The diffusion approximation (DA) is widely used in the analysis of stochastic population dynamics, from population genetics to ecology and evolution. DA is an uncontrolled approximation that assumes the smoothness of the calculated quantity over the relevant state space and fails when this property is not satisfied. This failure becomes severe in situations where the direction of selection switches sign. Here we employ the WKB (large-deviations) method, which requires only the logarithm of a given quantity to be smooth over its state space. Combining the WKB scheme with asymptotic matching techniques, we show how to derive the diffusion approximation in a controlled manner and how to produce better approximations, applicable for much wider regimes of parameters. We also introduce a scalable (independent of population size) WKB-based numerical technique. The method is applied to a central problem in population genetics and evolution, finding the chance of ultimate fixation in a zero-sum, two-types competition.

I. INTRODUCTION

Populations – collections of individuals which involve some kind of a birth and death process – are a fundamental object of study throughout the biological sciences. The number of individuals in a population is by definition an integer, and the birth-death process is inherently stochastic. As a result, the study of population dynamics – in genetics, ecology and evolution – requires one to examine stochastic processes over the set of integers [1–3].

These processes are characterized by different rates: the birth rate, for example, reflects the chance (per unit of time) of a given individual to produce an offspring. When the rates are fixed in time the stochastic process is stationary and the noise is binomial: for a population of \( n \) individuals the standard deviation of the total number of offspring per unit time is proportional to \( \sqrt{n} \). The rates themselves vary in time when the reproductive success of entire populations fluctuates coherently as a result of macro-environmental changes. If these variations are stochastic, which is a reasonable assumption given the complexity of all biological environments, the amplitude of abundance variations scales with \( n \). The \( \mathcal{O}(\sqrt{n}) \) noise, which is uncorrelated among individuals, is known in the literature as demographic stochasticity, internal noise or drift, while the \( \mathcal{O}(n) \) noise, originating from macro-variations of the environment, is usually described as external noise or environmental stochasticity [3–5].

Mathematically speaking, such a stochastic process corresponds to a biased random walk over the integers, and the important quantities which are of interest for life scientists, like the probability of fixation or invasion and the persistence time of a system, all have equivalents in the theory of random walks and first passage times [6]. But unlike simple random walks, here (even in a fixed environment) the rate of jumps and the strength of the bias depend on \( n \). Therefore, the effective timescale associated with environmental variations (the typical number of birth-death events before an environmental shift, say) reflects both external factors, like the correlation time of the environment, and internal factors, like the abundance of a given population. This phenomenon makes the mathematical analysis more complicated. Another source of complexity is the need to consider, in a varying environment, both drift and environmental stochasticity: while the drift is negligible in large populations, it does control the low-\( n \) sector and...
hence its strength dictates the most important processes, extinction and fixation [3, 7].

The simplest and the most popular tool in the analysis of these systems is the diffusion approximation (DA) [8]. This approximation is based on the expansion of the relevant quantities in a power series and the retention of only the two leading orders, an approach that assumes the smoothness of these quantities over the integers. Since its introduction the diffusion approximation has gained a lot of popularity, as it provides a generic algorithm that reduces problems of this kind to relatively simple, second-order differential equations such as the Fokker-Planck or the Backward Kolmogorov equation. The central place of the diffusion approximation in the modern theory of population genetics was surveyed by Wakeley [9], who described how, because of its usefulness as a calculation tool, the diffusion approximation has shaped the conceptual framework of the field.

For reasons that are not quite clear, the performance of the diffusion approximation in a stable environment (when selection is fixed in time and drift is the only noise-producing mechanism) is excellent [10]. On the other hand, in the presence of environmental stochasticity and fluctuating selection – for the importance of which there is ever-increasing evidence in the literature [11–20] – the performance of DA, as we shall see below, is much poorer. This poses a severe challenge to theory: most of the old [21, 22] and new [23, 20] studies of the effects of fluctuating selection or environmental stochasticity are based on the diffusion approximation, but the parameter range in which this generic technique is applicable turns out to be rather narrow.

The existing alternatives to DA for systems with fluctuating selection have their own problems. Numerical surveys, as in [30], are case-specific and are limited to relatively small systems. The applicability of Haldane’s branching process approximation [31–33] is restricted to small densities (it cannot take into account density-dependent, nonlinear effects) and its use in a system with a varying environment is technically complicated. Other works use heuristic arguments that rely on an interpolation between the diffusive and the nearly-fixed regimes [5, 34–36]. While these may be effective in particular scenarios, a general method to treat diverse systems under (weak as well as strong) fluctuating selection – one that may take the place of DA – is still lacking.

