How Life History Can Sway the Fixation Probability of Mutants

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ABSTRACT In this work, we study the effects of demographic structure on evolutionary dynamics when selection acts on reproduction, survival, or both. In contrast to the previously discovered pattern that the fixation probability of a neutral mutant decreases while the population becomes younger, we show that a mutant with a constant selective advantage may have a maximum or a minimum of the fixation probability in populations with an intermediate fraction of young individuals. This highlights the importance of life history and demographic structure in studying evolutionary dynamics. We also illustrate the fundamental differences between selection on reproduction and selection on survival when age structure is present. In addition, we evaluate the relative importance of size and structure of the population in determining the fixation probability of the mutant. Our work lays the foundation for also studying density- and frequency-dependent effects in populations when demographic structures cannot be neglected.

KEYWORDS demography; evolutionary dynamics; population structure; reproduction; survival

THE emergence and subsequent dynamics of mutants play important roles in determining the trajectory of evolution (Crow and Kimura 1970). The fate of a mutant is strongly influenced by its relative fitness. The fitness of a mutant or, rather, the fitness landscape of the whole population is not static but ever changing under the influence of many factors, including density- and frequency-dependent effects (Nowak and Sigmund 2004).

Depicting the trajectories of survival and reproduction along the lifespan, life history is well known to have great influence on evolution in general (Nunney 1991, 1996; Charlesworth 2001; Vindenes *et al.* 2009). Life history has been recognized as being of fundamental importance in determining the trajectory of evolutionary dynamics (Wahl and DeHaan 2004; Lambert 2006; Hubbarde *et al.* 2007; Parsons and Quince 2007a,b; Wahl and Dai Zhu 2015). In addition, life history also modulates the actual effect that an increase in survival or reproduction has on the growth rate of the

population, and it accounts for part of the effective size of the population (Charlesworth 1994; Engen *et al.* 2005). For the frequency-dependent case, it has been shown that life-stage-dependent strategic interactions can promote diversity and push strategic behaviors away from the equilibrium determined by game-theoretic interactions alone (Li *et al.* 2015a). However, it is not obvious whether certain demographic structures of the population would help or hinder the spread and fixation of a beneficial mutant. This is the problem of interest in this work, which may be the first step toward further studies of the stochastic effects of the frequency-dependent case.

Pioneer work on this topic includes seminal papers by Felsenstein (1971) and Emigh (1979a,b). One major goal of this previous work was to understand the evolutionary dynamics in populations with overlapping generations. Overlapping-generation models are biologically more relevant to many species of interest, including humans, but they are inevitably associated with increased complexity owing to age or stage structure of the population. To fully capture the demographic architecture of age-structured populations, not only the absolute number and frequency of the mutant matter but also its distribution across different age classes must be determined. One important concept to note here is the reproductive value. The reproductive value of an individual

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was originally defined by Fisher (1930) as the “extent [to which] persons of this age (or sex), on average, contribute to the ancestry of future generations.” It does so by accounting for the remaining number of offspring an individual will produce, discounted by the increase in population size at the time of reproduction of this offspring. Fisher discovered that in a linear model, the total reproductive value in a population grows exactly exponentially regardless of whether the population age distribution has reached the demographically stable state. Thereafter, in population genetics models of age-structured populations, it is of great importance to look at the dynamics of reproductive value-weighted frequencies of alleles (Crow 1979; Engen *et al.* 2005, 2009b; Vindenes *et al.* 2009). This reduces the typically highly dimensional problem of dealing with alleles flowing through multiple age classes to the lesser-dimensional problem of tracking allele frequencies with the appropriate weights and essentially neglecting explicit age structure. More comprehensive explanations and examples are presented in the book by Caswell (2001). In populations with demographic structure, individuals of different ages have different reproductive values. The evolutionary fate can be summarized by the fixation probability of a mutant, *i.e.*, the probability that it ultimately takes over the entire population. This fixation probability can vary greatly with the fraction of young individuals in the population in populations with overlapping generations.

The pioneering researchers have made great analytical contributions under various simplifying assumptions, such as large population size (Felsenstein 1971; Emigh 1979a, b), neutral (Emigh 1979a) or weak selection (Emigh 1979b), and extreme demographic structures (Felsenstein 1971; Emigh 1979a, b). Under these conditions, good approximations can be made to facilitate mathematical analysis. For example, if the sizes of subsequent age classes differ greatly or are very close to each other, it is cogent to approximate hypergeometric sampling with binomial sampling to capture the process of individuals entering the next age class. With impressive analytical dexterity, the pioneers successfully summarized the vast complexity into a few easily understood parameters, such as the “effective population number” (Felsenstein 1971) and the “average reproductive value” (Emigh 1979a). They used these parameters to describe and analyze evolutionary dynamics.

Despite the beautiful analysis, the original work did not achieve the impact it deserves in our opinion. This is probably a result of the inevitable mathematical complexity or somewhat limited applications dictated by the stringent underlying assumptions. With the help of current increased computational power, we show that there are still surprises left uncovered in the original model first described by Felsenstein (1971), even in the simplest case with only two age classes in a well-mixed population under constant selection.

In the following, we first describe the model and recall the fixation probability of a neutral mutant in the first age class as a benchmark. Then we analyze the pattern of fixation probability of a beneficial mutant in populations with diverse

demographic structures. We explore one by one the evolutionary consequences of selecting on reproduction, on survival, and on both. Further, we evaluate the relative importance of population structure and size in determining the fixation probability of a beneficial mutant. Finally, we show that unexpected nonmonotonic patterns of fixation probability hold in populations with multiple age classes.

Model Description

Life history and population updating rules

First, we describe the life-history features of individuals and population updating rules, as illustrated in Figure 1. In contrast to the original model of Felsenstein (1971), we start from analyzing the simple case of only two age classes (and then go beyond it in the section *Beyond Two Age Classes*). In addition, we include different targets of natural selection, such as selecting on reproduction, on survival, or on both. Consider a haploid population in which individuals can live up to age two at maximum. The numbers of individuals in age one (young) and age two (old) are constant, denoted as N_1 and N_2 , respectively. In each time step, all individuals produce large numbers of offspring, proportional to their fitness. Among them, only N_1 survive and become the next generation of young individuals. Similarly, only N_2 of the young individuals at the previous time step survive to enter the old age class. All old individuals die and are removed from the population. The recruitment of young individuals from the pool of newborn offspring is treated as a process of sampling *with* replacement (similar to the classic Wright-Fisher process), while the recruitment of old individuals from young ones is treated as sampling *without* replacement. The fitness of the mutant is assumed to be constant and greater than the fitness of the wild type, which is normalized to 1. Selection may act on reproduction (fitter individuals have more offspring), survival (fitter individuals have a higher probability of survival to the next age class), or a combination of both.

