jorge Azpurua, Alexis I. Stein, and Michael Rosenzweig for their advice and English editing. I thank Josh Mitteldorf and anonymous reviewers for comments.

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