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Weini Huang, Arne Traulsen. Fixation probabilities of random mutants under frequency dependent selection. *Journal of Theoretical Biology*, 2010, 263 (2), pp.262. <10.1016/j.jtbi.2009.11.025>. <hal-00566754>

HAL Id: hal-00566754

<https://hal.science/hal-00566754v1>

Submitted on 17 Feb 2011

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PII: S0022-5193(09)00567-0
DOI: doi:10.1016/j.jtbi.2009.11.025
Reference: YJTBI5790

To appear in: *Journal of Theoretical Biology*

Received date: 22 October 2009
Revised date: 12 November 2009
Accepted date: 27 November 2009

Cite this article as: Weini Huang and Arne Traulsen, Fixation probabilities of random mutants under frequency dependent selection, *Journal of Theoretical Biology*, doi:10.1016/j.jtbi.2009.11.025

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Fixation Probabilities of Random Mutants under Frequency Dependent Selection

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Abstract

Evolutionary game dynamics describes frequency dependent selection in asexual, haploid populations. It typically considers predefined strategies and fixed payoff matrices. Mutations occur between these known types only. Here, we consider a situation in which a mutation has produced an entirely new type which is characterized by a random payoff matrix that does not change during the fixation or extinction of the mutant. Based on the probability distribution underlying the payoff values, we address the fixation probability of the new mutant. It turns out that for weak selection, only the first moments of the distribution matter. For strong selection, the probability that a new payoff entry is larger than the wild type's payoff against itself is the crucial quantity.

Key words: Moran process, evolutionary game theory, fixation probabilities

1. Introduction

Evolutionary game theory is a method to study frequency dependent selection in asexual populations. (Maynard Smith, 1982; Weibull, 1995; Hofbauer and Sigmund, 1998, 2003; Cressman, 2003; Nowak and Sigmund, 2004). Whenever the fitness of the individuals depends on the composition of the population, the dynamics of the evolving population can be described based on an evolutionary game. Constant selection, where the fitness of a type is fixed, can be considered as a special case in this context, where the payoff depends only on the strategy, but not on the frequencies of other types in the population.

The standard approach to evolutionary game dynamics is the replicator dynamics (Taylor and Jonker, 1978; Hofbauer et al., 1979; Zeeman, 1980). It describes the change in frequency x_i of strategy i as $\dot{x}_i = x_i(\pi_i - \langle \pi \rangle)$, where π_i is the

payoff of strategy i and $\langle \pi \rangle$ is the average payoff in the population.

More recently, the focus of research has turned to finite populations. The most popular model for evolutionary game dynamics in finite populations is the frequency dependent Moran process introduced by Nowak et al. (2004). Although, mutations are often disregarded, they can be incorporated without any problems. Typically, the mutations produce types that are pre-defined in the payoff matrix and one considers the mutation-selection equilibria of the system (Bomze and Buerger, 1995; Nowak et al., 2004; Imhof et al., 2005; Imhof and Fudenberg, 2006; Traulsen et al., 2009; Antal et al., 2009a,b,c; Van Segbroeck et al., 2009).

Here, we consider a different possibility in which mutants are characterized by a new payoff matrix game with randomly chosen entries. For low mutation rates, only one mutant is present at a time. The average fixation time under neutral selection is N generations. Thus, it is unlikely that several mutants are present at the same time when the mutation rate μ fulfills $\mu \ll N^{-2}$. This estimate holds for situations in which the mutant is advantageous or disadvantageous for all abundances or if it is first disadvantageous and becomes advantageous at high abundances (Antal and Scheuring, 2006). When there is a stable coexistence between the types, however, the average fixation time diverges exponentially with the intensity of selection and the population size. In this case, our approach is only valid when the mutation rates go to zero. When the mutation rate is low, the crucial quantity of the population dynamics is the fixation probability ϕ_1 , the probability that a new mutant takes over the population. We address the fixation probability for the simple case of a 2×2 game. The entries of the payoff matrix, however, are chosen from a probability distribution, excluding the interaction of the wild type with itself, which should not be affected by the mutation. But during the course of evolution, the payoff matrix remains fixed. Due to the probabilistic payoff matrix, the fixation probability ϕ itself becomes a random number. Since Kimura (1968) introduced the neutral theory, many evolutionary biologists believe that changes in evolutionary confer only small or even vanishing selective advantages. It is very unlikely that a new mutation leads to a large selective advantage in a well adapted population. Thus, small intensities of selection seem to be biologically highly relevant (Ohta, 2002). It turns out that in our case, weak selection approximation corresponds to a moment expansion of the probability distribution, such that only the first few moments of the probability distribution of the payoff values matter. On the other hand, for strong selection the fixation probability is governed by the probability that a random mutant can invade the population.

The remainder of this paper is organized as follows: In Sec. 2, we recall the Moran process as a standard model of frequency dependent evolutionary dynam-

ics in finite populations. In Sec. 3, we address payoff matrices with Gaussian distributed entries and generalize the findings to arbitrary distributions in Sec. 4. Finally, in Sec. 5 we discuss how our findings relate to fitness distributions found empirically, based on frequency independent selection, and relate our results to this scenario.