Fixation probability of a selectively neutral mutant

We denote the state of the population at time t as a tuple $x_1 x_2^{(t)}$, in which x_1 is the number of mutants in the young age class, and x_2 is the number of mutants in the old age class. The transition probability from $x_1 x_2^{(t)}$ to $x_1 x_2^{(t+1)}$ is

$$p(x_1 x_2^{(t)} \rightarrow x_1 x_2^{(t+1)}) = B\left(x_1^{(t+1)}; N_1, \frac{x_1^{(t)} + x_2^{(t)}}{N_1 + N_2}\right) \times H\left(x_2^{(t+1)}; N_1, x_1^{(t)}, N_2\right) \quad (1)$$

where $x_i^{(t)}$ is the number of mutants in age class i at time t ,

$$B(k; n, q) = \binom{n}{k} q^k (1-q)^{n-k}$$

denotes the probability of obtaining k mutants in n draws with replacement, and q is the frequency of mutants in the

Figure 1 Population updating rules. The numbers of individuals in the first and second age classes are fixed (N_1 and N_2). Individuals produce large numbers of offspring proportional to their fitness if selection acts on reproduction. Otherwise, they all produce the same numbers of offspring. Offspring enter the first age class following binomial sampling, assuming that the number of offspring is much greater than N_1 . Entering the second age class of the age-one individuals follows hypergeometric sampling. If selection acts on survival, fitter individuals have a higher probability of survival to the next age class. Consequently, the sampling process becomes noncentral hypergeometric sampling. Compared to the original model described by Felsenstein (1971), we use only two age classes for simplicity, while the original model had an arbitrary number of age classes ω (we discuss this case in the section *Beyond Two Age Classes*). However, we explore the differences between selection on reproduction, selection on survival, and selection on both. These different sources of selective force were not considered in Felsenstein's original model.

population. We use this binomial sampling to model the process of picking N_1 individuals from the offspring pool in order to form the new young age class. Similarly,

$$H(k; N, K, n) = \frac{\binom{K}{k} \binom{N-K}{n-k}}{\binom{N}{n}}$$

denotes the probability of obtaining k mutants in n draws without replacement, in which N is the total number of individuals, and K is the current number of mutants. We use this hypergeometric sampling for drawing N_2 young individuals that enter the old age class in the next time step. There are $(N_1 + 1)(N_2 + 1)$ different states of the age-structured population; therefore, the state transition matrix $\hat{\mathbf{P}}$ [with elements $p(x_1 x_2^{(t)} \rightarrow x_1 x_2^{(t+1)})$] has dimension $(N_1 + 1)(N_2 + 1) \times (N_1 + 1)(N_2 + 1)$. The fixation probability vector $\hat{\mathbf{p}} = (\rho_{00}, \rho_{01}, \dots, \rho_{0N_2}, \rho_{10}, \rho_{11}, \dots, \rho_{1N_2}, \dots, \rho_{N_1 0}, \rho_{N_1 1}, \dots, \rho_{N_1 N_2})^{\text{con}}$ contains the fixation probabilities of the mutant type from each of the $(N_1 + 1)(N_2 + 1)$ distinct population states.

The transition matrix $\hat{\mathbf{P}}$ is stochastic and has unique eigenvalue 1. Given the absence of mutation, we have $\rho_{00} = 0$ and $\rho_{N_1 N_2} = 1$. In practice, we can thus remove the first row and first column of the transition matrix $\hat{\mathbf{P}}$ to form a new transition matrix $\mathbf{P}$ that corresponds to the fixation probability vector $\mathbf{p}$, which is $\hat{\mathbf{p}}$ having the first

Figure 2 Fixation probability of a neutral mutant in a population of total size 20. Symbols are results from numerical calculations (based on the transition matrix); the solid line is the known analytical solution (see Appendix A). The dashed line marks the fixation probability when age structure is absent. There are two age classes in this example; therefore, the fraction of young individuals ranges from 0.5 to 1. The neutral mutant has a higher probability of reaching fixation in populations with more old individuals than in populations with more young individuals. A *Mathematica* notebook file for generating this figure can be found in Supplemental Material, File S1.

element 0 removed. To calculate $\mathbf{p}$, we compute the eigenvector that corresponds to eigenvalue 1 of the transition matrix $\mathbf{P}$ numerically and then normalize it by setting $\rho_{N_1 N_2}$ to 1.

As a benchmark for later comparisons, we show in Figure 2 the fixation probability of a single neutral mutant arising from the young age class. We can see that a neutral mutant is more likely to reach fixation in populations with more old individuals than in populations with more young individuals.

A natural explanation of this pattern is the differentiated reproductive values in the population. In an age-structured population, the fixation probability of a neutral mutation equals the initial frequency of the mutant subpopulation weighted by reproductive values (Emigh 1979a). The reproductive value of an individual of a given age expresses the contribution of that individual to the future ancestry of the population. We can use a matrix population projection model to compute the reproductive values of different ages (Caswell 2001). This model is a square matrix that describes the vital rates (*i.e.*, fertility and survival) of the population organized by demographic class, for example:

$$\begin{pmatrix} F_1 & F_2 & F_3 & \dots & F_{\omega-1} & F_{\omega} \\ S_1 & 0 & 0 & \dots & 0 & 0 \\ 0 & S_2 & 0 & \dots & 0 & 0 \\ 0 & 0 & S_3 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & S_{\omega-1} & 0 \end{pmatrix} \quad (2)$$

In the case of an age-structured population, the first row of the projection matrix contains the fertilities of each age

class. The fertility F_k at the top of the k th column gives the number of offspring born to an individual in age class k that successfully enter the first age class at the next time step. The subdiagonal of the matrix contains the age-specific survival probabilities. S_k stands for the fraction of individuals in age class k that will enter age class $k + 1$ at the next time step. All other matrix entries are zero. The matrix population model can be right-multiplied by the population state vector. The result of this multiplication is the projection of the population state to the next time step. If this operation is iterated, the vector representing the population state eventually becomes proportional to the leading right eigenvector of the matrix population model. At this point, the population is in a demographically stable state, and its growth rate corresponds to the leading eigenvalue of the matrix. With appropriate scaling, the leading left eigenvector gives the reproductive value of each age class (Caswell 2001). Because this model only involves matrix algebra, it is entirely deterministic. In our case, the matrix population model is a 2×2 matrix because we have only two age classes. Because we assume a constant size, the leading eigenvalue of this matrix must be 1.

