

Fixation probabilities in evolutionary game dynamics in finite diploid populations (進化ゲームダイナミクスにおける 2 倍体集団での変異遺伝子の固定確率)

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Fixation processes in evolutionary game dynamics in finite diploid populations are investigated. Traditionally, frequency dependent evolutionary dynamics is modeled as deterministic replicator dynamics. This implies that the infinite size of the population is assumed implicitly. In nature, however, population sizes are finite. Recently, stochastic processes in finite populations have been introduced in order to study finite size effects in evolutionary game dynamics. One of the most significant studies on evolutionary dynamics in finite populations was carried out by Nowak *et al.* which describes the “one-third law.” It states that under weak selection, if the fitness of strategy α is greater than that of strategy β when α has a frequency $1/3$, strategy α fixates in a β -population with selective advantage. In this study, we apply their framework to a diploid population that plays a two-strategy game. The fixation probabilities of mutant alleles in diploid populations are derived. A “three-tenth law” for a completely recessive mutant allele and a “two-fifth law” for a completely dominant mutant allele are found; moreover, other cases are also discussed.

Traditionally, evolutionary game dynamics [1–3] is modeled as deterministic equations, for example, the well-known replicator equation [4]. However, in such equations, the population size is intrinsically assumed to be infinite, and the equations fail to consider the stochastic effects. In natural, population sizes are finite and deterministic processes are disturbed by stochastic effects. This fact has long been recognized in population genetics [5–8]. Only recently, some stochastic processes are introduced in order to investigate evolutionary game dynamics in finite populations, and it has been shown that the finiteness of population sizes may occasionally play a significant role in an evolutionary process [9–20]. In a finite population, the fate of a mutant is determined in a stochastic process. Even an advantageous mutant could become extinct and a deleterious mutant could fixate in the population by chance. A natural definition of an advantageous mutation in a finite population was introduced by comparing the fixation probability of a mutant strategy with that of a neutral strategy [11]. If the probability that the descendant of a single strategy α mutant invading a population of $(N - 1)$ strategy β individuals takes over the entire population is higher than the corresponding probability for the case of a neutral mutant, strategy α is advantageous. Further, it is shown that under weak selection, if the fitness of an α individual is higher than that of a β individual when the frequency of α individuals is $1/3$, strategy α is advantageous. This is called the one-third law.

Since the main focus area of evolutionary game dynamics in its early stage was the evolution of strategies in animal conflicts [1, 21–23], the evolution of phenotypes were primarily considered, and genetic mechanisms were often neglected. Also in recent years, inheritance is assumed to be asexual in most studies. Making a model simple is always important; however, at the same time it is also

true that sexual combination can play an important role and be a key factor in the evolutionary process. In fact, evolutionary game dynamics in sexual populations has also long been considered in many studies [1, 24–33].

In this study, we apply the framework proposed by Nowak *et al.* [11] to a diploid population and derive the fixation probability of a mutant allele in a diploid population playing a two-strategy game. In diploid populations, each individual has two homologous copies of each chromosome – one from its mother and the other from its father. Let us consider two alleles A and B on a single locus. Therefore, there are three genotypes AA , AB , and BB . The genotype of a new offspring will be determined by those of its parents according to the probability distributions shown in Table I. Let x_{AA} , x_{AB} , and x_{BB} denote the frequencies of the genotypes AA , AB , and BB , respectively. It should be noted that in a large population, the frequency distribution of the genotypes in each sex is approximately identical to that in the entire population since the genotype of a new offspring does not depend on the sex of the offspring but depends only on the genotypes of its parents as shown in Table I. For simplicity, we assume that the fitness of an individual depends only on the genotype on the locus.