2. The Moran Process and fixation probabilities

To model frequency dependence, we consider two player games, which can be represented by the payoff matrix

$$\begin{array}{cc} & \begin{array}{cc} A & B \end{array} \\ \begin{array}{c} A \\ B \end{array} & \begin{pmatrix} a & b \\ c & d \end{pmatrix} \end{array}$$

When A interacts with another A , it obtains a , and when it interacts with any B , it obtains b . Similarly, B obtains c or d , when interacting with A or another B respectively. Assuming there are i type A individuals and $N - i$ type B individuals, the average payoffs of A and B in a mixed population are

$$\pi_A = \frac{i-1}{N-1}a + \frac{N-i}{N-1}b, \quad (1a)$$

$$\pi_B = \frac{i}{N-1}c + \frac{N-i-1}{N-1}d. \quad (1b)$$

Here, we have explicitly assumed that there are no self-interactions. Note that the payoff difference is always a linear function in i ,

$$\Delta\pi = \pi_B - \pi_A = ui + v, \quad (2)$$

where $u = \frac{-a+b+c-d}{N-1}$ and $v = \frac{a-Nb+Nd-d}{N-1}$. The impact of the game on fitness is determined by the intensity of selection β . While commonly it is assumed that fitness f is a linear function for the payoffs, it is often mathematically more convenient to choose f as an exponential function of the payoff. Both approaches can be justified by mathematical simplicity. But the exponential function allows to address a strong selection limit, that can be relevant in specific biological situations where a certain trait is necessary for survival, e.g. resistance towards toxins. Moreover, the exponential function guarantees that that fitness is always positive, even when the payoffs π are negative (Traulsen et al., 2008). This leads to

$$f_A = e^{+\beta\pi_A}, \quad (3a)$$

$$f_B = e^{+\beta\pi_B}. \quad (3b)$$

We consider this game in the context of a frequency dependent Moran process (Nowak et al., 2004; Taylor et al., 2004; Antal and Scheuring, 2006). Suppose there is a finite population of N individuals. One individual is chosen at random, but proportional to fitness, to give birth to a new individual of the same type. Before the new offspring is added, one individual chosen at random is removed to keep the population size constant. The probability to increase the number of type A individuals from i to $i + 1$ is T_i^+ , and the probability to decrease the number of type A individuals from i to $i - 1$ is T_i^- . For the Moran process, we have

$$T_i^+ = \frac{if_A}{if_A + (N-i)f_B} \frac{N-i}{N}, \quad (4a)$$

$$T_i^- = \frac{(N-i)f_B}{if_A + (N-i)f_B} \frac{i}{N}. \quad (4b)$$

Due to the choice of an exponential function as payoff to fitness mapping, the ratio of the transition probabilities becomes particularly simple,

$$\frac{T_i^-}{T_i^+} = \frac{f_B}{f_A} = e^{+\beta(\pi_B - \pi_A)}. \quad (5)$$

In the absence of mutations, we have $T_0^+ = 0$ and $T_N^- = 0$, cf. Eqs. 4. Thus, there are two absorbing states, the state with all A , and the state with all B . The fixation probability ϕ_i describes the probability of i type A individuals to take over the entire population. Obviously, the fixation probabilities fulfill the equation $\phi_i = T_i^- \phi_{i-1} + T_i^+ \phi_{i+1} + (1 - T_i^- - T_i^+) \phi_i$, see e.g. (Goel and Richter-Dyn, 1974) for a full derivation. Solving this recursion with the boundary conditions $\phi_0 = 0$ and $\phi_N = 1$ leads to (Nowak, 2006; Antal and Scheuring, 2006)

$$\phi_i = \frac{1 + \sum_{k=1}^{i-1} \prod_{l=1}^k \frac{T_l^-}{T_l^+}}{1 + \sum_{k=1}^{N-1} \prod_{l=1}^k \frac{T_l^-}{T_l^+}}. \quad (6)$$

In particular, we are interested in ϕ_1 , for which the numerator is simply one. Together with Eq. (5), we can write ϕ_1 as

$$\phi_1 = \frac{1}{1 + \sum_{k=1}^{N-1} \exp\left[+\beta \sum_{i=1}^k (\pi_B - \pi_A)\right]}. \quad (7)$$

The two sums in Eq. (7) can be solved analytically, leading to closed expressions for the fixation probabilities (Traulsen et al., 2007a). However, for our numerical and analytical considerations, we consider Eq. (7) in the form given above.

3. Fixation of Random Mutants

We consider type B as the wild type and type A as the mutant type. Typically, one is interested in the fixation probability of a mutant with fixed values in the payoff matrix. But sometimes, the payoff of the mutant may not be fixed or even unpredictable. For this reason, we focus on payoff matrices with random entries. First, we analyze the case in which the payoff values a , b , and c that describe the mutant's interactions are Gaussian random variables with mean μ and standard deviation σ . Alternative scenarios are discussed below. Note that the payoff matrix is constant, in contrast to the work of Fudenberg and Harris (1992), where the payoff is subject to noise.