To illustrate our approach, let us first consider the case of a neutral mutant, in which mutant and wild type have the same fitness. Using the description of the life history in our population given earlier, our matrix population model is written as

$$\begin{pmatrix} \frac{N_1}{N_1 + N_2} & \frac{N_1}{N_1 + N_2} \\ \frac{N_2}{N_1} & 0 \end{pmatrix} \quad (3)$$

The right eigenvector of this matrix corresponding to the eigenvalue of 1 is

$$\mathbf{e}_R = \left(\frac{N_1}{N_1 + N_2}, \frac{N_2}{N_1 + N_2} \right)^T$$

This vector is already scaled to give the stable age distribution in the asymptotic population. The corresponding left eigenvector

$$\mathbf{e}_L = \left(\frac{N_1 + N_2}{N_1}, 1 \right)$$

gives the reproductive values. With these two vectors, we can now give reproductive value weights to the initial frequency of a neutral mutant of young age in our population at demographic stability. The mutant's reproductive value thus equals

$$\frac{N_1 + N_2}{N_1}$$

The reproductive value in the total population is the population size N multiplied by the scalar product $\mathbf{e}_L \bullet \mathbf{e}_R$,

which is the total reproductive value at stability in the unit-size population $N(\mathbf{e}_L \bullet \mathbf{e}_R) = N_1 + 2N_2$ (Caswell 2001). Taking the ratio of the initial mutant reproductive value to the total reproductive value in the population, we obtain

$$\frac{1}{N_1} \frac{N_1 + N_2}{N_1 + 2N_2}$$

which corresponds to the fixation probability of the mutant (Emigh 1979a). Observing that $N = N_1 + N_2$ is fixed, the derivative of this last quantity with respect to N_1 is

$$-\frac{2N(N - N_1)}{N_1^2(2N - N_1)^2}$$

which is strictly negative. Therefore, the fixation probability of a neutral mutant decreases as the fraction of young individuals increases.

Another way to understand this pattern is to calculate the age structure-dependent fixation probability directly (Charlesworth 1994). With the fraction of young individuals in the population $f = N_1/N$, the fixation probability of a single mutant in a population of size N is $[Nf(2-f)]^{-1}$, which is identical to our earlier result. A derivation of the fixation probability with this approach can be found in Appendix A.

To set the basis for later comparisons, we have first focused on the fixation probability of a neutral mutant in the first age class. In the following, we focus on the population dynamics and fixation probability of a beneficial mutant that has a constant selective advantage $r > 1$. This corresponds to the traditional notation of $r = 1 + s$ in the classic population genetics literature. We explore one by one the effects of selection on reproduction, on survival, and on both.

Selection on Reproduction

If selection acts only on reproduction, the mutant produces r times more offspring than the wild type. The transition probability from state $x_1 x_2^{(t)}$ to $x_1 x_2^{(t+1)}$ is then

$$p(x_1 x_2^{(t)} \rightarrow x_1 x_2^{(t+1)}) = B \left[x_1^{(t+1)}; N_1, \frac{r(x_1^{(t)} + x_2^{(t)})}{r(x_1^{(t)} + x_2^{(t)}) + N_1 - x_1^{(t)} + N_2 - x_2^{(t)}} \right] \times H(x_2^{(t+1)}; N_1, x_1^{(t)}, N_2) \quad (4)$$

It seems difficult to find a closed form of the fixation probability without making additional assumptions, such as approximating the noncentral hypergeometric distribution, which arises from biased sampling, with a binomial distribution, which requires that N_{i+1} is either very small or close to N_i (Emigh 1979a,b). However, we can obtain some first insights from calculating $E(x_1^{(t+1)} + x_2^{(t+1)})$, i.e.,

Figure 3 Constant selection on reproduction in populations with fixed total size of 20. Symbols represent the fixation probability of a single young mutant with fitness r . The solid line in A represents the fixation probability in the neutral case when $r = 1$. There is always a minimum of the fixation probability for an intermediate fraction of young individuals. (B–D) The fraction of young individuals at the minimum decreases when r increases. A *Mathematica* notebook file for generating this figure can be found in File S2.

the expected total number of mutants in the next time step. Thus,

$$\begin{aligned} E(x_1^{(t+1)} + x_2^{(t+1)}) &= E(x_1^{(t+1)}) + E(x_2^{(t+1)}) \\ &= \frac{r(x_1^{(t)} + x_2^{(t)})N_1}{(r-1)(x_1^{(t)} + x_2^{(t)}) + N_1 + N_2} \\ &\quad + \frac{x_1^{(t)}N_2}{N_1} \end{aligned} \quad (5)$$

Although $E(x_1^{(t+1)} + x_2^{(t+1)})$ is not a proxy of the fixation probability per se, it illustrates an important aspect of the fixation dynamics.

Given that the total size of the population is fixed, the state of the population is determined by the relative numbers of young and old individuals. Replacing N_2 by $N - N_1$, we observe a minimum of the expected number of mutants in the next time step, where $dE(x_1^{(t+1)} + x_2^{(t+1)})/dN_1 = 0$. The corresponding number of young individuals is

$$N_1^* = \sqrt{x_1^{(t)}N \left[1 + \frac{N - x_1^{(t)} - x_2^{(t)}}{r(x_1^{(t)} + x_2^{(t)})} \right]} \quad (6)$$

Because the expected number of mutants in the next time step depends on the number of young individuals in a nontrivial way once we depart from neutrality, the fixation probability of the mutant could in principle also have an extremum in populations with an intermediate fraction of young individuals. A numerical consideration of fixation probabilities shows that the fixation probability indeed has a minimum for an intermediate fraction of young individuals, as shown for a population of total size 20 in Figure 3. Appendix B shows that a weak selection analysis also recovers the U-shaped pattern of fixation probability, although there are foreseeable

disagreements on the exact values, especially when the selective advantage of the mutant becomes large.

Selection on Survival

If selection only works on survival, the mutant type has the same fecundity as the wild type but is r times more likely to survive to age two. Because of the selective advantage of the mutant, the survival step follows the Wallenius noncentral hypergeometric distribution instead of the standard hypergeometric distribution (Fog 2008b). The stochastic process can be illustrated conveniently with an urn model. Think of an urn with black and white balls. We take n balls one by one from the urn without replacement. With every removal, a black ball is r times more likely to be chosen than a white ball. The Wallenius noncentral hypergeometric distribution tells us the probability of obtaining x black balls by the end of the experiment. Similarly, in our case, there are N_1 mutant and wild-type individuals in the first age class. Among them, N_2 will be chosen to form the next age class. At each draw, a mutant is r times more likely to be chosen than a wild type. The Wallenius noncentral hypergeometric distribution tells us the probability of obtaining x_2 mutants in the next time step.