TABLE I: Probability distributions of genotypes of a new offspring for all possible combinations of parents.

pairs of parents	genotypes of offspring		
	AA	AB	BB
$AA \times AA$	1	0	0
$AA \times AB$	$1/2$	$1/2$	0
$AA \times BB$	0	1	0
$AB \times AB$	$1/4$	$1/2$	$1/4$
$AB \times BB$	0	$1/2$	$1/2$
$BB \times BB$	0	0	1

Consider a process in which a pair of individuals – a male and a female – is chosen as parents for reproduction in proportion to their fitnesses, and their offspring replaces a randomly chosen individual. Thus, in this process, the number of individuals is constant. Let N denote the number of individuals; we assume a large but finite value of N . The sex ratio of offsprings is an arbitrary constant. Let f_{AA} , f_{AB} , and f_{BB} denote the average fitnesses of the three genotypes AA , AB , and BB , respectively. The probabilities that the genotype of a new offspring is AA , AB , or BB are given by

$$p_{AA} = \psi_A^2, \quad p_{AB} = 2\psi_A\psi_B, \quad p_{BB} = \psi_B^2, \quad (1)$$

respectively, where

$$\begin{aligned} \psi_A &= x_{AA} \frac{f_{AA}}{\bar{f}} + \frac{x_{AB}}{2} \frac{f_{AB}}{\bar{f}}, \\ \psi_B &= x_{BB} \frac{f_{BB}}{\bar{f}} + \frac{x_{AB}}{2} \frac{f_{AB}}{\bar{f}}. \end{aligned} \quad (2)$$

$\bar{f}$ denotes the average fitness of the population ($\bar{f} = x_{AA}f_{AA} + x_{AB}f_{AB} + x_{BB}f_{BB}$). Further, the probabilities that the genotype of the individual replaced by the offspring is AA , AB , or BB are given by x_{AA} , x_{AB} , and x_{BB} , respectively. The process is a kind of a Moran process [7], and it is called the frequency dependent Moran process [11, 12] for diploid populations. It defines a Markov process. For example, in a single time step of this process, the number of genotype AA individuals increases by one and that of AB individuals decreases by one with a probability $\text{Prob}(AA \uparrow, AB \downarrow) = p_{AA}x_{AB}$. Probabilities in other possible cases are calculated in the same manner ($\text{Prob}(AB \uparrow, BB \downarrow) = p_{AB}x_{BB}$ and so on).

Let us assume that N individuals interact with each other through a game and that the genotype of the locus determines the strategy of the game. Because there exist three genotypes, they can correspond to three strategies in general. In this study, we assume that the game played by the population has two strategies – α and β . Let $\begin{pmatrix} m_{\alpha\alpha} & m_{\alpha\beta} \\ m_{\beta\alpha} & m_{\beta\beta} \end{pmatrix}$ denote the payoff matrix of the game. We also assume that α and β are the best replies to themselves, i.e., $m_{\alpha\alpha} > m_{\beta\alpha}$ and $m_{\beta\beta} > m_{\alpha\beta}$. This assumption allows us to deduce that $\mu = m_{\alpha\alpha} + m_{\beta\beta} - m_{\alpha\beta} - m_{\beta\alpha}$ is positive and that an unstable equilibrium $(q_\alpha, q_\beta) = (m_{\beta\beta} - m_{\alpha\beta}, m_{\alpha\alpha} - m_{\beta\alpha})/\mu$ exists. Further, we consider a situation in which an AA individual plays the pure strategy α , a BB individual plays the pure strategy β , and an AB individual plays a mixed strategy comprising α and β , i.e. $s_\alpha\alpha + s_\beta\beta$ ($s_\alpha, s_\beta \geq 0$, $s_\alpha + s_\beta = 1$). The frequencies of the strategies α and β played in the population are given by $\pi_\alpha = x_{AA} + s_\alpha x_{AB}$ and $\pi_\beta = x_{BB} + s_\beta x_{AB}$, respectively. The average payoffs for the strategies are given by $f_\alpha = m_{\alpha\alpha}\pi_\alpha + m_{\alpha\beta}\pi_\beta$ and $f_\beta = m_{\beta\alpha}\pi_\alpha + m_{\beta\beta}\pi_\beta$. Then,

the average fitnesses of the genotypes AA , AB , and BB are given by

$$\begin{aligned} f_{AA} &= 1 - w + wf_\alpha, \\ f_{AB} &= 1 - w + w(s_\alpha f_\alpha + s_\beta f_\beta), \\ f_{BB} &= 1 - w + wf_\beta, \end{aligned} \quad (3)$$