No matter which kind of randomness we consider in the payoff matrix, the fixation probability of a mutant in the population is the expectation value of ϕ_1 . Thus, we have to calculate the expectation value of the right hand side of Eq. (7).

When the new payoff values a , b , c are continuous random variables with probability density functions $p(a)$, $p(b)$, and $p(c)$ respectively, we can write the expectation of the fixation probability, Eq. (7), as follows

$$E(\phi_1) = \iiint \frac{1}{1 + \sum_{k=1}^{N-1} \exp\left[+\beta \sum_{i=1}^k (\pi_B - \pi_A)\right]} p(a)p(b)p(c) da db dc. \quad (8)$$

For a given population size N , and given probability density functions, this equation can be solved by numerical integration in three dimensions, see Fig. 1. However, the asymptotic for strong selection, $\beta \rightarrow \infty$, can be inferred directly, because for strong selection the fixation probability is either zero or one Altrock and Traulsen (2009a). For weak selection, $\beta \ll 1$, we obtain an analytical approximation for the solution of the integrals.

3.1. Weak selection approximation

To address the case of weak selection, we expand the fixation probability ϕ_1 , Eq. (7) at $\beta = 0$. First, we expand the exponential function in Eq. (7) up to second order for $\beta \ll 1$,

$$\exp\left[+\beta \sum_{i=1}^k (\pi_B - \pi_A)\right] \approx 1 + \beta \sum_{i=1}^k (\pi_B - \pi_A) + \frac{\beta^2}{2} \left(\sum_{i=1}^k (\pi_B - \pi_A)\right)^2. \quad (9)$$

Hence, we find for the fixation probability

$$\begin{aligned}\phi_1 &\approx \frac{1}{1 + \sum_{k=1}^{N-1} \left(1 + \beta \sum_{i=1}^k (\pi_B - \pi_A) + \frac{1}{2} \beta^2 \left(\sum_{i=1}^k (\pi_B - \pi_A) \right)^2 \right)} \quad (10) \\ &= \frac{1}{N + \underbrace{\beta \sum_{k=1}^{N-1} \sum_{i=1}^k (\pi_B - \pi_A)}_{C_1} + \beta^2 \frac{1}{2} \underbrace{\sum_{k=1}^{N-1} \left(\sum_{i=1}^k (\pi_B - \pi_A) \right)^2}_{C_2}}.\end{aligned}$$

After another expansion for $\beta \ll 1$ we obtain

$$\phi_1 \approx \frac{1}{N} - \beta \frac{C_1}{N^2} + \beta^2 \left(\frac{C_1^2}{N^3} - \frac{C_2}{N^2} \right). \quad (11)$$

Note that this expansion is valid for any payoff difference $\pi_B - \pi_A$. For example, let us consider the situation in which $\Delta\pi = \pi_B - \pi_A$ is constant. This occurs for frequency independent selection, but also for $a + d = b + c$, which is often referred to as “equal gains from switching” (Nowak and Sigmund, 1990). In this case, we have $C_1 = N(N-1)\Delta\pi/2$ and $C_2 = N(N-1)(2N-1)\Delta\pi^2/6$. This leads to

$$\phi_1 \approx \frac{1}{N} \left[1 - \beta(N-1) \frac{\Delta\pi}{2} - \beta^2(N^2-1) \frac{\Delta\pi^2}{12} \right]. \quad (12)$$

For a first order expansion to be meaningful, $\beta \ll 1$ is not enough. Instead, we have to ensure $\beta N \Delta\pi \ll 1$.

In principle, we could assume any function for $\pi_B - \pi_A$. The most important case, however, are 2×2 games, which lead to a linear dependence of the payoff difference $\Delta\pi = \pi_B - \pi_A = u i + v$, cf. Eq. (2). In this case, we have

$$\begin{aligned}C_1 &= \sum_{k=1}^{N-1} \sum_{i=1}^k (u i + v) \quad (13) \\ &= \sum_{k=1}^{N-1} \left(\frac{u k^2}{2} + \frac{(u + 2v)k}{2} \right) \\ &= u \frac{N(N^2-1)}{6} + v \frac{N(N-1)}{2}.\end{aligned}$$

For the second order term in Eq. (10), we obtain

$$\begin{aligned}
C_2 &= \frac{1}{2} \sum_{k=1}^{N-1} \left(\sum_{i=1}^k (u i + v) \right)^2 \\
&= \frac{1}{2} \sum_{k=1}^{N-1} \left(\frac{u k^2}{2} + \frac{(u + 2v)k}{2} \right)^2 \\
&= \frac{u^2}{8} \sum_{k=1}^{N-1} k^4 + \left(\frac{u^2}{4} + \frac{uv}{2} \right) \sum_{k=1}^{N-1} k^3 + \left(\frac{u^2}{8} + \frac{uv}{2} + \frac{v^2}{2} \right) \sum_{k=1}^{N-1} k^2 \\
&= N(N-1) \left[u^2 \frac{3N^3 + 3N^2 - 2N - 2}{120} + uv \frac{3N^2 + N - 2}{24} + v^2 \frac{2N - 1}{12} \right].
\end{aligned} \tag{14}$$