Therefore, the transition probability from state $x_1x_2^{(t)}$ to $x_1x_2^{(t+1)}$ is

$$p(x_1x_2^{(t)} \rightarrow x_1x_2^{(t+1)}) = B(x_1^{(t+1)}; N_1, \frac{x_1^{(t)} + x_2^{(t)}}{N_1 + N_2}) H^W(x_2^{(t+1)}; N_1, x_1^{(t)}, N_2, r) \quad (7)$$

in which H^W is the Wallenius noncentral hypergeometric distribution, for which closed-form implementations are numerically cumbersome (Fog 2008a).

When the selective advantage of the mutant r is small, H^W can be approximated by the corresponding standard hypergeometric distribution, and thus the fixation probability of the mutant is similar to that of the neutral case (Figure

Figure 4 Constant selection on survival in populations with a total fixed size of 20. Symbols represent the fixation probability of one single mutant in the young age class with fitness r . The solid line in A represents the fixation probability in the neutral case when $r = 1$. When r is small, the fixation probability decreases monotonically, resembling the neutral case. But when r becomes larger (B–D), there is an intermediate maximum of fixation probability. The corresponding fraction of young individuals increases when r increases. A *Mathematica* notebook for generating this figure can be found in File S3.

4A). However, when r is large, we numerically observe a remarkable increase in the fixation probability in populations with an intermediate fraction of young individuals (Figure 4B–D).

Although we cannot calculate the exact fixation probability analytically owing to the complexity associated with the Wallenius noncentral hypergeometric distribution, it is still possible to understand the pattern of having a maximum of fixation probability in populations with intermediate fraction of young individuals intuitively. First, we consider the change in the expected number of mutants in the young age class as the fraction of young individuals increases. We keep in mind that selection works on survival, and there is no selection on reproduction. Therefore, the expected number of young mutants in the next time step is simply proportional to the global fraction of mutants in the whole population. As N_1 increases by 1, the expected number of mutants in the young age class in the next time step increases by $(x_1^{(t)} + x_2^{(t)})/N$, which is between 0 and 1. This is irrespective of the value of N_1 .

Next, we consider the change in the expected number of mutants in the old age class as the fraction of young individuals increases. In the limit of very large selective advantage r , basically all mutants in the young age class will be selected to survive into the old age class if there is enough space; *i.e.*, namely, if N_2 is greater than the total number of mutants. Otherwise, among all the mutants in the young age class, N_2 of them will survive and enter the old age class. Therefore, the expected number of mutants in the old age class in the next time step is the minimum between the current number of mutants in the young age class and the total number of old individuals in the population. In short, if $r \gg 1$, then $x_2^{(t+1)} \approx \min\{x_1^{(t)}, N_2\}$. When the fraction of young individuals is small, $N_1 < N - x_1^{(t)}$, the expected number of mutants in the old age class in the next time step does not change as N_1 increases by 1 because each of these mutants will survive. But when the number of young individuals is large, *i.e.*, $N_1 > N - x_1^{(t)}$, the expected number of mutants in the old

age class is limited by N_2 . In this case, as N_1 increases by 1, N_2 and thus $x_2^{(t)}$ must decrease by 1 because of the constant population size.

Thus, the change in the expected total number of mutants in one time step is the sum of the change in the expected number of mutants in the young age class and the expected number of mutants in the old age class. As N_1 increases by 1, on the one hand, the expected number of mutants in the young age class in the next step should increase by between 0 and 1. On the other hand, the expected number of mutants in the old age class does not change when N_1 is small but decreases by 1 when N_1 becomes large. Therefore, the expected total number of mutants in the next time step should first increase and then decrease as N_1 increases. The corresponding fixation probabilities are explored numerically in Figure 4.

Selection on Both Reproduction and Survival

In the two preceding sections, we have shown that if selection only acts on survival, there is a minimum of the fixation probability when the number of young individuals is intermediate. But if selection acts on survival and the selective advantage of the mutant is sufficiently large, there is a maximum of the fixation probability when the number of young individuals is intermediate.

If selection works on both reproduction and survival, we assume that a beneficial mutant not only may produce more offspring but also is more likely to survive to the next age. This double effect could result from the fact that the mutant allocates extra payoff to both reproduction and survival. Consider a mutant that has increased access to food resources compared to the wild type. As a result, it may choose to (or be genetically programmed to) consume the extra food immediately, thereby allocating most of the benefits to reproduction and relatively little to improving its chance of surviving to the next round of reproduction. However, the mutant may choose

Figure 5 A comparison between selecting on reproduction, on survival, and on both. The figure shows the fixation probability of a single beneficial mutant in the young age class. Solid lines represent the fixation probability in the neutral case when $r = 1$. The pattern of selecting on both reproduction and survival shows a combined effect. The magnitude of the fixation probability across different age structures is closer to the case when selecting solely on reproduction, but the shape of having an intermediate maximum when r is large is similar to selecting on survival (note the different scale on the y-axis). Total population size $n = 20$. A *Mathematica* notebook for generating this figure can be found in [File S4](#), [File S5](#), and [File S6](#).

to save most of the food for provision, thereby having little improvement in the current round of reproduction but substantial improvement in the chance of survival. There exists a well-established body of allocation theory with different functional forms for allocating limited resources to reproduction and survival. This further leads to different patterns of aging in different species and populations. For a recent review, see Baudisch and Vaupel (2012). In the case where selection acts on both reproduction and survival and the mutant allocates its payoff benefit to both, the transition probability from state $x_1 x_2^{(t)}$ to $x_1 x_2^{(t+1)}$ is

$$p(x_1 x_2^{(t)} \rightarrow x_1 x_2^{(t+1)}) = B \left[x_1^{(t+1)}; N_1, \frac{r_1 (x_1^{(t)} + x_2^{(t)})}{r_1 (x_1^{(t)} + x_2^{(t)}) + N_1 - x_1^{(t)} + N_2 - x_2^{(t)}} \right] \times H^W(x_2^{(t+1)}; N_1, x_1^{(t)}, N_2, r_2) \quad (8)$$

in which the mutant produces r_1 times more offspring than the wild type and is r_2 times more likely to survive to the next age.

In this study, we focus on demonstrating the distinct effects of different selective forces on the fixation probability of mutants. Therefore, we choose arbitrarily the simple case where $r_1 = r_2$ to study the model, as Altrock and Traulsen (2009) did in studying the evolutionary dynamics of stochastic birth-death processes. Appendix C provides examples of allocating fitness benefits between reproduction and survival following a linear pattern, where r_1 and r_2 are different. Following the same method, the effects of allocating benefits in

other ways can be studied. We also show in Appendix C that mutants taking a different life-history tradeoff strategy also have complex nonlinear patterns of fixation probabilities depending on the population demographic structure. We provide an example showing that trading for higher reproduction at the cost of reduced survival produces very different patterns of fixation probability from the other way around. Considering the complexity of this question and the vast diversity in the range of life-history tradeoff strategies, it is better to study this in detail in a separated work.

