



Absorption and fixation times for neutral and quasi-neutral populations with density dependence

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ABSTRACT

We study a generalisation of Moran's population-genetic model that incorporates density dependence. Rather than assuming fixed population size, we allow the number of individuals to vary stochastically with the same events that change allele number, according to a logistic growth process with density dependent mortality. We analyse the expected time to absorption and fixation in the 'quasi-neutral' case: both types have the same carrying capacity, achieved through a trade-off of birth and death rates. Such types would be competitively neutral in a classical, fixed-population Wright–Fisher model. Nonetheless, we find that absorption times are skewed compared to the Wright–Fisher model. The absorption time is longer than the Wright–Fisher prediction when the initial proportion of the type with higher birth rate is large, and shorter when it is small. By contrast, demographic stochasticity has no effect on the fixation or absorption times of truly neutral alleles in a large population. Our calculations provide the first analytic results on hitting times in a two-allele model, when the population size varies stochastically.

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1. Introduction

The time to fixation or extinction of a mutant allele in a finite population is a classical problem of population genetics, and one in which there has been sustained interest (Kimura and Ohta, 1969a,b; Littler, 1975; van Herwaarden and van der Wal, 2002; Ewens, 2004; Taylor et al., 2006). For reasons of mathematical tractability, previous studies have typically assumed fixed population sizes. In such models with deterministic population size, birth events are followed immediately by death events. In natural populations, however, birth and death events are independent, and the total population size varies stochastically around a typical value, often governed by density dependence. Here we study fixation times in a model that allows for stochastic population sizes, which is therefore more realistic than the standard Wright–Fisher formulation (Wright, 1931; Fisher, 1958; Ewens, 2004).

We have recently demonstrated (Parsons and Quince, 2007a,b) that when population size varies stochastically, the probability of fixation differs qualitatively from that of fixed or deterministic population size models (Kimura, 1957, 1962; Moran, 1958; Ewens,

1967; Kimura and Ohta, 1974; Otto and Whitlock, 1997). Similar results appear in Lambert (2006). In particular, in the case of two types that have the same carrying capacity, but achieve this carrying capacity through different life-history strategies – what we call the quasi-neutral case – the probability of fixation depends not only on the initial density of the mutant type, as would be expected from a fixed-population size model, but also on the initial population size.

Here, we study the expected time to absorption or fixation for two quasi-neutral types. We use the framework introduced in Parsons and Quince (2007a): a two-dimensional Markov chain that models competition between discrete individuals of two types (mutant and resident) in continuous time. Competition is modelled via density dependent mortality, whose strength varies inversely with 'system size' N . The system size reflects the availability of resources, and it determines the carrying capacity of all types. We use singular perturbation analysis (Grasman and van Herwaarden, 1999) of a diffusion approximation to obtain asymptotic expressions for the mean time to absorption or fixation. These approximations increase in accuracy with increasing N . Consistent with our previous findings, we find that for types with different birth rates, the time to fixation grows with the difference in birth rates. We also determine the expected absorption and fixation times for an arbitrary number of

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truly neutral types – all having the same birth and death rates. In this case, we obtain the classical expressions with the total population number replaced by the carrying capacity – thereby demonstrating that under strict neutrality the classical results remain valid even when the assumption of fixed population size is relaxed. Lastly, we verify our approximations by comparison with exact numerical computations, and we investigate the accuracy of our approximations at small population sizes over a range of parameters.

In what follows, we present our model and our asymptotic results with discussion, with the details of the derivation in the appendices.

2. A model of allele fixation with density dependent mortality

We consider a population consisting of K types, subject to density dependent regulation. All types have the same carrying capacity, which is proportional to the ‘system size’ N . The system size represents the pool of available resources; as the system size is enlarged, carrying capacity of all types increases.

We denote the number of individuals of each type by $\mathbf{X}^N = (X_1^N, \dots, X_K^N)$. Here, X_i^N is the number of individuals of type i . We emphasise N , as we will be interested in the asymptotic behaviour as the system size becomes large. We assume that the number of the each type changes as a result of stochastic birth and death events in continuous time, for which the transition rates – probabilities per unit time – depend only on the current state of the system. This gives a Markov chain on $(\mathbb{Z}^{\geq 0})^K$ with transitions only to neighbouring states, i.e., a K -dimensional birth-and-death process (van Kampen, 1992), with transition rates as given in Table 1.

Here β_i and δ_i represent the birth and intrinsic death rates of type i , respectively, and the system size N determines the carrying capacity. δ_i gives a lower bound for the per capita death rate, which increases in proportion to the total number of individuals and is inversely proportional to the system size.

Our model naturally generalises the Moran model (Moran, 1958) by making births and deaths independent events, thereby allowing the total population number to vary stochastically with the same events that cause changes in allele number.

We previously determined fixation probabilities in the case $K = 2$ (Parsons and Quince, 2007a,b) for a closely related process with density dependent fecundity. While the model here may appear different, due to density dependence in the mortality term, the arguments and results for fixation times presented here are identical for both models (unpublished results).

In this study, we assume that all types are quasi-neutral – i.e. that the ratio of birth rates to intrinsic death rates is fixed, $\frac{\delta_i}{\beta_i} = \alpha$, for all types i . This corresponds to the case when all types have the same value for Kimura’s selection coefficient, s . Thus, in a Wright–Fisher model assuming fixed population size, all such types would be competitively neutral. However, when the population size is allowed to vary stochastically, the population dynamics correspond to a form of r vs. K selection (MacArthur and Wilson, 1967; Pianka, 1972): types with higher birth rates are favoured at small initial population sizes and types with lower mortality are favoured as the population size becomes large (Parsons and Quince, 2007b).