respectively. $w \in [0, 1]$ is called “the selection intensity parameter” [11]. If $w \ll 1$, this game provides a small perturbation to the fitness of an individual and the selection with this game is termed as “weak selection.” In previous studies [11, 18–20], it is assumed that selection is sufficiently weak. In the study by Traulsen *et al.* [19], it is asserted that weak selection is an important concept for two reasons: (i) many analytical results can be obtained only in the limit of weak selection; however, a good approximation can also be obtained for a larger value of w and (ii) many factors affect the fitness of an individual; however, only a particular game is under consideration. For these reasons, we restrict the value of w to the domain of weak selection; i.e., in this study, we assume that $Nw \ll 1$.

Nowak *et al.* introduced a natural definition of an advantageous mutation by comparing the fixation probability of a mutant strategy with that of a neutral strategy [11]. For a mutant allele in a diploid population, the definition is modified as follows. The fixation probability ρ_A of mutant allele A is defined as the probability that a population consisting of $(N - 1)$ BB individuals and a single AB individual is eventually taken over by AA individuals. If allele A is always neutral, the fixation probability is equal to the reciprocal of the total number of genes in the population, i.e., $\frac{1}{2N}$. Let $\bar{\rho}$ denote the fixation probability of allele A in a neutral case ($\bar{\rho} = \frac{1}{2N}$). Therefore, allele A is deemed advantageous if the fixation probability ρ_A is greater than $\bar{\rho}$.

Since this is a two-dimensional Markov process, it is difficult to obtain the exact value of the fixation probability. However, in the limit of weak selection, $Nw \ll 1$, the population goes close to the Hardy-Weinberg equilibrium (H-W eq.). Let ϕ_A and ϕ_B denote the frequencies of A and B (i.e., $\phi_A = x_{AA} + \frac{1}{2}x_{AB}$ and $\phi_B = x_{BB} + \frac{1}{2}x_{AB}$). In the H-W eq., x_{AA} , x_{AB} , and x_{BB} satisfy

$$x_{AA} = \phi_A^2, \quad x_{AB} = 2\phi_A\phi_B, \quad x_{BB} = \phi_B^2. \quad (4)$$

Thus, in the H-W eq., $h = x_{AB}^2 - 4x_{AA}x_{BB} \in [-1, 1]$ is zero. By evaluating the expected change in h in a single step at time t , denoted by $\langle h_t \rangle$, it can be proved that $\langle h_t \rangle = -\frac{h_t}{N} + O(N^{-2})$ with the assumption $Nw \ll 1$. This implies that the population tends to the H-W eq. even though demographic stochasticity constantly perturbs the system state. Furthermore, h is almost zero in the initial state, $h_{t=0} = N^{-2}$. Thus, the population is very close to the H-W eq. right from the beginning. These facts help us to obtain an approximate value of the fixation probability. By the approximation that the

population is always in the H-W eq., we can substitute a simple gene pool model for the original diploid population model. The simple gene pool model is described as follows. There exist two types of genes in the pool – A and B – and the total number of genes is $2N$. A (or B) is reproduced with a probability ψ_A (or ψ_B) and it replaces a randomly chosen gene. ψ_A and ψ_B are determined by Eqs. (2), (3), and (4). When the diploid population is in the H-W eq., a single step of the original process is equivalent to two steps of this simplified process. The simplified process is a one-dimensional Markov process. The number of gene A can increase by one, stay the same, or decrease by one. The transition matrix of the process is tri-diagonal and defines a birth-death process given by

$$R_{i,i+1} = \psi_A \phi_B, \quad R_{i,i} = \psi_A \phi_A + \psi_B \phi_B, \quad R_{i,i-1} = \psi_B \phi_A. \quad (5)$$

where i denotes the number of A ($i = 2N\phi_A$). The fixation probability ρ_A in the original process can be approximated by the fixation probability of A , denoted by ρ'_A , in the process defined by Eq. (5). It is given by

$$\rho_A \approx \rho'_A = \left(1 + \sum_{k=1}^{2N-1} \prod_{i=1}^k \frac{R_{i,i-1}}{R_{i,i+1}} \right)^{-1}$$