Thus, we find for the expectation value of ϕ_1 under weak selection

$$E(\phi_1) \approx \frac{1}{N} - \beta \frac{E(C_1)}{N^2} - \beta^2 \frac{E(C_2)}{N^2} + \beta^2 \frac{E(C_1^2)}{N^3}. \tag{15}$$

Note that C_1 is linear in the payoffs, whereas C_2 is quadratic in the payoffs.

So far, this equation is valid for any distribution of payoffs $p(x)$. Next, we focus on the case in which a , b , and c follow Gaussian distributions with mean μ and standard deviation σ^2 , $p(x) = \frac{1}{\sigma \sqrt{2\pi}} \exp\left[-\frac{(x-\mu)^2}{2\sigma^2}\right]$. In our expectation value Eq. (15), we have only terms involving the first and the second moment of the distribution. Using $E(x) = \mu$ and $E(x^2) = \mu^2 + \sigma^2$, we find

$$E(u) = -\frac{d - \mu}{N - 1} \tag{16a}$$

$$E(v) = d - \mu \tag{16b}$$

$$E(u^2) = \frac{(d - \mu)^2}{(N - 1)^2} + \frac{3\sigma^2}{(N - 1)^2} \tag{16c}$$

$$E(v^2) = (d - \mu)^2 + \frac{N^2 + 1}{(N - 1)^2} \sigma^2 \tag{16d}$$

$$E(uv) = -\frac{(d - \mu)^2}{N - 1} - \frac{N + 1}{(N - 1)^2} \sigma^2. \tag{16e}$$

With these terms, Eq. (15) reduces to

$$\begin{aligned}
 E(\phi_1) \approx & \frac{1}{N} \\
 & -\beta \frac{N-2}{3N} (d-\mu) \\
 & +\beta^2 \frac{N-2}{N-1} \frac{16N^2-57N+47}{360N} (d-\mu)^2 \\
 & +\beta^2 \frac{N-2}{N-1} \frac{6N^2-7N+7}{120N} \sigma^2.
 \end{aligned} \tag{17}$$

In the simplest case, the average payoff entry associated with the mutant is identical to the wild type's payoff interacting with himself, such that we have $\mu = d$. Then, the linear term in Eq. (17) vanishes and only a second order weak selection approximation will lead to deviations from the neutral case. We obtain

$$E(\phi_1) \approx \frac{1}{N} + \beta^2 \frac{N-2}{N-1} \frac{6N^2-7N+7}{120N} \sigma^2. \tag{18}$$

Now, the variance σ can be absorbed into the selection intensity. In other words, changing the variance of the Gaussian distribution is equivalent to changing the intensity of selection. In Fig. 1, the quadratic approximation Eq. (18) is compared to the numerical solution of the integrals in Eq. (8) and to individual based simulations. For the third order weak selection approximation, we refer to the Appendix.

3.2. Strong selection limit

For strong selection, $\beta \rightarrow \infty$, only those mutants that are advantageous from the beginning of their invasion until the time they finally reach fixation take over the population. This means the mutant type A will reach fixation only if $a > c$ and $b > d$, see Eq. 1. In this case, the fixation probability is 1 for $\beta \rightarrow \infty$.

However, the fixation probability is not only one for $a > c$ and $b > d$. It also converges to one with $\beta \rightarrow \infty$ in coexistence games with $a < c$ and $b > d$ if we have $a + b > c + d$ in addition. This situation occurs for $\mu = d$ with probability $1/8$. However, for such games the average fixation times diverge rapidly with population size and intensity of selection (Antal and Scheuring, 2006; Traulsen et al., 2007a). Thus, for practical purposes we can neglect the fixation in coexistence games under strong selection, as it can hardly ever be observed.

Thus, we only consider $a > c$ and $b > d$ here for the fixation probability. The probability for this payoff ranking is the fixation probability for strong selection.

First, let us consider the situation when a , b , and c follow a Gaussian distribution with mean $\mu = d$ and standard deviation σ . The probability that a is larger than c is $1/2$. The probability that b is larger than d is also $1/2$. Therefore, the fixation probability is simply $1/4$, see Fig. 1.

In frequency independent mutant scenarios, the payoff of both type does not depend on its interaction partner, i.e. $a = b$ and $c = d$. In this case, the fixation probability of a random mutant is $1/2$ for $\mu = d$.

3.3. Computer simulations

We simulate the population dynamics exactly as described in Sec. 2. In each time step, each individual interacts with all others in the population and obtains a payoff. However, our results for weak selection would not change significantly if they interact only with a random subset of the population (Traulsen et al., 2007b; Woelfing and Traulsen, 2009). Then, an individual is selected with probability proportional to its fitness and produces identical offspring. Another individual chosen at random is removed. To compute fixation probabilities, we simulate this birth-death process many times, each time with a new, different payoff matrix. Note that we are combining two sources of randomness, as the fixation process itself and the payoff matrix are stochastic.