As N approaches infinity, $N^{-1}\mathbf{X}^N$ approaches a deterministic dynamical system,

$$\dot{x}_i = \beta_i x_i - \delta_i x_i \left(1 + \sum_{j=1}^K x_j \right). \tag{1}$$

Under the assumption of quasi-neutrality, every point on the line $\sum_{j=1}^K x_j = \frac{1}{\alpha} - 1$ is a possible equilibrium point of the deterministic

Table 1
Density dependent mortality

Transition	Rate
$X_i^N \rightarrow X_i^N + 1$	$\beta_i X_i^N$
$X_i^N \rightarrow X_i^N - 1$	$\delta_i X_i^N \left(1 + \frac{\sum_{j=1}^K X_j^N}{N} \right)$

system, corresponding to coexistence of all types. When N is finite, the total number of individuals will rapidly approach $(\frac{1}{\alpha} - 1)N$, and will remain near this value for a long time, before demographic stochasticity leads to the extinction of one of the types. We thus refer to $N^* = (\frac{1}{\alpha} - 1)N$ as the carrying capacity of the system. We are primarily concerned with the case when α is much smaller than 1, so that the population spends most of its time near the carrying capacity.

3. Results

Strictly speaking, the only absorbing state of the model above is extinction of all types. However, the total population number, obtained by summing all types, obeys a logistic process, for which the time before such extinction is exponentially large in the system size, N (Newman et al., 2004). Long before the entire population goes extinct, the population will become monomorphic for one of the K types.

We are concerned here with the the first time at which the population is monomorphic, which we call the absorption time. Focusing on one particular type, i , we define the fixation time as the absorption time conditioned on monomorphism of type i . We will obtain asymptotic expressions for the expected time to absorption and the expected (conditional) time to fixation for two quasi-neutral types, and for an arbitrary number of strictly neutral types. These expressions become exact as N approaches infinity, and, as we confirm with numerical analysis, they are already very accurate for N of the order of hundreds. We present our results below, with details of the derivation in the appendices.

Asymptotically, both hitting times depend only on the initial state of the system. We express these hitting times as a function of new co-ordinates σ_i , which parameterise the flows of the deterministic system Eq. (A.6) (Appendix A.3). If the types are strictly neutral or if the population size starts at carrying capacity, then σ_i is simply the initial proportion of type i in the population, namely

$$\sigma_i = \frac{X_i(0)}{\sum_{j=1}^K X_j(0)}.$$

In general, explicit expressions for the σ_i do not exist, although they are well-defined and can be calculated numerically for any parameters and initial population sizes (Appendix A.3).

3.1. Absorption and fixation times for two quasi-neutral types

For two quasi-neutral types, the expected time to first absorption of either type is:

$$T(\sigma_1) = -\frac{N^*}{2\beta_1\beta_2} \left[(\beta_1(1 + \sigma_1) + \beta_2(1 - \sigma_1))(1 - \sigma_1) \ln(1 - \sigma_1) + (\beta_1\sigma_1 + \beta_2(2 - \sigma_1))\sigma_1 \ln \sigma_1 + \frac{(\beta_1 - \beta_2)^2}{\beta_1 + \beta_2} \sigma_1(1 - \sigma_1) \right], \tag{2}$$

while the conditional expected time to fixation for type 1 is

$$T_1(\sigma_1) = -\frac{1}{\pi_1(\sigma_1)} \frac{N^*}{2\beta_1\beta_2} [(\beta_1(1 + \sigma_1) + \beta_2(1 - \sigma_1)) (1 - \sigma_1) \ln(1 - \sigma_1) + \frac{1}{3} \frac{\beta_1 - \beta_2}{(\beta_1 + \beta_2)^2} \sigma_1(1 - \sigma_1) (2(\beta_1^2 - \beta_2^2)\sigma_1 + (\beta_1 + 2\beta_2)(3\beta_1 + \beta_2))], \quad (3)$$

where π_1 is the asymptotic probability that type 1 fixes (Parsons and Quince, 2007b):

$$\pi_1(\sigma_1) = \sigma_1 + \frac{\beta_2 - \beta_1}{\beta_1 + \beta_2} \sigma_1(1 - \sigma_1). \quad (4)$$

In subsequent sections we compare these hitting times to those expected under a neutral model. For now, we note the time to fixation of a single mutant of type 1 invading a resident population of type 2 is:

$$\frac{1}{12} \frac{N^*(5\beta_1^2 + 14\beta_1\beta_2 + 5\beta_2^2)}{\beta_1\beta_2(\beta_1 + \beta_2)}, \quad (5)$$

as N gets large. This is obtained by taking the limit $\sigma \rightarrow 0$ in Eq. (3). This expression is symmetric: a single mutant of type 2 invading a large resident population of type 1 has the same expected time to fixation. This result is interesting in light of Eq. (4), which shows that the type with lower birth rate has higher probability of fixation. The symmetric behaviour of the fixation time arises because we have conditioned on fixation. We discuss this issue further below.

Our analysis requires that the population size spend a long period of time near carrying capacity. This condition will be met provided α is much less than unity, $\frac{1}{\alpha}$ is strictly larger than the expected lifetime reproductive success of an individual, so as α approaches unity, the carrying capacity approaches zero and the entire population will rapidly go extinct. We are thus not interested in the behaviour of the system for α near unity, as the population behaviour degenerates in this regime. For intermediate values of α , however, our results are in excellent agreement with numerically determined times (neutral case in Fig. 2, quasi-neutral absorption times in Fig. 3, and quasi-neutral fixation times in Fig. 4). Our results agree with simulations for carrying capacities as small as fifty individuals.

In Fig. 1A, we compare Eq. (3) with numerical calculations of the fixation time for a single mutant for large and small values of N . In agreement with our analytic expressions, fixation time increases linearly in N . The slopes of both predicted and numerically determined lines are equal to the limit of machine precision. The lines differ only in their intercept – the result of lower order terms – which we have not determined for Eq. (3), but which are negative for the numerical results. Consequently we are slightly overestimating the fixation time by a fixed amount. This remains true as the population size is decreased, until around twenty individuals (Fig. 1B), where the numerical results deviate positively from the linear relationship to intercept the origin. Much of this effect can be attributed to events where one or both species vanish before the population arrives at the centre manifold. Numerical investigations reveal that using the harmonic mean population size in place of carrying capacity in our expressions above provides a slight improvement in the intercept, with the difference diminishing as N increases. Subsequent determination of the quasi-stationary distribution shows that the harmonic mean population size converges to the carrying capacity with increasing values of N (Parsons and Plotkin, in preparation).