From the numerical calculation results (for the special case of $r_1 = r_2 = r$) shown in Figure 5, we see that the pattern of fixation probability of a single mutant in the young age class has combined effects from selecting on both reproduction and survival. On the one hand, the value of the fixation probability is more similar to the case where selection works solely on reproduction. (Note that the end points in the first and third panels are identical because at these points the effect of age structure disappears.) On the other hand, the pattern of having an apparent maximum of the fixation probability in populations with an intermediate fraction of young individuals is more similar to the case where selection works solely on survival.

Effects of Population Size

Up to now, we have shown the effects of demographic population structure on the fixation probability of mutants. It is important to study how the magnitude of the effects scales

Figure 6 (A–C) Population size has a larger effect on the fixation probability if the relative fitness advantage of the mutant is small, in this case $r = 1.005$. (D–F) Demographic population structure has a larger effect on the fixation probability if the relative fitness advantage of the mutant is large, in this case $r = 1.2$. Symbols of different colors represent different population sizes. Color-coding is consistent in all panels. A *Mathematica* notebook for generating this figure can be found in [File S7](#) and [File S8](#).

with the strength of selection and population size. In this section, we show that the relative importance of population size and demographic population structure depends crucially on the strength of selection; in this case, it depends on the relative fitness of the mutant compared to the wild type.

If the relative fitness of the mutant is small (e.g., $r = 1.005$, as shown in Figure 6, A–C), population size has a larger effect. It does not matter too much if selection works on reproduction, survival, or both because in this limit, instead of demographic structure, the size of the population plays the most important role in determining the fixation probability. Fixation and extinction are mainly driven by drift. Therefore,

the general pattern is that the fixation probability decreases with population size. But if the fitness of the mutant is large (e.g., $r = 1.2$, as shown in Figure 6, D–F), the demographic structure of the population plays an essential role. Note that symbols of different color represent different population sizes. In this case, the symbols corresponding to population sizes 80 and 100 almost overlap for selecting on reproduction, survival, or both. Therefore, the effect of demographic structure on the fixation probabilities does not diminish with population size, but there is convergence for large populations to a certain effect size. The pattern of having an intermediate minimum of fixation probability when selecting

Figure 7 Fixation probability of a single mutant from the first age class in a population of three age classes depending on the size ratio between age classes $\gamma = N_2/N_1 = N_3/N_2$. Circles and crosses represent results from the numerical solution (by calculating the corresponding eigenvector of the eigenvalue 1 of the population state transition matrix) and simulation, respectively. The solid line represents the analytical result (details in Appendix A). Each data point in the simulation result is calculated from 10^7 realizations. The dotted line marks $1/N$, the fixation probability of a single mutant in a well-mixed age-homogeneous population when selection is absent. (A) For a population size of $N = 30$, we show results from both the numerical solution and simulation. The slight wiggling of the fixation probability curves is the result of rounding errors when constructing the three age classes. The wiggling diminishes when population size increases. (B) For $N = 100$, we only show results from simulation because it is computationally costly to calculate the eigenvectors for large matrices. Python codes and a Mathematica notebook file for generating this figure can be found in File S9 and File S10.

on reproduction is preserved irrespective of population size. The intermediate maximum of the fixation probability when selecting on survival exists when the relative fitness of the mutant is not too small.

Another interesting observation is that the fixation probability of a single mutant is higher in larger populations than in smaller populations, when r is large, and when selecting on reproduction or both reproduction and survival. This is similar to a feature of the Wright-Fisher process (details in Appendix D).

We also assume that population size is fixed over time. It also would be interesting to study how population size fluctuations may change the dynamics. In general, although the Markov approach we used in this work allows us to calculate the exact fixation probability and has lead us to find the interesting nonmonotonic patterns, it does have limitations in numerically analyzing large or fluctuating population sizes. In such cases, we need to update the population state transition matrix dynamically, depending on the detailed population updating processes. Every time the population changes its size, the state space is updated. Consequently, the transition probabilities from one state to another also have to change. Although the fixation probability still can be obtained from simulations, it would be challenging to derive analytical results. Compared to the Markov approach, the branching-process approach and the diffusion-approximation approach may be more suitable modeling frameworks for analyzing the effects of population size fluctuations. See Patwa and Wahl (2008) and Wahl (2011) for comprehensive reviews on different approaches to studying the fixation probability of mutants.

In Appendix B, the results we derived from weak selection analysis only require the assumption that the resident population have size N when the initial mutant is first introduced, but they do not require this population size to be kept constant thereafter. The diffusion approximation is meant to work when the population size fluctuates over time despite having unity geometric growth in the limit of infinite size. In populations of finite size, as a result of demographic stochasticity, the total number of individuals fluctuates with time. The smaller the population size, the greater are the fluctuations. This is so because random independent variation in survival and reproduction between individuals is hard to average out when the population size is very small (Vindenes *et al.* 2009). This suggests, qualitatively, that the result of having a U-shaped pattern of fixation probability when selecting on reproduction should not be restricted to situations in which the population size is kept constant over time.

Besides the classic works of Ewens (1967), Kimura and Ohta (1974), Crow (1979), and Otto and Whitlock (1997), there are a number of recent works that study the effects of population size fluctuation on the fixation probability of mutants, including Parsons and Quince (2007a), Orr and Unckless (2008), Engen *et al.* (2009a,b), Parsons *et al.* (2010), Uecker and Hermisson (2011), and Waxman (2011). Important insights from recent developments include the great importance of studying the detailed processes of population dynamics and to distinguish and examine the effects of selection, drift, and the interactions of both. For example, Waxman (2011) pointed out that changes in population size are not equivalent to corresponding changes in selection, for they can result in less drift than anticipated. Uecker and Hermisson (2011) showed that even for the same logistic growth of the

population, depending on whether it results from a reduction of fertility while keeping mortality constant or an increase of mortality while keeping fertility constant, the fixation probability can be very different as a result of the stronger effects of drift in the second scenario.

Beyond Two Age Classes

So far we have only considered the case of two age classes. In this section, we give a proof of principle that the results shown in preceding sections are not artifacts of the assumption of two age classes. Instead, the nontrivial effects of population demographic structure on the fixation probability of a mutant are also preserved in populations with multiple age classes.