When we compare our analytical results to computer simulations, a further difficulty appears: Formally, we are always considering a Markov chain with two absorbing states $i = 0$ and $i = N$. Eventually, we will end up in one of them. But the time until we reach these states diverges with the intensity of selection and the population size if $a < c$ and $d < b$ (Antal and Scheuring, 2006; Traulsen et al., 2007a; Altrock and Traulsen, 2009b), see above. Thus, we have two choices: Either, we include coexistence games and say that no fixation has occurred if we have waited for a very long time and still both types are present. However, then we cannot expect that our numerical results coincide with the analytical theory, because only the latter approach takes the possibility of fixation in coexistence games into account. This approach is appropriate when selection is not too strong. For strong selection, Alternatively, we can exclude coexistence games from the beginning, both in our numerical solution of the integrals in Eq. (8) and in our simulations. If we do this and assume that fixation never occurs in coexistence games, we find a convergence for strong selection towards a fixation probability of $1/4$.

As shown in Fig. 1, the simulations and the numerical results agree nicely both under strong selection and weak selection if we take these complications into account. However, under strong selection the fixation probability from simulations

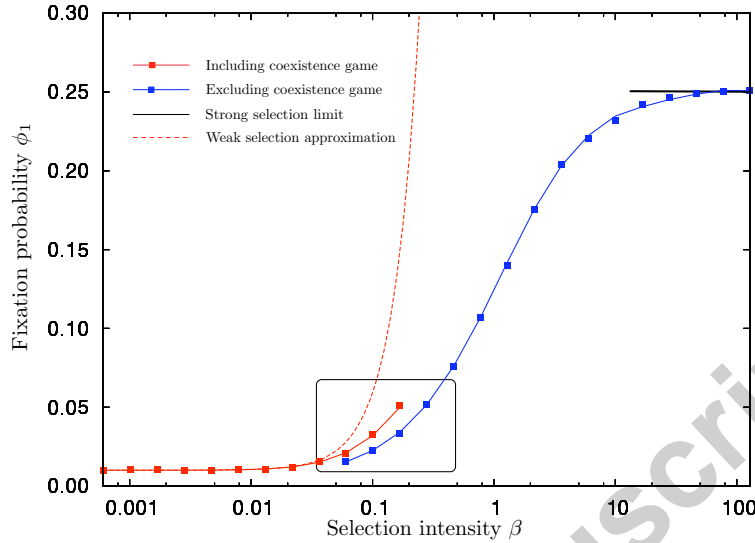


Figure 1: Fixation probability of a single mutant with random payoff values under different selection intensities. The payoff values are Gaussian distributed with the mean equal to the wild type individual's payoff. We start from a single mutant and wait until it is either lost or it takes over the whole population. The fixation probability is the fraction of runs in which the mutants took over. Coexistence games are only taken into account for weak selection, see text. The black box represent the region between strong selection and weak selection (population size $N = 100$, averages over 10^5 runs).

temporarily exceeds the strong selection limit. The reason is that in those games in which wild type only slightly dominates the mutant, the latter may still occasionally reach fixation. This makes the fixation probability of the mutant type slightly higher than it should be theoretically. For $\beta \rightarrow \infty$, however, the fixation probability converges to $1/4$, as expected.

4. Alternative fitness distributions

So far, we have concentrated on Gaussian distributed payoff entries. Next, we relax this restriction and consider more general distributions. It turns out that for weak selection, only the first moments of the distribution matter, whereas for strong selection, fixation is governed by the probability that a payoff value is larger than the average. Thus, our results from above generalize easily to general distributions.

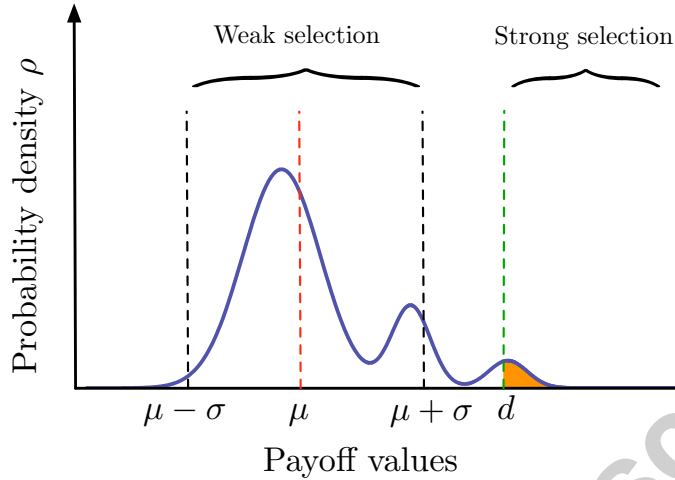


Figure 2: The probability of fixation of a random mutant for general payoff value distributions is determined by different properties of the distribution. For weak selection, the fixation probability is determined by the first moments of the distribution of the new payoff values a, b and c . If we approximate up to second order, only $d - \mu$, the difference between mean μ and the wildtype's payoff d against itself and the standard deviation σ affect the fixation probability. For strong selection, the fixation probability of mutant type is determined by the product of the probability that the mutant is advantageous when it invades, $b > d$ and the probability that it is advantageous when it is frequent, $a > c$. The latter probability is $\frac{1}{2}$ and the former probability is given by the shaded part of the distribution in the figure.