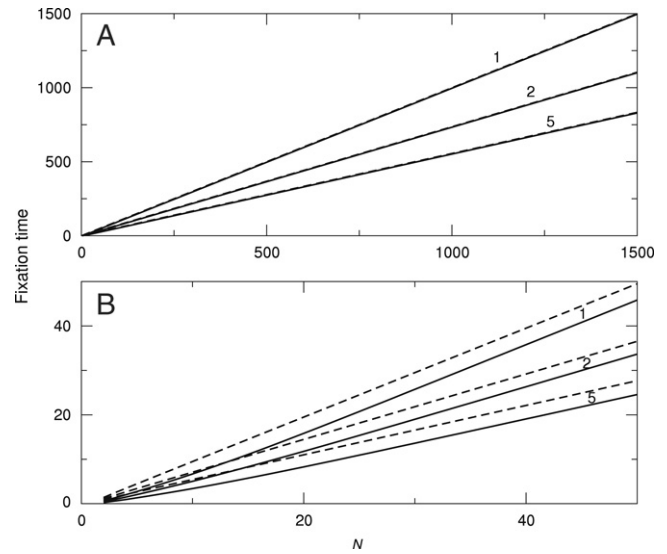


Fig. 1. A comparison of the analytic approximation (dashed lines) for fixation time of a single mutant, Eq. (3) with exact numerical results (solid lines), for varying values of N , (A) $\alpha = 0.5$, $\beta_2 = 1.0$, and $\beta_1 = 1.0, 2.0$, and 5.0 , as indicated on the graph. (B) detailed view of the same figure for small N .

3.2. Absorption and fixation times for K neutral types

Under the assumption of true neutrality, $\beta_i \equiv \beta$ and $\delta_i \equiv \delta$ for all i , the results of the previous section can be used to obtain fixation probabilities and times for an arbitrary number of types: when the types are truly neutral, we can calculate the probability of fixation and expected time to fixation for type i by considering it as one type, and collapsing all other types into a single, second type. Using Eqs. (3) and (4), we have

$$\pi_i(\sigma_i) = \sigma_i$$

$$T_i(\sigma_i) = -\frac{N^*}{\beta} \frac{(1 - \sigma_i) \ln(1 - \sigma_i)}{\sigma_i}. \quad (6)$$

Moreover, the absorption time is simply

$$T(\sigma_1, \dots, \sigma_K) = \sum_{i=1}^K \pi_i(\sigma_i) T_i(\sigma_i) \quad (7)$$

$$= \sum_{i=1}^K -\frac{N^*}{\beta} (1 - \sigma_i) \ln(1 - \sigma_i) \quad (8)$$

where σ_i is exactly equal to the initial density of type i :

$$\sigma_i = \frac{X_i^N(0)}{\sum_{j=1}^K X_j^N(0)}.$$

Dividing by the expected age to first reproduction, $\frac{1}{\beta}$, we get the expected number of generations until absorption or fixation. Our expressions agree with the classical expressions (Ewens, 2004) for absorption and fixation times in a population of fixed size equal to the carrying capacity, N^* , and are in excellent agreement with numerically exact results (Fig. 2A). In other words, in the case of strict neutrality, classical results on fixation times in constant-size populations still hold even when the population size varies stochastically.

As we remarked above, we expect our estimated fixation time to be less accurate for values of α near unity – in which case the population spends significant periods away from carrying capacity. In Fig. 2B, we compare our expression with numerically

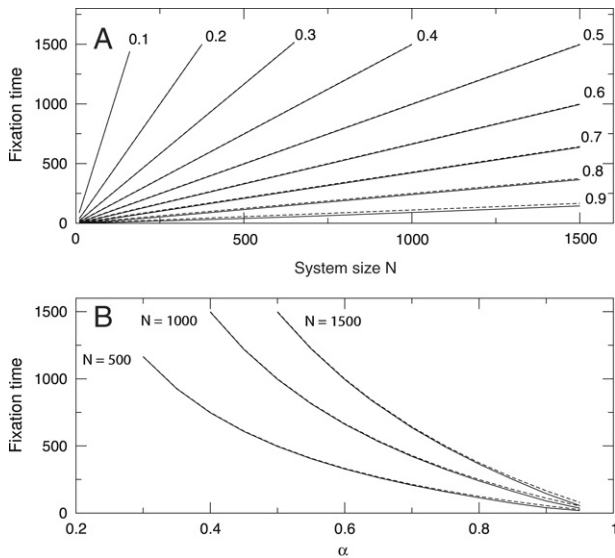


Fig. 2. A comparison of the analytic approximation (dashed lines) for fixation time Eq. (6) in the neutral case ($\beta_1 = \beta_2 = 1$) with exact numerical results (solid lines). (A) N varied at fixed $\alpha = 0.1, \dots, 0.9$. (B) α varied at fixed $N = 500, 1000, 1500$.

exact absorption times over a range of values of α , for three different values of N . We see that for the intermediate system size, $N = 1000$, our results remain accurate for $\alpha < 0.8$, corresponding to a carrying capacity of only 250 individuals. At smaller carrying capacities, our analytical expression overestimates the fixation time.

3.3. Comparison with fixed population size models

For strictly neutral types, (i.e. $\beta_i \equiv \beta$), we have shown that our expressions for mean absorption and fixation time coincide with the classical expression for a population with fixed total size. In this section, we compare absorption and fixation times in the quasi-neutral case against equivalent fixed-size models. Defining a corresponding fixed-size model for the quasi-neutral case is more complicated than for the strictly neutral case, as the two types have different birth and death rates. We address this by using two fixed-size models. Both models are formulations of the continuous time Moran model (Ewens, 2004) with types that are neutral and with fixed population size equal to the carrying capacity. In the first model, we assume all types are identical, with common birth rate equal to the harmonic mean of the birth rates in our quasi-neutral model:

$$\bar{\beta} = \frac{2}{1/\beta_1 + 1/\beta_2}. \tag{9}$$

For this choice of birth rate, each individual has mean time to first reproduction equal to the average reproduction time in an equilibrium quasi-neutral population. To keep the population size fixed, we assume that each birth is immediately followed by the death of a randomly chosen individual. The diffusion approximation to this process, obtained in the large population size limit, is equivalent to a haploid Wright–Fisher model with effective population size one half of census size. In this limit the fixation and absorption times are given by Eq. (6) and Eq. (7) respectively, with β as defined in Eq. (9).