(see [34]). In the limit of weak selection, $Nw \ll 1$, we obtain

$$\rho_A \approx \frac{1}{2N} - \frac{w\mu}{6} \left\{ s_\beta \left(q_\alpha - \frac{3}{10} \right) + 2s_\alpha \left(q_\alpha - \frac{2}{5} \right) + \frac{1}{5} s_\alpha s_\beta \right\} \quad (6)$$

by neglecting orders higher than the first order of w . From this equation, we observe that the threshold value of q_α for allele A to be advantageous depends on genetic mechanisms. If allele A is completely recessive, an AB individual plays the pure strategy β (i.e. $(s_\alpha, s_\beta) = (0, 1)$). Therefore, in this case, Eq. (6) is simplified into

$$\rho_A \approx \frac{1}{2N} - \frac{w\mu}{6} \left(q_\alpha - \frac{3}{10} \right). \quad (7)$$

In Fig. 1(a), $\rho_A/\bar{\rho}$ obtained by Eq. (7) for three values of w are plotted. The numerically evaluated values of $\rho_A/\bar{\rho}$ are also plotted. From Fig. 1(a), we observe that Eq. (7) approximates the fixation probability quite well not only when $Nw \ll 1$ but also when w is significantly large ($Nw = 1/2$). Equation (7) suggests that when the mutant allele A is completely recessive, A is advantageous if strategy α has a higher payoff than strategy β when the frequency of α individuals is $3/10$ (i.e., $\rho_A \geq \bar{\rho} \iff q_\alpha \leq \frac{3}{10}$). This is a “three-tenth law” for a completely recessive mutant allele. On the other hand, if allele A is completely dominant, an AB individual plays the pure strategy α , and this indicates that $(s_\alpha, s_\beta) = (1, 0)$. In this case, Eq. (6) is simplified into

$$\rho_A \approx \frac{1}{2N} - \frac{w\mu}{3} \left(q_\alpha - \frac{2}{5} \right). \quad (8)$$

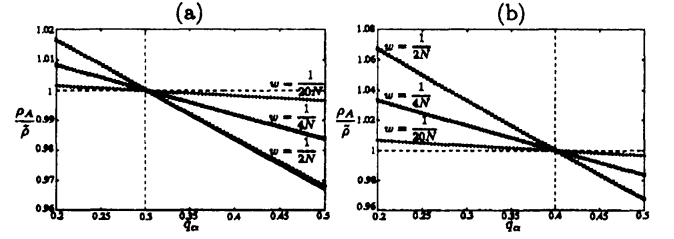


FIG. 1: Ratio of ρ_A to $\bar{\rho}$ plotted as a function of q_α . Allele A is completely recessive in (a), $s_\alpha = 0$, and completely dominant in (b), $s_\alpha = 1$. The points denote $\rho_A/\bar{\rho}$ evaluated numerically for three values of w which are indicated in the figures. The lines are obtained with Eq. (7) in (a) and Eq. (8) in (b). The system parameters are given by $N = 100$, $m_{\alpha\alpha} = 1 - q_\alpha$, $m_{\alpha\beta} = m_{\beta\alpha} = 0$, and $m_{\beta\beta} = q_\alpha$.

Equation (8) provides a “two-fifth law” for a completely dominant mutant allele, $\rho_A \geq \bar{\rho} \iff q_\alpha \leq \frac{2}{5}$ (see Fig. 1(b)). If the two alleles A and B have an additive effect on the fitness, i.e., an AB individual plays α and β in equal proportions, $(s_\alpha, s_\beta) = (1/2, 1/2)$, we obtain $\rho_A \approx \frac{1}{2N} - \frac{w\mu}{4} (q_\alpha - \frac{1}{3})$ from Eq. (6). Thus, in this case, the “one-third law” appears again.

Since Eq. (6) can be rewritten as $\rho_A \approx \frac{1}{2N} - \frac{w\mu}{6} (1 + s_\alpha) \left\{ q_\alpha - \frac{3}{10} - \frac{s_\alpha^2}{5(1+s_\alpha)} \right\}$, A is advantageous if q_α is smaller than $Q_\alpha = \frac{3}{10} + \frac{s_\alpha^2}{5(1+s_\alpha)}$, i.e., $\rho_A \geq \bar{\rho} \iff q_\alpha \leq Q_\alpha$. Since Q_α is a monotone increasing function of s_α , it is concluded that a more dominant allele is advantageous in a wider domain of q_α (see Fig. 2).