In a demographically stationary population with ω age classes and a total size N , assuming the average survival probability $\gamma \in [0, 1]$ is constant from one age class to the next, the number of individuals in each age class is determined by the equations

$$\begin{aligned} N_j &= \gamma N_{j-1} = \gamma^{j-1} N_1 \quad \text{for } j = 2, 3, \dots, \omega \\ \sum_{j=1}^{\omega} N_j &= N \end{aligned} \quad (9)$$

Because we are only considering integer N_j , the number of individuals in each age class has to be rounded. We do this by calculating N_j under the condition of a fixed integer N first and perform the rounding afterward. We only show simulations where the N_j add up to our choice of N .

The choice of a constant γ corresponds to species such as the freshwater hydra (*Hydra magnipapillata* and *H. vulgaris*) living under controlled laboratory conditions (Martínez 1998; Schaible *et al.* 2015). In field studies, approximately constant survival probabilities after the age of reproductive maturity also have been observed in birds, frogs, invertebrates, and plants (Baudisch *et al.* 2013; Jones *et al.* 2014).

For other species, the survival (mortality) rate can differ widely over different ages or life stages. For example, most mammals including humans have decreasing survival rates after adulthood (γ decreases with age). However, for the desert tortoise, the survival probability increases monotonically with age; see Jones *et al.* (2014) for a review of the diverse patterns of age/life-stage-dependent mortality rates.

We show in Figure 7 the patterns of fixation probability for a single mutant from the first age class in a population of three age classes with constant γ ($m = 3$). When selection is absent, the fixation probability of the mutant decreases monotonically as the survival rate γ decreases. In the boundary case, where $\gamma = 0$, all individuals in the population are in the first age class. Therefore, $N_1 = N$, and the fixation probability of the mutant reduces to $1/N$. In the case where selection works on reproduction or survival, we show that the intermediate minimum or maximum of the fixation probability still persists.

Data availability

The authors state that all data necessary for confirming the conclusions presented in the article are represented fully within the article.

Discussion and Conclusion

Although it is clear that the likelihood of incorporating a beneficial mutation in the gene pool is a function of the life-history architecture of the population, little has been done to pinpoint the direct effects of different life-history patterns on promoting or hindering adaptive evolution. In this work, we approach this problem by building on the seminal Felsenstein model of populations with overlapping generations (Felsenstein 1971). We explore the effects of different sources of evolutionary force, including selecting on reproduction, on survival, and on a combination of both numerically. We also study the relative importance of the size and demographic structure of the population.

First, our work reveals fundamental differences between selection on reproduction and on survival in populations with demographic structures. The differences are remarkable even in the simple case where the population is spatially well mixed, and neither density nor frequency affects the relative fitness of the mutant. It is known that in well-mixed populations under constant selection, selecting on reproduction or on survival is equivalent when mutation is absent (Ewens 2004; Kaiping *et al.* 2014). In spatially structured populations, selecting on reproduction and on survival is different in general, but it is possible to produce the same effects (Zukewich *et al.* 2013; Hindersin and Traulsen 2015; Kaveh *et al.* 2015). For example, under the Moran process scheme, selecting on reproduction with a birth-death updating rule is still equivalent to selecting on survival with a death-birth updating rule in any population with “homogeneous” structures (*e.g.*, lattices, cycles, and island models) and symmetric dispersal (Taylor *et al.* 2011). It is worthwhile to note that in degree-heterogeneous graphs, the fixation probability of an advantageous mutant depends crucially on whether selection works on reproduction or on survival (Antal *et al.* 2006; Hindersin and Traulsen 2015; Kaveh *et al.* 2015). Even when selection works only on reproduction, the sequence of birth and death events can lead to completely different evolutionary dynamics (Zukewich *et al.* 2013; Kaveh *et al.* 2015). For almost any random graph, a selectively advantageous mutant almost always has a higher-than-neutral fixation probability if birth takes place before death but has a lower-than-neutral fixation probability if death happens first (Hindersin and Traulsen 2015). Although the differences in selecting on reproduction and on survival are relatively well recognized and studied in spatially structured populations, less is known in populations with a demographic structure.

Even under constant selective advantage, the life history of individuals in the population makes the evolutionary dynamics differ drastically with different sources of selective force

(Houston and McNamara 1999; Caswell 2001). In the future it would be interesting to go beyond the simple case of constant selection and investigate the effects of density- and frequency-dependent fitness of the mutants. In the well-mixed case, low density favors individuals who direct their efforts toward exploring the ecological environment and thereby maximizing their reproduction rates. But under high-density conditions, because most resources have already been absorbed into the population, it is more efficient to direct one's effort toward exploiting other population members through interactions (Blute 2011). Usually, the successfulness of a strategy is not determined by its nature alone but rather by the presence and frequency of other strategies in the population. Density and frequency effects are hardly disconnected from each other in natural populations, and it is often necessary to take both into account to capture the important features of evolutionary dynamics, especially when there is substantial change in population size (Novak *et al.* 2013; Huang *et al.* 2015; Li *et al.* 2015b). Under the framework of evolutionary game theory, elegant conditions such as the one-third rule have been obtained (Nowak *et al.* 2004; Imhof and Nowak 2006; Lessard and Ladret 2007) that determine whether strategies such as cooperation can evolve in the first place. But it is unclear whether such conditions still hold in populations with demographic structures. Therefore, it seems interesting to study the co-evolution between population demography and game-theoretic strategies in future work.

In natural populations, species display an enormous variety of life-history patterns (Jones *et al.* 2014). Often mutations affect the fitness of individuals in both reproductive and survival aspects. A classical example is the thoroughly discussed ornamented trains of male peacocks, which are sublimely beneficial in terms of mating success but at the same time tremendously costly when it comes to the ability to escape from predators. Another beautiful example is the shape of the wings in migrating birds. Pointed wings are aerodynamically desirable for fast and long-distance flights (Mönkkönen 1995; Berthold 1996; Hedenström 2002; Bowlin and Wikelski 2008; Minias *et al.* 2015), but they reduce the maneuverability that helps birds with foraging and courtship displays (Alatalo *et al.* 1984; Swaddle and Lockwood 2003). Precisely due to the high benefits and high costs of pointed wings, the change in selective pressure leads to the change of wing morphology in bird populations. This has been observed in many passerine species, *e.g.*, the fast evolution of stonechats (*Saxicola torquata*) in response to changing environmental conditions (Baldwin *et al.* 2010). It is interesting also to note that evolution can go to great detail in balancing the cost and benefits of a single morphologic trait, and life history serves as a channel through which evolutionary forces fine-tune the balance. As an example and also a demonstration of its plastic potential, it has been found that the juveniles of migrating birds have less pointed wings than adults. This could be due to the fact that juveniles are more naive and thus more vulnerable to predators. Under elevated predation

pressure, improved maneuverability is more important than migration performance, particularly in the early stage of life (Pérez-Tris and Tellería 2001). For more examples of the amazing variety of survival and reproduction trajectories over the life course of various species, Jones *et al.* (2014) provide a recent review.