The model above is the fixed population size equivalent of our density-dependent model when the two types are identical. However, this confounds two different effects. To investigate the effect of fixed population size alone, we use a variant of the Moran model that separates the fitness contributions of birth and death rates (Parsons and Quince, 2007a). This is done by allowing the

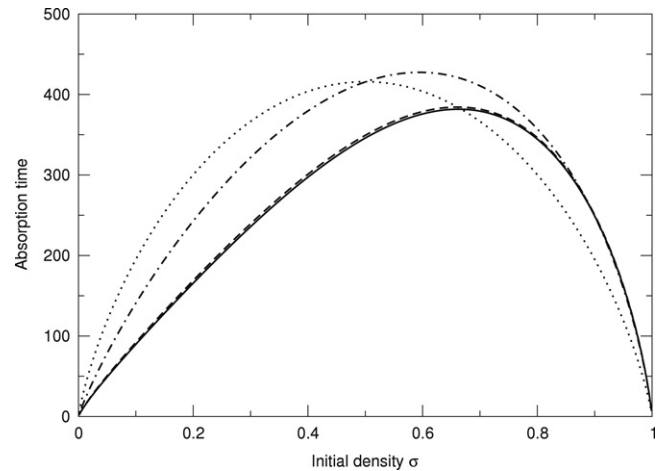


Fig. 3. Time to absorption for two quasi neutral types as a function of initial frequency, σ , of type 1. Total population size starts at carrying capacity, N^* . The graph shows exact numerical results (solid line) and the asymptotic approximation Eq. (2) (dashed line). Parameters are $\beta_1 = 5, \beta_2 = 1, \alpha = 0.5$ and $N = 1000$. Results from the equivalent neutral fixed size models, with identical types and birth rate equal to the harmonic mean (dotted line) and different birth rates (dot-dash) are also shown.

types to differ in their birth rates, and also in their probability of being replaced subsequent to a birth event. To parameterise this model in the quasi-neutral case, we simply take the birth rates to be equal to those in our quasi-neutral model, β_1 and β_2 , and then weight the probability of replacement by the birth rates. This ensures that the two types are neutral. It differs from the standard Moran model in that the normalisation for the deaths results in an extra frequency dependence in the rate at which events occur. As a result, in the limit of large population size there is no corresponding Wright–Fisher model. Since it is a one dimensional stochastic process, the absorption and fixation times can be written down explicitly and efficiently calculated numerically (van Kampen, 1992).

In Fig. 3, we plot the time to absorption for two quasi-neutral types as a function of initial frequency σ , starting with an initial total population at carrying capacity (solid line). Comparing these with the identical-type fixed-size model (dotted line), we see that the quasi-neutral absorption times are skewed, with a longer mean absorption time when the type with higher birth rate forms a larger initial proportion of the population. Examining the equivalent fixed size model with different types (dot-dashed line) we see that this skew does not depend on a fluctuating population size, but is rather a result of having types with different birth rates. Fluctuations in the total population size reduce absorption times when the type with higher birth rate is initially at low frequency. This reflects the lower fixation probability for this type in a fluctuating population, and the consequent increased likelihood of its relatively rapid elimination from the population.

In Fig. 4, we show the mean time to fixation of type 1 and type 2 for the density-dependent model and the two fixed-size models. When the types are identical (dotted line), the fixation time is independent of type and a decreasing function of initial density. The effect of having types with different birth rates at fixed population size (dot-dashed lines) is to increase the fixation times for the higher birth rate type 1 and decrease them for the lower birth rate type 2. This counter-intuitive effect is most pronounced at intermediate initial densities. This suggests that the dynamics of fixation are controlled not by the birth rate of the fixing type, but by the death rate of the displaced type. Comparing these results to our density dependent model (solid and dashed lines) it is apparent that demographic stochasticity reduces fixation times for both types, an effect that is more pronounced when the initial frequency is smaller.

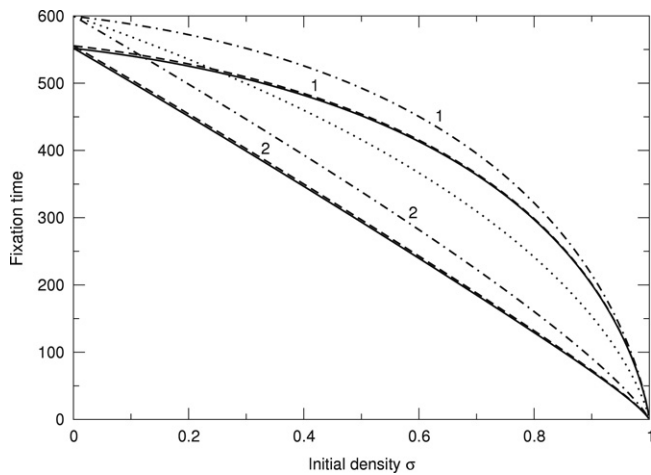


Fig. 4. Time to fixation for two quasi neutral types as a function of initial frequency σ , starting from carrying capacity: exact numerical results (solid line) and the asymptotic approximation Eq. (2) (dashed line). Parameters are $\beta_1 = 5$, $\beta_2 = 1$, $\alpha = 0.5$ and $N = 1000$. The times are shown for both type 1 and type 2 (type indicated on graph). Results from the equivalent neutral fixed size models, with identical types and birth rate equal to the harmonic mean (dotted line) and different birth rates (dot-dash) are also shown.

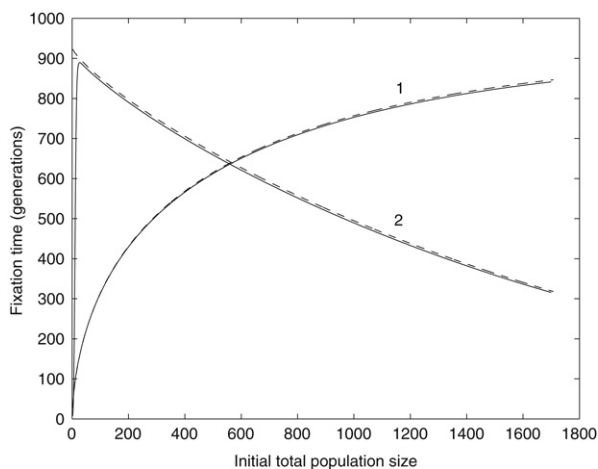


Fig. 5. Generations to fixation for each of two quasi-neutral types (type indicated on graph) as a function of initial population size, starting from equal numbers of each type: exact numerical results (solid line) and the asymptotic approximation Eq. (3) (dashed line). Parameters are $\beta_1 = 5$, $\beta_2 = 1$, $\alpha = 0.5$, and $N = 1000$.