4.1. Weak selection approximation

The weak selection approximation Eq. (17) corresponds to a moment expansion of the probability distribution: For the linear term, only the difference between average μ and the wild type's payoff against himself d matters. For the quadratic term, we have to take into account the second moment as well. Thus, Eq. (17) holds for any distribution with mean μ and standard deviation σ . The same reasoning holds when we take higher order terms in β into account, see Appendix. When $\mu = d$, the moments of the distribution matter up to the order of our approximation in β , see Fig. 2.

4.2. Strong selection limit

For strong selection, $\beta \rightarrow \infty$, only those mutants whose fitness always exceeds that of the wild type, will eventually reach fixation. In game theory, such types

are called dominant. The probability of the mutant type to be dominant is based on the fitness distribution.

If a , b , and c follow a symmetric distribution p with mean μ and standard deviation σ , and $\mu = d$, we obtain the same strong selection limit as for the Gaussian distribution with $\mu = d$, see Sec. 3.2. This is because in our strong selection argument, we only have to consider the probability that a certain payoff entry is larger than another one or larger than the mean. If the fitness distribution is asymmetric or $\mu \neq d$, this argument no longer holds and different strong selection limits will be reached under special fitness distributions. Since both a and c are chosen from the same distribution, the probability p_1 that a is larger than c , and thus the probability that the new mutant dominates when it has high abundance, is simply $p_1 = \int_{-\infty}^{\infty} p(x)p(y)\Theta(x-y)dx dy = 0.5$, where $\Theta(x-y)$ is the step function. Therefore, the only influence of the details of the distribution occurs through the payoff entry b . The mutant will be dominant if in addition b is larger than d , which is the condition that the mutant is advantageous when it enters the population. This occurs with probability $p_2 = \int_d^{\infty} p(x)dx$. For $d = \mu$ and distributions in which the median is equal to the mean, we obtain $p_2 = 1/2$. But in general, the value of p_2 depends on the precise shape of the distribution, see Fig. 2, and the fixation probability is given by $p_1 p_2$.

For example, let us assume a , b , and c follow an exponential distribution with mean λ , e.g. $p(a) = \frac{1}{\lambda} \exp\left[-\frac{a}{\lambda}\right]$, such that $a, b, c \geq 0$. Thus, we obtain $p_2 = \lambda^{-1} \int_d^{\infty} \exp\left[-\frac{x}{\lambda}\right] dx = \exp\left[-\frac{d}{\lambda}\right]$. Even for $\lambda = d$, we have $p_2 = \exp[-1] \approx 0.368$. Thus, the probability that the mutant dominates the wild type is $p_1 p_2 = \exp[-1]/2 \approx 0.184$. The asymptotic limit of the fixation probability for strong selection, $\beta \rightarrow \infty$, is also $p_1 p_2$. For $\lambda = d/\ln 2$, we would obtain the same asymptotic limit as for the Gaussian distribution.

5. Discussion

We have introduced a model in which a new mutant in asexual population is characterized by a new payoff matrix. We have calculated the probability that such a mutant interacting with the wild type in a novel, unpredictable way can take over a population. This depends on the details of the interactions, which are in our case based on the distribution of payoff values. How does this relate to the usual approaches of population genetics that discuss fitness distributions? One simplifying assumption of evolutionary game theory is that individuals are haploid and reproduction is asexual. So we should first aim at e.g. comparing to experimental data from bacteria.

Recent works in population genetics have attempted to measure fitness distributions experimentally (Zeyl and DeVisser, 2001; Cowperthwaite et al., 2005; Kassen and Bataillon, 2006). Also in our case, we have a distribution of fitness values, reflected by the entries of a payoff matrix. However, our model is looking at the invasion and fixation of mutants from a different perspective. The first and most important point is the way we define fitness. Mutations bring variety, and fitness is to describe the advantages of one type over others. In the traditional population genetic view, fitness is typically constant, but our model considers fitness under frequency dependent selection. The evolutionary dynamics under these two approaches will be quite different, especially when selection is not weak, see Fig. 3. For constant fitness, a mutant in an asexual population is either advantageous or disadvantageous compared to the wild type. Therefore, the fixation or extinction of the mutant type is usually fast for strong selection. But for frequency dependent fitness, mutant and wild type may coexist with each other for a long time. This occurs when a mutant performs better than the wild type when it is rare, but the wild type has a fitness advantage when the mutant is frequent. One would expect that frequency dependence is the rule rather than the exception, because the success of a strategy typically depends on the actions and abundance of others.