Here we present just such a generic approach, by combining the large-deviations (WKB) method with asymptotic matching techniques. Our approach may be adopted for a wide variety of problems in population genetics, ecology and evolution where the sign and the amplitude of the selection vary stochastically in time.

Large-deviations theory has been applied in the past to continuum (no drift) systems under large-amplitude external noise [37] and to systems with only drift (intrinsic noise) [38]. The combined effect of both types of stochasticity has been studied when the environmental fluctuations reflect an underlying Ornstein-Uhlenbeck process [4, 39, 40] or are modeled as an auxiliary species [41, 42]. Under these conditions the problem becomes two-dimensional and must be solved numerically.

Here we would like to break free of the limitations in existing approaches and to treat generic temporal environmental fluctuations as a one-dimensional problem, by combining the WKB method with the asymptotic matching technique that was employed with great success for the diffusion approximation [25, 27, 43, 44]. We consider the common case in which the fixation time is much larger than the correlation time of the environment (this is the “annealed” case of [34]; the chance of fixation otherwise depends strongly on the initial state of the environment). This allows us to average over different states of the environment and to map the problem onto a biased random walk, where step sizes reflect effective selection and effective (both drift-induced and environmental) stochasticity. The WKB method then yields a simple, single-parameter transcendental equation for which we present efficient approximate solutions. These
solutions are employed separately in the inner regime (close to extinction), in the outer regime (close to fixation), and in the intermediate regime (where the drift is negligible with respect to the environmental variations), and are matched to each other in the regions of overlap.

The range of applicability of this generic approach turns out to be much wider than that of DA, and it converges to DA when a given parameter is small, so its usage makes the DA technique a controlled approximation. Moreover, our approach allows further improvements, such as by adding more regimes to the asymptotic matching procedure or by modifying the transcendental equation to reflect better the details of the underlying process (see discussion). We also show how to implement our method as a scalable numerical technique that works even when $N$, the total community size, is too small to allow asymptotic analysis.

To clarify the discussion we stick here to the calculation of the simplest and the most important quantity in the theory of population genetics and evolution, namely the chance of ultimate fixation. The environmental stochasticity is modeled by erratic fluctuations between two states (dichotomous noise), as explained below. These assumptions impose no restrictions on the implementation of the technique presented here, which, *mutatis mutandis*, may be used to calculate other quantities (like the time to fixation, the time to absorption and the quasi-stable distribution function) under different realizations of stochasticity.

This paper is organized as follows. We begin, in the next section, with the case of fixed selection. DA works well in this case, so the goal of the discussion here is didactic: it allows us to present two critical elements of our method, the WKB technique and the two-destination approximation, and to demonstrate our ability to derive the same results using DA and using the new technique. The two-destination approximation yields naturally the fundamental transcendental equation, and its solutions in different sectors (that we name small-$q$, medium-$q$ and large-$q$, as explained below) are presented in Section III.

Section IV defines the stochastic dynamics of systems with fluctuating selection, and explains how to solve numerically for the chance of ultimate fixation using matrix inversion. In section V we employ the solutions presented in Section III and establish a scalable numerical scheme where (unlike the exact numerics which involve the inversion of an $N \times N$ matrix) the numerical effort is almost $N$-independent. The fully analytical analysis is first presented in Section VI. The analytical solution is based on a large-$N$ asymptotic matching technique that depends on the existence of an intermediate regime where the drift is negligible. In this section we determine the conditions (on the magnitude of $N$) for such an intermediate regime to exist. In Section VII we first rederive the results of DA as obtained in [26, 27], and then extend the solution to the small-$q$ sector. In Section VIII we present an approximate solution in the medium-$q$ sector, and the emerging general picture is reexamined in the discussion section.