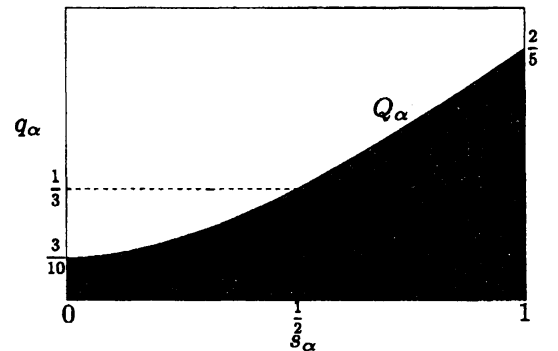


FIG. 2: The threshold Q_α of q_α for allele A to be advantageous is plotted as a function of s_α . In the shaded region ($q_\alpha < Q_\alpha$), A is advantageous.

We compared the fixation probability of A with the corresponding probability under neutral drift. Here, we compare the fixation probability of A with that of B , which is given by $\rho_B \approx \frac{1}{2N} - \frac{w\mu}{6} \{ s_\alpha (q_\beta - \frac{3}{10}) + 2s_\beta (q_\beta - \frac{2}{5}) - \frac{1}{5} s_\alpha s_\beta \}$. From this and Eq. (6), it is shown that $\rho_A \geq \rho_B \iff q_\alpha \leq \frac{1}{2}$ (see

Fig. 3) regardless of the strategy of AB . This is closely related to the concept of “risk-dominance”: strategy α is risk-dominant over strategy β if α gets higher payoff than β when the two strategies have the same frequencies of $1/2$. Our result can be restated as follows: if the strategy of AA is risk-dominant over the strategy of BB , regardless of the strategy of AB , ρ_A is larger than ρ_B , which suggests that in a process with infrequent mutations, A dominates the population more frequently than B .

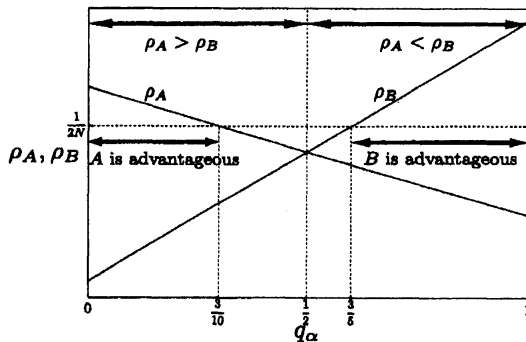


FIG. 3: ρ_A and ρ_B are plotted as functions of q_α where A is a completely recessive gene (i.e., $(s_\alpha, s_\beta) = (0, 1)$). ρ_A is larger (smaller) than ρ_B when q_α is less (greater) than $1/2$.

We have studied a frequency dependent Moran process for a diploid population in order to investigate game dynamics in a finite diploid population and we have derived the fixation probabilities of mutant alleles under weak selection. The criterion of the internal equilibrium of the game for a mutant allele to be advantageous is derived, and its dependency on genetic mechanisms is revealed. Similar to the $1/3$ law, there are several laws of the criterion for the determination of advantageous mutant genes; the $3/10$ law for a completely recessive allele and the $2/5$ law for a completely dominant allele. Further, it is shown that whether the fixation probability of A is higher than that of B does not depend on the strategy of AB , instead, it depends only on the position of the internal equilibrium.

In this study, an AB individual plays a mixed strategy comprising the strategies of AA and BB . There exist other possible cases; AA or BB plays a mixed strategy. Moreover, the genotypes can correspond to completely different strategies; this indicates three-strategy game. Further, although we consider only a single game in this study, several games are played simultaneously in general. This situation is described by “multi-game” [35]. Furthermore, it is assumed that every individual joins the game irrespective of its sex. However, it is observed that some games in nature are played only in a single sex.

Studies for these situations will be reported in future.

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