3.4. Dependence on initial population sizes

In Fig. 5 we compare the time to fixation for the two types as obtained from expression Eq. (3) with exact numerical computations. The two agree very well for all but extremely small population sizes, a consequence of very small populations tending to go extinct before reaching carrying capacity. More importantly, the figure shows the consequence of the trade-off on fixation times: types that allocate toward higher birth-rates at the cost of higher death rates will on average fix very rapidly in unsaturated environments, but will take substantially longer than a type with fewer births and deaths when the population is near carrying capacity. This result likely has important consequences when the population is subject to exogenous fluctuations, such as bottlenecks. In particular, repeated extreme bottlenecks are likely to favour the fixation of types with higher vital rates.

4. Discussion

The expressions in Section 3.1 are, to the best of our knowledge, the first analytic results for the time to absorption

and fixation in a two-allele model with stochastically varying population sizes. These are asymptotic results, and they can be expected to be precise only for populations with large carrying capacity. Nonetheless, numerical experiments confirm that they are quite accurate for populations of one hundred or fewer haploid individuals.

Our study focused on the quasi-neutral case: both types have the same carrying capacity and would be considered neutral in a fixed population size model. We have shown that in the quasi-neutral case, the mean absorption and fixation times for intermediate sized populations are skewed relative to a model with identical types. This effect is independent of the presence of a fluctuating population size. The effect of demographic stochasticity is to reduce fixation times and absorption times. For quasi-neutral mutants, fixation times are substantially smaller than for the equivalent fixed size model, something we had noted previously for deleterious mutants (Parsons and Quince, 2007a).

Interestingly, we observed that when a single individual invades a resident population at equilibrium, the expected time to fixation does not depend upon whether the invader has a higher or lower birth rate than the resident. In other words, the advantage of a high birth rate at low population density is exactly compensated by the disadvantage of high death rates at large population density. By contrast, when the number of invaders is significantly larger than one, invaders with a higher birth rate take longer to fix than invaders with a lower birth rate. In Maruyama and Kimura (1974) and van Herwaarden and van der Wal (2002) a similar result was found for the Wright–Fisher model with selection: a single mutant that is negatively selected will on average take the same time to fix as a positively selected mutant. More recently, Antal and Scheuring (2006) have shown that fixation times are equal in a population of fixed size consisting of two types competing according to a 2×2 matrix game, while Taylor et al. (2006) show that for all one-dimensional discrete time Markov chains on $\{0, \dots, N\}$ satisfying a detailed balance condition, if 0 and N are absorbing states, then the distribution of first exit times conditioned on first exit through 0 or through N are equal. Inspired by their elegant argument, in Appendix B, we show that for diffusions on an interval $I = (r_0, r_1)$, subject to a similar condition, the conditional first exit time distributions across r_0 and r_1 are equal. The result in Taylor et al. (2006) and our result are consequences of time-reversibility (Kent, 1978; Ewens, 2004): after a relaxation period, for all pairs of points $x, y \in \{1, \dots, N-1\}$ ($x, y \in (r_0, r_1)$ respectively), the probability that the process following a path of length t from x to y is equal to the probability that the process goes from y to x in equal time. This explains the equality in expected fixation times observed above, and also ensures that all higher moments of the fixation time are equal as well.

Lastly, we found that in the limit of true neutrality, when all types have the same birth and death rates, our expressions for times to absorption and fixation simplify to those derived in the neutral case by Ewens, Littler, and Kimura and Ohta (Kimura and Ohta, 1969a,b; Littler, 1975; Ewens, 2004), with the carrying capacity in place of population size. In other words, our results are compatible with classical theory. In addition, our results demonstrate that the theory of neutral types with a fixed population size remains asymptotically correct in predicting fixation times for stochastically varying populations. This is due in large part to the fact that the total population will rapidly grow to carrying capacity and will thereafter spend a long period fluctuating about carrying capacity. This is also true for the quasi-neutral case, which indicates that one must use caution in making separation of time-scale arguments. The differences between the neutral and quasi-neutral cases arise from these fluctuations: in the quasi-neutral case, the size of the fluctuations about carrying capacity are not uniform, but rather vary according to the proportion of the two types, which leads to fixation probabilities and times that differ qualitatively from models with a fixed population size.

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Appendix A. Deriving the asymptotic expressions

In this appendix, we give a sketch of the mathematical details of the derivation of equations Eqs. (2) and (3). Our argument proceeds by three steps. We

- (1) approximate the Markov chain \mathbf{X}^N by a diffusion process \mathbf{X}_N ,
- (2) express the expected absorption and fixation times as solutions to a Dirichlet problem,
- (3) and lastly, reduce the Dirichlet problem to an analytically solvable one-dimensional boundary value problem.

We elaborate on each of these steps below.

A.1. Diffusion approximation

For large N , we can approximate the process $N^{-1}\mathbf{X}^N$ by a diffusion process \mathbf{X}_N (Ethier and Kurtz, 1986; van Kampen, 1992; Gardiner, 2004). If X_N has probability density $p(\mathbf{y}, t|\mathbf{x})$ – for all $A \subseteq \mathbb{R}^K$,

$$\mathbb{P}_{\mathbf{x}} \{ \mathbf{X}_N(t) \in A \} = \int_A p(\mathbf{y}, t|\mathbf{x}) d\mathbf{y},$$

where $\mathbb{P}_{\mathbf{x}}$ denotes the probability conditioned on initial value \mathbf{x} – then p must satisfy the Fokker–Planck equation

$$\partial_t p(\mathbf{y}, t|\mathbf{x}) = - \sum_{i=1}^K \partial_{y_i} [b^i(\mathbf{y}) p(\mathbf{y}, t|\mathbf{x})] + \frac{1}{2} \sum_{i,j=1}^K \partial_{y_i}^2 [a^{ij}(\mathbf{y}) p(\mathbf{y}, t|\mathbf{x})],$$