## II. FIXED SELECTION

Under fixed selection (both positive and negative), the diffusion approximation performs excellently. Our goal in this section is not to improve this approximation but to provide a methodological and technical introduction to the use of the WKB technique. For this purpose we rederive the DA expression, first using the traditional method and then as a limit of the WKB expression.
A. General considerations

We consider a population with \( N \) individuals, \( n \) mutants and \( N - n \) wild-type individuals. If \( x = n/N \) is the frequency of the mutants, \( 1 - x \) is the frequency of the wild type. The mutant fitness is \( W = e^s \) so \( s \), the selection parameter, is the log-fitness. We consider a simple haploid non-overlapping generation (Wright-Fisher) dynamics: in each generation (without loss of generality, assumed to be a year) all the individuals die and their offspring (seed, larvae, etc.) compete for the \( N \) empty slots. The probability of the mutant type to capture any given slot is given by

\[
r = \frac{ne^s}{ne^s + (N - n)},
\]

(1)

Accordingly, the chance of a mutant population of size \( n \) to reach, in the next haploid generation, the size \( n + m \) \((-n \leq m \leq N - n)\) is

\[
W_{n\rightarrow n+m} = \left( \frac{N}{n+m} \right) r^{n+m} (1 - r)^{N-n-m}.
\]

(2)

The mean change of the mutant population size after one year is

\[
E[m] \equiv \sum_m m W_{n\rightarrow n+m} = N(r - x),
\]

(3)

and the variance of this quantity is

\[
E[m^2] - (E[m])^2 = N(r - r^2).
\]

(4)

B. The diffusion approximation

The chance of ultimate fixation starting from \( n \) individuals, \( \Pi_n \), satisfies the Backward Kolmogorov Equation,

\[
\Pi_n = \sum_m W_{n\rightarrow n+m} \Pi_{n+m}.
\]

(5)

This difference equation admits two independent solutions. Since \( \sum_m W_{n\rightarrow n+m} = 1 \), one solution is always a constant, so the general solution takes the form \( \Pi_n = C_1 + C_2 F_n \), where \( F_n \) is some non-trivial function of \( n \). The boundary conditions,

\[
\Pi_0 = 0 \quad \text{and} \quad \Pi_N = 1,
\]

(6)

are satisfied by a specific linear combination of the two solutions, which determines the constants \( C_1 \) and \( C_2 \).

The diffusion approximation is based on the assumption that \( N \) is large so that \( \Pi_n \) is smooth enough over the integers. This allows one to approximate (for \( x = n/N \))

\[
\Pi_{n+m} = \Pi(x + m/N) \approx \Pi(x) + \frac{m}{N} \Pi'(x) + \frac{m^2}{2N^2} \Pi''(x) + \frac{m^3}{6N^3} \Pi'''(x) + \text{higher order terms},
\]

(7)

where a prime denotes a derivative with respect to \( x \). Assuming that \( N \) is large and \( N s^2 \ll 1 \) [15], one finds that (see Appendix A for details)

- Only the first two terms (\( \Pi' \) and \( \Pi'' \)) must be taken into account, and all the higher-order terms (including \( \Pi''' \)) are negligible.
• The difference between the second moment, \( E[m^2] \), and the variance, \( \text{Var}[m] \equiv E[m^2] - (E[m])^2 \), is negligible. Accordingly, the diffusion approximation for Eq. (5) takes its canonical form,

\[
\frac{\text{Var}[m]}{2N^2} \Pi'' + \frac{E[m]}{N} \Pi' = 0.
\]

Specifically, for the model at hand one obtains

\[
\Pi'' + 2sN\Pi' = 0, \quad \text{with} \quad \Pi(0) = 0 \quad \text{and} \quad \Pi(1) = 1,
\]

and the solution is the well-known formula \[1, 2, 46\],

\[
\Pi(x) = 1 - \frac{e^{-2sx}}{1 - e^{-2sN}}.
\]

We emphasize that the diffusion equation depends on the assumption that \( \Pi \) is smooth over the integers, such that \( \Pi_{n+m} \) may be approximated by Eq. (7). When \( \Pi \) is not smooth enough, the diffusion approximation (DA) fails [38]. Note that \( N \to \infty \) is not a sufficient condition for smoothness: as may be seen from Eq. (10), when \( s \) is positive (beneficial mutation) the chance of fixation rises from zero at \( n = 0 \) to almost one when \( n = xN = 1/s \). The gradient of \( \Pi \) may be large even when \( N \) diverges.

C. WKB approximation and the two-destination scheme

Let us now take the WKB approach. As mentioned above, here our aim is not to improve the result in Eq. (10), but to demonstrate its derivation using the WKB technique and to discuss some details and limitations of WKB as employed here.

WKB is a generic perturbation scheme that allows one to derive a perturbation series that converges (asymptotically) to the correct result. Here we will calculate only the first term (the controlling factor) of this series. At this level the interpretation of our technique is quite simple: instead of assuming that \( \Pi_n \) is smooth over the integers, we assume that its logarithm, \( S_n = \ln \Pi_n \), is smooth. It is, of course, possible that even when a function is not smooth enough, its logarithm is.