In this work, we focused mostly on the simple case of two age classes. But it is possible to extend our results to cases with multiple age classes, as demonstrated in the section *Beyond Two Age Classes*. We have shown how the fixation probability of a mutation with an effect on certain components of the life history is influenced by the demographic structure of the resident population, *i.e.*, the relative fraction of young vs. adult individuals. We note that a natural interpretation of the same results also can be given in terms of the rate of aging that characterizes the resident population. In fact, the relative abundances of young and adult individuals depend on the probability of newborn survival to young age and the probability of surviving from young age to old age. Aging is defined as an age-related deterioration in survival. Aging features in a large number of species is one of the most salient life-history traits. It follows from the definition of aging in our model that populations that are composed of a higher fraction of young individuals are characterized by a higher rate of aging (*i.e.*, stronger deterioration of survival with age). Conversely, populations with a higher representation of old individuals may possess no aging at all or even negative aging (*i.e.*, survival does not decline but it may even increase with age) [see Baudisch and Vaupel (2012) and Jones *et al.* (2014)].

In this way, our results can be linked directly to the effect that an important life-history trait exerts on adaptive evolution. If natural selection acts on reproduction, for any beneficial mutant, intermediate rates of aging always reduce the fixation probability, although the chance of fixation may be higher in populations with low or negative rates of aging, depending on the difference in fitness between the mutant and the wild type. If natural selection acts on survival and the fitness difference between the beneficial mutant and the wild type is not too small, there is a maximum of fixation probability in populations with intermediate rates of aging, while in populations with extremely positive or negative rates of aging, the fixation probability of the beneficial mutant is reduced. In this regard, it would be of interest to study variation in the rate of adaptation in systems that have already been established for within-species comparisons of the rate of aging across populations. For example, populations of guppies living under different environmental conditions have proven to be a valuable model to understand ecologically induced variation in aging within a single species (Reznick *et al.* 2004; Bronikowski and Promislow 2005). Similarly, different life-history ecotypes of the garter snake show different aging patterns (Sparkman *et al.* 2007; Robert and Bronikowski 2010). If natural selection acts on both survival and reproduction, depending on how fitness advantages are allocated and the magnitude of the fitness difference between mutants and

wild types, complex patterns with multiple extrema of the fixation probability with respect to the rate of aging can emerge.

Summary

To summarize, in this work, we have studied the direct effects of population demographic structures on stochastic evolutionary dynamics under the constant selection regime. Using a model with two age classes and constant population size, we have compared the fixation probability of mutants under different population demographic structures. Different targets of selective force, as well as the relative impacts of the size and structure of the populations, are also evaluated in our analyses. Through this work, we hope to call attention to the importance of considering life history when studying evolutionary dynamics. Facilitated by modern computational power, we now have the opportunity to delve into many interesting questions that were technically difficult to approach a few decades ago. Our work opens up new directions for future research, including the co-evolution of population structure, resource allocation, and strategic dynamics; the impacts of demography on the rate of adaptive evolution; and the density/frequency-dependent fitness effects in populations with different life-history patterns.

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Appendix A: Fixation Probability of a Single Mutant in the Young Age Class

Fisher's reproductive value v_k of an individual in age class k in an age-structured population with prebreeding census is (Charlesworth 1994)

$$v_k = \frac{\lambda^k}{Tb l_k} \sum_{x=k}^{\omega} l_x F_x \lambda^{-x} \quad (A1)$$

in which λ is the asymptotic growth rate of the population, $l_k = S_1 S_2 \cdots S_{k-1}$ is the probability of an individual surviving at least to age class k with $l_1 = 1$, F_k is the expected number of offspring to an individual in age class k , T is the generation time in the stable population, b is the birth rate in the stable population, and ω is the maximum attainable age.

In our specific model of two age classes ($\omega = 2$), the parameter values are $\lambda = 1$ (constant population size), $l_1 = 1$, $l_2 = N_2/N_1$, and $F_1 = F_2 = N_1/N$, where $N = N_1 + N_2$. We have $v_1 = 1$ and $v_2 = N_1/N$. Following Emigh (1979a), the fixation probability of a selectively neutral mutant is

$$\frac{v_1}{v_1 N_1 + v_2 N_2} = \frac{1}{N_1 (2 - \frac{N_1}{N})} \quad (A2)$$

In the case of multiple age classes, as in the section *Beyond Two Age Classes*, $l_k = \gamma^{k-1}$, in which γ is the survival probability to the next age class $F_k = N_1/N = 1/\sum_{i=0}^{\omega-1} \gamma^i$, for all k . The size of the k th age class is $N_k = N \gamma^{k-1} / \sum_{i=0}^{\omega-1} \gamma^i$. Therefore, the reproductive value of the k th age class in a stationary population is

$$v_k = \frac{\sum_{i=0}^{\omega-k} \gamma^i}{Tb \sum_{i=0}^{\omega-1} \gamma^i} \quad (A3)$$

The fixation probability of a single mutant in the first age class is then

$$\frac{v_1}{\sum_{k=1}^{\omega} v_k N_k} = \frac{1}{N} \frac{(\sum_{k=1}^{\omega} \gamma^{k-1})^2}{\sum_{k=1}^{\omega} k \gamma^{k-1}} \quad (A4)$$

In the case of two age classes, $\omega = 2$ and $\gamma = N_2/N_1$. Denote the fraction of young individuals as $f = N_1/N$, and the fixation probability recovers $[Nf(2-f)]^{-1}$.

Appendix B: Weak Selection Analysis for Selecting on Reproduction

Following Kimura (1957, 1962), Emigh (1979a,b), and Vindenes *et al.* (2009), in an age-structured population of haploid individuals, the fixation probability of a single mutant with selective advantage s in age class i can be approximated by

$$\frac{1 - \exp(-2sv_i/\sigma^2)}{1 - \exp(-2sN/\sigma^2)} \quad (B1)$$

where N is the resident population size, σ^2 is the expected variation in geometric growth of the wild-type population, and v_i is the reproductive value of a wild-type individual in the same age class as the initial mutant. The selective advantage s of a beneficial mutation is computed as the absolute value of the difference between the stable growth rate of the wild-type, which is the leading eigenvalue of its projection matrix (Caswell 2001), and the stable growth rate that would be observed in a population composed entirely by mutants (*i.e.*, the leading eigenvalue of the mutant Leslie matrix). Following Engen *et al.* (2005) in assuming no covariances between matrix elements, the demographic variance σ^2 can be approximated by

$$\sigma^2 \approx \sum u_i \left[v_{i+1}^2 S_i (1 - S_i) + v_1^2 \text{Var}(F_i) \right] \quad (B2)$$

In this expression, S_i is the $(i + 1)$ th element of column i of the (prebreeding census) Leslie matrix, representing the survival rate of an individual in age class i , F_i is the i th element of the first row of the matrix, representing the numbers of offspring

Figure B1 Weak selection approximation to the fixation probability of a mutant with reproductive advantage r .

produced by an individual currently in age class i , and u_i and v_i are the i th elements of the right and left leading eigenvectors, respectively, of the Leslie matrix and are scaled so that $\sum u_i = 1$ and $\sum u_i v_i = 1$.