The distribution of fitness values is a central concept in population genetics. Gillespie (1983) and Orr (2002, 2003) have proposed that the fitness distribution of beneficial mutants would be approximately exponential. Alternative distributions like gamma distribution, L-shaped distribution and slightly bell-shaped distribution are also considered to be possible. The fitness distribution is a function of the environment and thus it is influenced by many factors, such as the adaptation of the wild type to the environment. It also makes a difference if only single-step mutations are considered or if also mutants with several mutations are taken into account. However, these attempts are typically based on the assumption of fixed fitness values. If fitness is frequency dependent, as in our model, the selective advantage of a novel type depends on its frequency. A new mutation may be able to invade, but not to take over the population. Alternatively, new mutants may be disadvantageous, but turn highly successful when they have crossed a certain threshold.

Payoff matrices with random entries have been considered before: In a seminal paper, Fudenberg and Harris (1992) have shown that a game with time-dependent random payoff matrix can be described by a stochastic form of the replicator equation. They have argued that the system spends most time in the vicinity of the risk dominant equilibrium. This is the strategy with the larger basin of attraction under

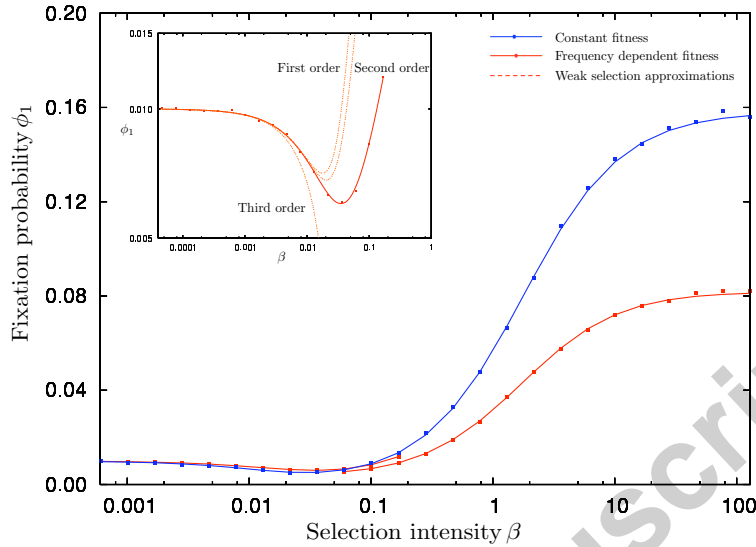


Figure 3: In the main panel, we compare the probability of fixation under constant fitness and frequency dependent fitness. Here, wild type's payoff against itself d is larger than mean μ of the Gaussian random variables in the payoff matrix ($d = 2, \mu = 1$). This is consistent with the notion in population genetics that deleterious mutants are more common than beneficial ones. For weak selection, the dynamics under both approaches are similar. However, the scenarios under strong selection are quite different. In the inset, we show the weak selection approximations of the fixation probability under frequency dependent fitness. As the probability to be deleterious is higher, the fixation probability of a random mutant decreases first with the intensity selection, before it starts to increase again. It is obviously that the approximation becomes more accurate when higher order terms are considered. In particular, the linear term cannot capture the fixation probability when the intensity of selection is increased here (population size $N = 100$, averages over 10^5 runs).

positive frequency dependent selection. The approach of Fudenberg and Harris leads to much faster convergence to the risk dominant equilibrium than the approach of Kandori et al. (1993), looking at mutations only under strong selection. Our model assumes that the nature of interactions, i.e. the payoff matrix, does not change in time, whereas Fudenberg and Harris (1992) consider a situation in which fitness is not only frequency, but also time dependent, such that fixation probabilities are not meaningful.

Berg and Engel (1998) as well as Galla (2007) have considered random bi-matrix games with a large number of strategies to address the number of Nash equilibria and the fraction of strategies contributing to mixed Nash equilibria.

Eriksson and Lindgren (2001) have asked what kind of strategies is most successful if the payoff matrix is chosen at random and change in every round of game. These papers either consider large numbers of strategies, sophisticated decision processes or temporal changes of the payoff matrix that do not affect the identity of the strategies. Our approach is different in many aspects: Players do not switch between strategies or choose a particular way to play in each game. Rather, they play a fixed strategy that they also pass on to their offspring. We consider an ensemble of fixed games and explore how the probability that a mutant can take over a population depends on that ensemble. It turns out that the dependence on the underlying distribution of interaction parameters corresponds to a moment expansion for weak selection and to an integral of a part of the fitness distribution for strong selection.

Acknowledgement

W.H. gratefully acknowledges funding by the Chinese Scholarship Council and the American Association of University Women. A.T. is funded through the Emmy-Noether program of the German Research Foundation (DFG).