With the substitution \( \Pi_n = e^{S_n} \), Eq. (6) takes the form

\[
e^{S_n} = \sum_m W_{n \to n+m} e^{S_{n+m}} \approx \sum_m W_{n \to n+m} e^{S(n) + mS'(n)}
\]

where the last approximation is based on the (assumed) smoothness of \( S \).

To continue we would like to get rid of the sum over \( m \). This may be done by introducing another approximation that has nothing to do with the WKB method itself (except for simplifying its calculations): the two-destination scheme. Instead of the random walk described in Eq. (2), we consider an “effective walk”: an asymmetric random walk whose possible destinations are given by the mean, plus or minus the standard deviation (the square root of the variance). For the mean and the variance we employ the same approximations used above, i.e., \( s \) and \( Ns^2 \) are assumed to be small, so for \( x = n/N \) and \( \Delta x \equiv m/N \), \( E[\Delta x] \approx sx(1-x) \) and \( \sqrt{\text{Var}[\Delta x]} \approx \sqrt{x(1-x)/N} \). The transition probabilities are thus,

\[
W_{x \to x+sx(1-x)+\sqrt{x(1-x)/N}} = 1/2 \quad \text{and} \quad W_{x \to x+sx(1-x)-\sqrt{x(1-x)/N}} = 1/2.
\]
Plugging (12) into (11) and substituting \( q \) for \( S'(n) \), one obtains
\[
e^S = \frac{e^S}{2} \left( e^{q(\sqrt{x(1-x)} + \sqrt{x(1-x)/N})} + e^{q(\sqrt{x(1-x)} - \sqrt{x(1-x)/N})} \right),
\]
(13)
or
\[
e^{q sx(1-x)} \cosh \left( q \sqrt{\frac{x(1-x)}{N}} \right) = 1.
\]
(14)

Note that here, and in what follows, we have suppressed the \( n \)-dependence of \( q \) and \( S \) (and \( \Pi \)) for notational convenience, though we will occasionally write them out as \( q(n) \), \( q(x) \), \( S(n) \), \( S(x) \), etc. (or \( q_n \), \( S_n \), etc., to highlight the discreteness of \( n \)) if we want to show the argument explicitly.

As we shall see below, the two-destination approximation yields generically equations that have the general form of Eq. (14). For the moment, let us assume that \( q \) is \( \mathcal{O}(1) \) (or, at least, is not a large parameter). In that case, the smallness of \( s \) and \( 1/N \) allows us to expand in Taylor series both the exponent and the \( \cosh \) functions, and the resulting expressions for \( q \) (where again we have assumed the smallness of \( s^2 N \)) are
\[
q_1 = -2sN \quad \text{and} \quad q_2 = 0.
\]
(15)

These two solutions yield the two independent solutions. Since \( S_1 = \int q_1 dx = -2sNx \) and \( S_2 = \int q_2 dx = \) constant, these two solutions are \( \Pi(x) = C_1 \) and \( \Pi(x) = C_2 \exp(-2sNx) \). The boundary conditions [6] are satisfied if \( C_1 = -C_2 = 1/[1 - \exp(-2sN)] \), which again yields the solution [10].

D. An outlook

As explained above, our goal in this section is not to improve (10) but to rederive it using the WKB technique. Let us review the steps involved:

- We employ only the controlling factor of the WKB expansion. This approximation has a simple interpretation: it assumes, instead of a smooth \( \Pi \), a smooth \( S = \ln \Pi \). This approximation may fail: in some cases even \( S \) is not smooth enough, in which case one has to use higher orders of WKB and/or to match it with other types of approximate solutions in the regions where they are available [38]. However, in most cases the controlling-factor analysis is adequate [4], and our problem is no exception.