In our model, when selecting on reproduction, a mutant produces r times the offspring of the wild type. Hence, the selective advantage s of the mutant can be calculated as the absolute value of the difference between the leading eigenvalue of the Leslie matrix of the wild type (which is unity in our case of constant size) and the leading eigenvalue of the same matrix with the first row multiplied by r , *i.e.*, the leading eigenvalue of the matrix

$$\begin{pmatrix} r \frac{N_1}{N_1 + N_2} & r \frac{N_1}{N_1 + N_2} \\ \frac{N_2}{N_1} & 0 \end{pmatrix} \quad (\text{B3})$$

To compute the demographic variance, we calculate $\text{Var}(F_i)$ by treating first-row elements of the resident Leslie matrix as averages of Poisson distributions. Figure B1 (corresponding to Figure 3 in the text) and Figure B2 (corresponding to Figure 5, A and B, in the text) show the results of using Equation B1 with the same r and N values used in our numerical solutions.

Figure B2 Weak selection approximation to the fixation probability of a mutant with reproductive advantage for different population sizes and selective advantages. Note that in the right panel, when selective advantage of the mutant is relatively large ($r = 1.2$), the symbols representing different population sizes overlap with each other (especially from $N = 40$ to $N = 100$).

Figure C1 Effects on fixation probability of a mutant that has an extra fitness benefit of $s = 0.2$. (A) The fixation probability increases monotonically with the fraction of benefits allocated to reproduction. In the older population, the fraction of young individuals is 0.55, and in the younger population, the fraction of young individuals is 0.95. (B) If the fraction of benefits that can be allocated to reproduction is fixed, the fixation probability varies in a

nonlinear way in populations with different demographic structures. Here a is the fraction of extra benefits allocated to reproduction ($N = 20$). A *Mathematica* notebook for generating this figure can be found in File S1.

Despite the foreseeable quantitative disagreements, especially when the selective advantage becomes large, the weak selection approximation results preserve the U-shaped pattern of fixation probability under different selection intensities and at different population sizes.

Appendix C: Allocation and Tradeoff of Fitness Benefits

Earlier we showed the combined effects of selecting on reproduction and survival at the same time. There we used an arbitrary example of $r_1 = r_2 = r$ for simplicity. In this case, the mutant type not only produces r times more offspring than the wild type but also is r times more likely to survive to the next age class. This, of course, is a very special case. It corresponds to the scenario where the mutant happens to split its payoff increment “equally” on improving reproduction and survival. In nature, mutants can, in principle, allocate the payoff increment in any combination of improving reproduction and survival. The mutant can even commit so much to improving one of them at the cost of reducing or eliminating the other. This leads to the “life-history tradeoff.” Depending on the physiologic nature of the species and social interactions in the population, the consequence of putting more weight on one aspect at the cost of reducing the other can be very complex. To illustrate this, in the following, we give examples of allocating increments of benefit in different ways and their consequences on the fitness probability of the mutant.

First, imagine that the mutant allocates its extra benefit in a linear way. Relative to wild types, the mutant has an extra payoff s . The mutant allocates fraction a of s to increase its reproduction and uses the rest to improve its survival. Therefore, the mutant’s

Figure C2 The effects of trading on reproduction or survival. When selection works on both reproduction and survival, a beneficial mutant may have an increase in both of them (the “trade-on scenario”) or an increase in one of them at the cost of decreasing the other (the “tradeoff scenario”) or the maintenance of the other (“zero-tradeoff scenario”). We use r_1 to denote the selective advantage on survival and r_2 to denote the selective advantage on reproduction. In the left panel, keeping selective advantage on reproduction fixed, we change the selective advantage on survival, with two trade-on scenarios, two tradeoff scenarios, and one zero-tradeoff scenario. In the right panel, keeping the selective advantage on survival fixed, we change the selective advantage on reproduction, also with two trade-on scenarios, two tradeoff scenarios, and one zero-tradeoff scenario.

Figure D1 Fixation probability of a single beneficial mutant in the Wright-Fisher process calculated numerically from the transition matrix. In the left panel, when the selective advantage of the mutant is small, as population size grows, the fixation probability approaches the classic result of $2(r-1)$. In the right panel, when the conditions of diffusion approximation are not satisfied, the fixation probability first decreases and then increases again as population size increases. A *Mathematica* notebook for generating this figure can be found in File S1.

relative fitness for reproduction is $r_1 = 1 + as$, and its relative fitness for survival is $r_2 = 1 + (1 - a)s$. Figure C1 shows the effects of this particular manner of allocating extra benefits on the fixation probability of mutants.

It is also very interesting to consider the reproduction vs. survival tradeoff. Considering the great variety in life history and different ways of allocating resources, here we present very briefly an example in Figure C2 showing that trading on reproduction or trading on survival has very different influences on the fixation probability. Given the apparent complexity of the result, it seems challenging to analyze in its whole extent.

Appendix D: Fixation Probability Increases with Population Size in the Wright-Fisher Process when r Is Large

Because we are interested in small populations, here we explore the fixation probability in the Wright-Fisher process numerically directly from the associated transition matrix. When r is small, the fixation probability of a beneficial mutant decreases with increasing size of the population, approaching $2s = 2(r-1)$. But when r is large, the fixation probability first decreases and then increases again, although the magnitude of this effect is small (Figure D1).

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Supporting Information

<http://www.genetics.org/lookup/suppl/doi:10.1534/genetics.116.188409/-/DC1>

How Life History Can Sway the Fixation Probability of Mutants

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File S1: Mathematica notebook file for generating Figure 2. (.zip, 8 KB)

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File S8: Mathematica notebook file for generating Figure 6 panel d-f. (.zip, 7 KB)

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File S9: Python codes for generating the simulation results in Figure 7. (.zip, 2 KB)

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File S10: Mathematica notebook file for generating Figure 7. (.zip, 18 KB)

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