A. Third order weak selection

The third order expansion of the fixation probability of a single mutant under weak selection is calculated here. We consider the fitness as frequency dependent. First, we expand the exponential function in Eq. (7) for $\beta \ll 1$,

$$\exp\left[+\beta \sum_{i=1}^k (\pi_B - \pi_A)\right] \approx 1 + \beta \sum_{i=1}^k (\pi_B - \pi_A) + \frac{\beta^2}{2} \left(\sum_{i=1}^k (\pi_B - \pi_A)\right)^2 + \frac{\beta^3}{6} \left(\sum_{i=1}^k (\pi_B - \pi_A)\right)^3 \quad (19)$$

Then, Eq. (7) can be written as

$$\phi_1 \approx \frac{1}{N + \beta C_1 + \beta^2 C_2 + \beta^3 \underbrace{\frac{1}{6} \sum_{k=1}^{N-1} \left(\sum_{i=1}^k (\pi_B - \pi_A)\right)^3}_{C_3}}, \quad (20)$$

where C_1 and C_2 are defined as Eq. (13) and Eq. (14) in the main text. Expanding Eq. (20) for $\beta \ll 1$, we have

$$\phi_1 \approx \frac{1}{N} - \beta \frac{C_1}{N^2} + \beta^2 \left(\frac{C_1^2}{N^3} - \frac{C_2}{N^2}\right) - \beta^3 \left(\frac{C_1^3}{N^4} - \frac{2C_1 C_2}{N^3} + \frac{C_3}{N^2}\right) \quad (21)$$

As $\pi_B - \pi_A = u i + v$, cf. Eq. (2), we have

$$\begin{aligned}
 C_3 &= \frac{1}{6} \sum_{k=1}^{N-1} \left(\sum_{i=1}^k (u i + v) \right)^3 & (22) \\
 &= N \left[u^3 \frac{15N^6 - 42N^4 + 35N^2 - 8}{630} + u^2 v \frac{5N^5 - 3N^4 - 10N^3 + 5N^2 + 5N - 2}{240} \right] \\
 &\quad + N \left[u v^2 \frac{12N^4 - 15N^3 - 10N^2 + 15N - 2}{240} + v^3 \frac{N(N-1)^2}{24} \right]
 \end{aligned}$$

When we assume that a, b, c follow an arbitrary distribution $f(x)$ with mean μ , variance σ^2 and skewness γ , the fixation probability under weak selection is the expectation value of ϕ_1 ,

$$E(\phi_1) \approx \frac{1}{N} - \beta \frac{E(C_1)}{N^2} + \beta^2 \left(\frac{E(C_1^2)}{N^3} - \frac{E(C_2)}{N^2} \right) - \beta^3 \left(\frac{E(C_1^3)}{N^4} - \frac{2E(C_1 C_2)}{N^3} + \frac{E(C_3)}{N^2} \right). \quad (23)$$

Compared with the second order approximation where only the first and the second moment of the distribution are involved, we need to include the third moment of the distribution $E(x^3) = \mu^3 + 3\mu\sigma^2 + \gamma$. Then, we obtain four new terms beside those in Eq.(16)

$$E(u^3) = -\frac{(d-\mu)^3}{(N-1)^3} - \frac{9(d-\mu)\sigma^2}{(N-1)^3} + \frac{\gamma}{(N-1)^3} \quad (24a)$$

$$E(v^3) = (d-\mu)^3 + \frac{3(N^2+1)}{(N-1)^2} (d-\mu)\sigma^2 - \frac{N^3-1}{(N-1)^3} \gamma \quad (24b)$$

$$E(u^2 v) = \frac{(d-\mu)^3}{(N-1)^2} + \frac{5N-1}{(N-1)^3} (d-\mu)\sigma^2 - \frac{\gamma}{(N-1)^2} \quad (24c)$$

$$E(u v^2) = -\frac{(d-\mu)^3}{N-1} - \frac{3N^2-1}{(N-1)^3} (d-\mu)\sigma^2 + \frac{(N^2-1)}{(N-1)^3} \gamma \quad (24d)$$

With all the items in Eq. (16) and Eq. (24), the fixation probability for a mutant in Eq.(23) becomes

$$\begin{aligned}
 E(\phi_1) \approx & \frac{1}{N} \\
 & -\beta \frac{N-2}{3N} (d-\mu) \\
 & +\beta^2 \frac{N-2}{N-1} \frac{16N^2-57N+47}{360N} (d-\mu)^2 \\
 & +\beta^2 \frac{N-2}{N-1} \frac{6N^2-7N+7}{120N} \sigma^2 \\
 & -\beta^3 \frac{N-2}{(N-1)^2} \frac{32N^4-345N^3+1106N^2-1347N+530}{15120N} (d-\mu)^3 \\
 & -\beta^3 \frac{N-2}{(N-1)^2} \frac{12N^4-293N^3+546N^2-541N+288}{5040N} (d-\mu) \sigma^2 \\
 & +\beta^3 \frac{N-2}{(N-1)^2} \frac{32N^4-177N^3+182N^2-255N+194}{15120N} \gamma.
 \end{aligned} \tag{25}$$

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