where

$$b^i(\mathbf{y}) = \beta_i y_i - \delta_i y_i \left(1 + \sum_{j=1}^N y_j \right)$$

$$Na^{ij}(\mathbf{y}) = \begin{cases} \beta_i y_i + \delta_i y_i \left(1 + \sum_{j=1}^N y_j \right) & \text{if } i = j, \\ 0 & \text{otherwise} \end{cases} \quad (\text{A.1})$$

with initial condition

$$p(\mathbf{y}, 0|\mathbf{x}) = \delta(\mathbf{x} - \mathbf{y}).$$

Under the assumption of quasi-neutrality, in the limit as $N \rightarrow \infty$, \mathbf{X}_N approaches a deterministic dynamical system

$$\dot{X}_i = \beta_i X_i \left(1 - \alpha \left(1 + \sum_{j=1}^N X_j \right) \right) \quad (\text{A.2})$$

with an attracting centre manifold along the hyperplane

$$\left\{ \mathbf{x} \in \mathbb{R}^K \mid \sum_{j=1}^K x_j = \frac{1}{\alpha} - 1 \right\}.$$

A.2. Exit probabilities and times

The diffusion process \mathbf{X}_N may be visualised as describing the motion of a particle in $(\mathbb{R}^{\geq 0})^K$. Extinction of a type i corresponds to the particle exiting this region through one of the faces $\Gamma_i = \{ \mathbf{x} | x_i = 0, x_j \neq 0, j \neq i \}$.

The problem of exit from a domain has been long studied, and it is a well known result (Gardiner, 2004) that the probability of exiting through Γ_i starting from an initial point \mathbf{x} , $\pi_i(\mathbf{x})$, satisfies the Komolgorov equation

$$\sum_{i=1}^K b^i(\mathbf{x}) \partial_{x_i} \pi_i(\mathbf{x}) + \frac{1}{2} \sum_{i,j=1}^K a^{ij}(\mathbf{x}) \partial_{x_i}^2 \pi_i(\mathbf{x}) = 0 \quad (\text{A.3})$$

with boundary conditions

$$\pi_i |_{\Gamma_j} = \delta_{ij},$$

while the expected time to first exit, across any face, starting from \mathbf{x} , $T(\mathbf{x})$ satisfies

$$\sum_{i=1}^K b^i(\mathbf{x}) \partial_{x_i} T(\mathbf{x}) + \frac{1}{2} \sum_{i,j=1}^K a^{ij}(\mathbf{x}) \partial_{x_i}^2 T(\mathbf{x}) = -1 \quad (\text{A.4})$$

with boundary condition

$$T |_{\Gamma_j} = 0 \quad \text{for all } j.$$

Lastly, the expected time to exit, conditioned on exit through Γ_i , T_i , satisfies

$$\sum_{i=1}^K b^i(\mathbf{x}) \partial_{x_i} (\pi_i(\mathbf{x}) T_i(\mathbf{x})) + \frac{1}{2} \sum_{i,j=1}^K a^{ij}(\mathbf{x}) \partial_{x_i}^2 (\pi_i(\mathbf{x}) T_i(\mathbf{x})) = -\pi_i(\mathbf{x}) \quad (\text{A.5})$$

with boundary condition

$$(\pi_i T_i) |_{\Gamma_j} = 0 \quad \text{for all } j.$$

A.3. Projection on the centre manifold

To proceed, we introduce co-ordinates σ_i and τ such that

$$x_i = \begin{cases} \left(\frac{1}{\alpha} - 1 \right) \sigma_i e^{-\beta_i \tau} & \text{if } i < K \\ \left(\frac{1}{\alpha} - 1 \right) \left(1 - \sum_{i=1}^{K-1} \sigma_i \right) e^{-\beta_K \tau} & \text{if } i = K. \end{cases} \quad (\text{A.6})$$

We obtain σ and τ via a change of time coordinates in the dynamical system Eq. (A.2): let $\mathbf{X}(t, \mathbf{x})$ denote the solution starting from \mathbf{x} at time $t = 0$, and define

$$\sigma(\mathbf{x}) = \left(\frac{1}{\alpha} - 1 \right)^{-1} \lim_{t \rightarrow \infty} \mathbf{X}(t, \mathbf{x}),$$

$$G(t, \mathbf{x}) = \int_t^\infty 1 - \alpha \left(1 + \sum_{j=1}^K X_j(s, \mathbf{x}) \right) ds,$$

and

$$\tau(\mathbf{x}) = G(0, \mathbf{x}).$$

Then if $\dot{Y}_i = \beta_i Y_i$ has solution $\mathbf{Y}(t, \mathbf{x})$, a simple calculation shows that

$$\mathbf{X}(t, \mathbf{x}) = \mathbf{Y}(G(t, \mathbf{x}), \left(\frac{1}{\alpha} - 1 \right) \sigma(\mathbf{x})). \quad (\text{A.7})$$

Thus, the two systems follow the same solution curves, but at different rates, with trajectories of \mathbf{Y} beginning at the endpoints

of the trajectories of \mathbf{X} at $t = \infty$. Now $Y_i(t, \mathbf{x})$ is simply an exponential function; combining this with Eq. (A.7) and evaluating at $t = 0$ yields Eq. (A.6). Intuitively, τ is a measure of the distance of the point \mathbf{x} from the centre manifold $\sum_{i=1}^K x_i = \frac{1}{\alpha} - 1$, while $\sigma(\mathbf{x})$ maps each trajectory of Eq. (A.2) to a unique point in the standard simplex

$$\Delta^K = \left\{ \mathbf{x} \in \mathbb{R}^K \mid \sum_{j=1}^K x_j = 1 \right\},$$

giving a convenient parameterisation of the flows. In the neutral case, we have

$$\sigma_i = \frac{x_i}{\sum_{j=1}^K x_j},$$

while in general, the dependence of σ_i on \mathbf{x} is more complicated, and the value of σ must be determined numerically.