- The two-destination approximation facilitates tremendously the implementation of the WKB method, and we use it throughout this manuscript. However, it should be noted that this scheme may fail. In particular, if both the destinations (i.e., both \( r + \sqrt{\text{Var}[m]/N^2} \) and \( r - \sqrt{\text{Var}[m]/N^2} \)) are to the left of the original location \( x = n/N \), then Eq. (14) allows only one solution, \( q = 0 \), because a two-destination walk of this type cannot end up in fixation. Similarly, when both the destinations are to the right of the original location, then the two-destination process does not allow extinction. This is an artefact of the approximation used. The actual process [Eq. (11)] still has a small chance of extinction or fixation, since the drift supports larger (although improbable) jumps. As a result, when \( \sqrt{x(1-x)/N} \) becomes too close to \( r - x \), the two-destination approximation fails while Eq. (11) is still valid.
Interestingly, in the case of fixed selection considered in this section, the two-destination approximation always fails in the large-$N$ limit. In the intermediate regime, where both $x$ and $1-x$ are $O(1)$, $r(x) - x$ is an $N$-independent number while the drift term $\sqrt{x(1-x)/N}$ goes to zero. However, under fixed selection (as opposed to the cases of fluctuating selection considered below) $\Pi(x)$ is almost fixed in this intermediate regime where $\sqrt{x(1-x)/N} \ll 1$. In the case of a beneficial mutant ($s > 0$), $\Pi$ grows and reaches values that are very close to one in the inner regime $x \ll 1$ (where $r(x) - x$ is $O(1/N)$, so it is comparable with $\sqrt{x/N}$), while for a deleterious mutant $\Pi$ is almost zero until the outer regime $1-x \ll 1$. Therefore, the technical failure of the two-destination WKB approximation in the intermediate regime has no effect on the outcome.

- The small-$q$ approximation, or more exactly small $q s x (1-x)$ and small $q \sqrt{x(1-x)/N}$, was used to derive Eq. (15) from Eq. (14). In the next sections, where the effect of a fluctuating environment is discussed, we will obtain analogous equations that have the same form as Eq. (14), for which the arguments of the exponent and cosh functions are not small. For these cases we will present alternate approximations.

### III. THE FUNDAMENTAL TRANSCENDENTAL EQUATION

The first-order WKB method, when employed using the two-destination approximation as described in the last section, yields naturally a transcendental equation of the form

$$e^{q s_e} \cosh(q \sigma_e) = 1. \quad (16)$$

In this equation $s_e$ is the effective deterministic bias of the population towards fixation or towards extinction, while $\sigma_e$ is the effective stochasticity (drift plus fluctuating selection). The value of $q$ depends strongly (see below) on the ratio between $s_e$ and $\sigma_e$. Equation (16) has no known closed-form solution in terms of elementary functions. In this section we present approximate solutions that work well in various sectors.

First, we write (16) as

$$\ln \cosh(q \sigma_e) = -q s_e. \quad (17)$$

Because the cosh function is symmetric, Eq. (17) reveals that $q(-s_e) = -q(s_e)$.

Second, with the definitions $\tilde{q} \equiv q \sigma_e$ and $\tilde{s} \equiv s_e/\sigma_e$, we obtain the one-parameter equation

$$e^{\tilde{q} \tilde{s}} \cosh(\tilde{q}) = 1. \quad (18)$$

Now we can identify three different sectors, and fit an approximate solution in each of them separately.

1. **In the small-$\tilde{q}$ sector**, one may expand the exponent and cosh functions in Eq. (18) to second order in $\tilde{q}$. This yields

$$\tilde{q} = -\frac{2 \tilde{s}}{\tilde{s}^2 + 1}, \quad (19)$$

or

$$q = -\frac{2 s_e}{s_e^2 + \sigma_e^2}. \quad (20)$$
Since DA assumes that $\Pi$ is smooth, when this approximation is applicable $S = \ln \Pi$ is clearly smooth as well, so $q = S'$ has to be small. Accordingly, one expects that when the diffusion approximation works, the system is in the small-$\tilde{q}$ sector. In fact, the diffusion approximation in its canonical form suggests that the parameter $2s_e/\sigma_e^2$ controls the results, so it corresponds to the subsector $s_e \ll \sigma_e^2$ of the small-$\tilde{q}$ sector.

2. In the large-$\tilde{q}$ sector, the $\cosh(\tilde{q})$ factor in Eq. (18) may be replaced by an exponent, $\cosh(\tilde{q}) \approx \exp(|\tilde{q}|)/2$. This leads to $\tilde{q}s_e + |\tilde{q}| = \ln 2$, so

$$\tilde{q} = \frac{\ln 2}{s_e - \text{sign}(s_e)}.$$  \hspace{1cm} (21)

and

$$q = \frac{\ln 2}{s_e - \text{sign}(s_e)\sigma_e}.$$ \hspace{1cm} (22)

As $\sigma_e$ approaches $|s_e|$ from above, the moves that are against the current (i.e., backward moves if $s_e > 0$ and forward ones if $s_e < 0$) become rarer and $q$ increases. Formally, Eq. (18) implies that $q$ diverges at $\sigma_e = |s_0|$, but this divergence does not reflect a discontinuous change in the chance of fixation. Instead it reflects the breakdown of the two-destination approximation. Once $\sigma_e \leq |s_0|$, moves against the deterministic current occur only through (rare) events at the tails of the jump distribution, so one cannot approximate the whole spectrum by its standard deviation. Therefore, the analysis suggested here becomes less reliable when the system enters deep inside the large-$\tilde{q}$ sector.