In (Parsons and Quince, 2007b), we showed that by making a change of variable $\tau = \frac{T}{\sqrt{N}}$ and looking for an asymptotic series expansion in powers of $N^{-\frac{1}{2}}$, the solution, π_1 , of Eq. (A.3) could be determined to order $O(N^{-\frac{1}{2}})$, from a lower dimensional problem on the centre manifold. An identical argument applies here; we refer the reader to our previous paper for details.

We now focus on the case $K = 2$, for which we are able to find analytical asymptotic expressions for the exit times and probabilities. In this case, the fixation of type 1 corresponds to the first exit across Γ_2 , while the centre manifold is simply the set of points $\{(\sigma_1, \tau) \mid 0 \leq \sigma_1 \leq 1, \tau = 0\}$. After projection to the centre manifold, our process reduces to a one dimensional diffusion $\Sigma(t)$ on $(0, 1)$, while Eqs. (A.3)–(A.5) become ordinary differential equations:

$$\frac{\beta_1 \beta_2 (1 - \sigma_1) \sigma_1}{(\frac{1}{\alpha} - 1) N (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1))^2} \times \left[(\beta_2 - \beta_1) \frac{d\pi_1}{d\sigma_1} + (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1)) \frac{d^2 \pi_1}{d\sigma_1^2} \right] = 0$$

$$\pi_1(0) = 0$$

$$\pi_1(1) = 1$$

for the fixation probability (see (Parsons and Quince, 2007b),)

$$\frac{\beta_1 \beta_2 (1 - \sigma_1) \sigma_1}{(\frac{1}{\alpha} - 1) N (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1))^2} \times \left[(\beta_2 - \beta_1) \frac{dT}{d\sigma_1} + (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1)) \frac{d^2 T}{d\sigma_1^2} \right] = -1$$

$$T(0) = T(1) = 0$$

for the expected time to absorption, and

$$\frac{\beta_1 \beta_2 (1 - \sigma_1) \sigma_1}{(\frac{1}{\alpha} - 1) N (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1))^2} \times \left[(\beta_2 - \beta_1) \frac{d}{d\sigma_1} (\pi_1 T_1) + (\beta_1 \sigma_1 + \beta_2 (1 - \sigma_1)) \frac{d^2}{d\sigma_1^2} (\pi_1 T_1) \right] = -\pi_1$$

$$\pi_1(0) T(0) = \pi_1(1) T(1) = 0$$

for the expected time to fixation of type 1.

These linear equations may be readily solved to give the expressions presented in 3.1.

Appendix B. Equality of fixation times in symmetric diffusions

In this appendix, we sketch a proof of the equality of the distribution of fixation times for a class of diffusions $X(t)$ defined on an open interval $I = (r_0, r_1)$ that includes our process $\Sigma(t)$.

Let X have distribution $p(t, y|x)$ satisfying the Fokker–Planck equation

$$\partial_t p(t, y|x) = \frac{1}{2} \partial_y^2 [a(y)p(t, y|x)] - \partial_y [b(y)p(t, y|x)]$$

with $a(y) > 0$ on I , with absorbing boundary condition

$$\lim_{y \rightarrow r_i} W(y) a(y) p(t, y|x) = 0 \tag{B.1}$$

where

$$W(y) = e^{-2 \int \frac{b(y)}{a(y)} dy}. \tag{B.2}$$

Thus, $p(t, y|x)$ also satisfies Komologorov's equation

$$\partial_t p(t, y|x) = \frac{1}{2} a(x) \partial_x^2 p(t, y|x) - b(x) \partial_x p(t, y|x)$$

with boundary condition

$$\lim_{x \rightarrow r_i} p(t, y|x) = 0 \tag{B.3}$$

(Feller, 1954a; McKean, 1956).

We assume additionally that $a(y)$ and $b(y)$ are in $C^2(I)$, $p(t, y|x)$ is in $C^2([0, \infty) \times I \times I)$, and that for $i = 0, 1$

$$0 < \lim_{y \rightarrow r_i} \left| \frac{b(y)}{a(y)} \right| < \infty. \tag{B.4}$$

Note that we do not require $\lim_{y \rightarrow r_i} a(y)$ or $\lim_{y \rightarrow r_i} b(y)$ to be non-zero or finite, so our assumptions include the process $\Sigma(t)$. We refer the reader to Feller (1954a,b) and McKean (1956) for detailed discussions of conditions under which these postulates apply.

For the exit time distributions to be sensible, we also require both boundaries of I to be accessible according to Feller's classification scheme (Feller, 1954a,b; Ethier and Kurtz, 1986; Ewens, 2004): let

$$m(y) = \int \frac{1}{a(y)W(y)} dy \quad \text{and} \quad p(y) = \int W(y) dy$$

be the speed measure and scale function, respectively. We then require that

$$u(y) = \int m(y) dp(y)$$

be finite in the limit as $y \rightarrow r_i$ (so both boundaries are exit or natural.) This implies that with non-zero probability, the process will exit across one or the other boundary in finite time: if

$$\tau_y = \inf\{t \geq 0 \mid X(t) = y\},$$

then for all $x \in I$,

$$\mathbb{P}_x \{ \tau_{r_i} < \infty \} > 0.$$

It may be readily verified that both 0 and 1 are accessible boundaries for Σ .

Under these assumptions, the diffusion is symmetric with respect to $w(y)$ (Kent, 1978):

$$\frac{p(s, y|x)}{w(y)} = \frac{p(s, x|y)}{w(x)}$$

where

$$w(y) = \frac{1}{a(y)W(y)}.$$

Moreover, the probability current,

$$J(t, z|x) = \lim_{y \rightarrow z} \frac{1}{2} \partial_y [a(y)p(t, y|x)] - b(y)p(t, y|x)$$

is continuous and finite everywhere on $\bar{I} = [r_0, r_1]$. Note that we require the use of a limit in our definition of the probability current so that it can be applied at the endpoints r_0 and r_1 of I . We also note that Eqs. (B.1) and (B.4) together imply that

$$J(t, r_i|x) = \lim_{y \rightarrow r_i} \frac{1}{2} \partial_y [a(y)p(t, y|x)], \tag{B.5}$$

while from Eq. (B.3) we have

$$\lim_{x \rightarrow r_j} J(t, r_i|x) = 0$$

for $i \neq j$.

Under our smoothness assumptions on $p(t, y|x)$, we may express the conditional exit-time distributions in terms of the probability current J (Gardiner, 2004):

$$\mathbb{P}_x \{ \tau > t | X(\tau) = r_i \} = \frac{\int_t^\infty J(s, r_i|x) ds}{\int_0^\infty J(s, r_i|x) ds}.$$

$J(s, r_i|x)$ is the flow of probability across r_i at time s , i.e. the probability that the diffusion process will exit in $[s, s + \Delta s)$. Thus, the numerator is the cumulative probability of exit at r_i for all times $s > t$, while the denominator is the flow across r_i for all time, and thus the probability of exit across r_i ; the fraction gives the conditional probability of exit across r_i at some time after t . We will use this expression to show that for a symmetric diffusion,

$$\lim_{x \rightarrow r_0} \mathbb{P}_x \{ \tau > t | X(\tau) = r_1 \} = \lim_{y \rightarrow r_1} \mathbb{P}_y \{ \tau > t | X(\tau) = r_0 \}. \tag{B.6}$$

The right hand side of this equality is

$$\begin{aligned} & \lim_{x \rightarrow r_0} \frac{\int_t^\infty J(s, r_1|x) ds}{\int_0^\infty J(s, r_1|x) ds} \\ &= \lim_{x \rightarrow r_0} \frac{\int_t^\infty a(x)w(x)J(s, r_1|x) ds}{\int_0^\infty a(x)w(x)J(s, r_1|x) ds}. \end{aligned}$$

Now, from Eq. (B.3), both numerator and denominator vanish as $x \rightarrow r_0$, so applying l'Hôpital's rule,

$$= \lim_{x \rightarrow r_0} \frac{\partial_x \left[\int_t^\infty a(x)w(x)J(s, r_1|x) ds \right]}{\partial_x \left[\int_0^\infty a(x)w(x)J(s, r_1|x) ds \right]}.$$

Using Eq. (B.5),

$$\begin{aligned} &= \lim_{x \rightarrow r_0} \frac{\partial_x \left[\int_t^\infty \lim_{y \rightarrow r_1} \frac{1}{2} \partial_y [a(y)a(x)w(x)p(s, y|x)] ds \right]}{\partial_x \left[\int_0^\infty \lim_{y \rightarrow r_1} \frac{1}{2} \partial_y [a(y)a(x)w(x)p(s, y|x)] ds \right]} \\ &= \lim_{x \rightarrow r_0} \frac{\partial_x \left[\int_t^\infty \lim_{y \rightarrow r_1} \frac{1}{2} \partial_y [a(y)a(x)w(y)p(s, x|y)] ds \right]}{\partial_x \left[\int_0^\infty \lim_{y \rightarrow r_1} \frac{1}{2} \partial_y [a(y)a(x)w(y)p(s, x|y)] ds \right]} \end{aligned}$$

where we have used the symmetry of $X(t)$: $\frac{p(s, y|x)}{w(y)} = \frac{p(s, x|y)}{w(x)}$. We have assumed $p(t, x|y)$, $a(x)$, and $a(y)w(y)$ are twice continuously differentiable, and their product has a continuous and bounded (and thus uniformly continuous) extension to \bar{I} , so we can interchange limits, derivatives and integrals with impunity to obtain

$$= \lim_{x \rightarrow r_0} \frac{\lim_{y \rightarrow r_1} \partial_y [a(y)w(y) \int_t^\infty \frac{1}{2} \partial_x [a(x)p(s, x|y)] ds]}{\lim_{y \rightarrow r_1} \partial_y [a(y)w(y) \int_0^\infty \frac{1}{2} \partial_x [a(x)p(s, x|y)] ds]},$$

and, provided the limits in the numerator and denominator exist,

$$\begin{aligned} &= \frac{\lim_{y \rightarrow r_1} \partial_y \left[a(y)w(y) \int_t^\infty \lim_{x \rightarrow r_0} \frac{1}{2} \partial_x [a(x)p(s, x|y)] ds \right]}{\lim_{y \rightarrow r_1} \partial_y \left[a(y)w(y) \int_0^\infty \lim_{x \rightarrow r_0} \frac{1}{2} \partial_x [a(x)p(s, x|y)] ds \right]}, \\ &= \frac{\lim_{y \rightarrow r_1} \partial_y [a(y)w(y) \int_t^\infty J(s, r_0|y) ds]}{\lim_{y \rightarrow r_1} \partial_y [a(y)w(y) \int_0^\infty J(s, r_0|y) ds]}. \end{aligned}$$

Since the flux is well defined at r_0 , this last line allows us to conclude that the limits do indeed exist. We conclude by applying l'Hôpital's rule again:

$$\begin{aligned} &= \lim_{y \rightarrow r_1} \frac{a(y)w(y) \int_t^\infty J(s, r_0|y) ds}{a(y)w(y) \int_0^\infty J(s, r_0|y) ds} \\ &= \lim_{y \rightarrow r_1} \mathbb{P}_y \{ \tau > t | X(\tau) = r_0 \}, \end{aligned}$$

yielding our desired result.

Note that

$$\frac{1}{2} \partial_y^2 [a(y)w(y)] - \partial_y [b(y)w(y)] = 0,$$

so $w(y)$, when integrable, is a stationary distribution for $X(t)$, which is the case provided $\lim_{y \rightarrow r_i} a(y) > 0$. When $a(y)$ degenerates at the boundaries, $w(y)$ is often a good approximation to the quasi-stationary distribution for $X(t)$, except near to the endpoints of I (Gardiner, 2004) – in this case, the only true stationary distribution is 0, as X will exit through one of the endpoints with probability 1.

We may use this fact to give an intuitive interpretation of Eq. (B.6): after a transient period, the distribution of X converges to $w(x)$, except perhaps very near the boundaries. Thus, X is time-reversible with respect to w : the probability of moving from x to y in time t is $w(x)p(t, y|x)$, which, by symmetry, is equal to the probability $w(y)p(t, x|y)$ of X moving from y to x in the same time (Kent, 1978). In particular, the probabilities of the process traversing a path from r_0 to r_1 in time t or from r_1 to r_0 in the same time are equal, yielding Eq. (B.6).

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