3. In the medium-$\tilde{q}$ sector, none of the above approximations work. Fortunately, when $\tilde{q}$ is plotted against $\tilde{s}$ on a semi-logarithmic scale, one finds that the small-$\tilde{q}$ approximation works well for $\tilde{s} < 0.25$, the large-$\tilde{q}$ solution works well for $\tilde{s} > 0.7$, and in the medium-$\tilde{q}$ sector $\ln \tilde{q}$ is nearly linear in $\tilde{s}$. This allows us to employ, in the medium-$\tilde{q}$ sector, the approximation

$$\tilde{q} = -\text{sign}(s_e)e^{3|\tilde{s}| - 1.3}.$$ \hspace{1cm} (23)

As a result,

$$q = -\text{sign}(s_e)\frac{e^{3|s_e|/\sigma_e} - 1.3}{\sigma_e}.$$ \hspace{1cm} (24)

Figure 1 shows how these three solutions cover the whole $\tilde{s}$-range. Table I summarizes the $q(s_e, \sigma_e)$ relationships used hereon as approximate solutions of the fundamental transcendental equation.

| $q$ | $|\tilde{s}| < 0.25$ | $|\tilde{s}| > 0.25$ |
|-----|-------------------|-------------------|
| small $\tilde{q}$ | $q \approx -\frac{2s_e}{(s_e^2 + \sigma_e^2)}$ |                    |
| medium $\tilde{q}$ | $0.25 < |\tilde{s}| < 0.7$ | $q \approx -\text{sign}(s_e)\frac{e^{3(s_e/\sigma_e)} - 1.3}{\sigma_e}$ |
| large $\tilde{q}$  | $0.7 < |\tilde{s}|$  | $q \approx \frac{\ln 2}{s_e - \text{sign}(s_e)\sigma_e}$ |
FIG. 1: Numerical solution of the transcendental equation (18) as a function of \( \tilde{s} \) (blue), together with the small-\( \tilde{q} \) approximation Eq. (20) (orange), the middle-\( \tilde{q} \) approximation Eq. (24) (red) and the large-\( \tilde{q} \) approximation Eq. (22) (green), using arithmetic (main) and semi-logarithmic (inset) scales [47].

IV. CHANCE OF ULTIMATE FIXATION UNDER FLUCTUATING SELECTION: THE MODEL AND ITS DIRECT NUMERICAL SOLUTION

We consider a population of size \( N \), with \( n \) mutant-type individuals and \( N - n \) wild-type individuals. Now the state of the system is fully characterized by \( N \), \( n \) and \( k \), the state of the environment. These quantities dictate the transition probabilities \( W_{n,k \rightarrow n+m,k'} \), where \( m \) is the change in a step in the abundance of the mutant type (and may be negative). The chance of ultimate fixation, \( \Pi_k^n \), satisfies the BKE,

\[
\Pi_k^n = \sum_{m,k'} W_{n,k \rightarrow n+m,k'} \Pi_{n+m,k'}^{k'},
\]

with the boundary conditions \( \Pi_0^n = 0 \) and \( \Pi_N^n = 1 \). As in the fixed selection case, since \( \sum_{m,k'} W_{n,k \rightarrow n+m,k'} = 1 \), any constant \( C_1 \) is a solution of (25) and the general solution is the linear combination, \( \Pi_k^n = C_1 + C_2 \Pi_n^k \), where \( C_1 \) and \( C_2 \) are determined by the absorbing boundary conditions.

The diffusion approximation approach assumes that \( \Pi \) is smooth over its state space [1, 2, 21, 22, 26, 27]. In systems with fluctuating selection, DA requires \( \Pi \) to be smooth also over the different environmental states \( k \), for instance assuming \( \Pi_n^\sigma - \Pi_n^{-\sigma} \ll 1 \) [25, 26]. This fails when the persistence time of the environment is comparable to the fixation time [34, 35]; in what follows we assume that \( N \) is large enough such that this condition is satisfied, which allows us to deal only with the non-smoothness of \( \Pi \) over the population states, and to average all \( \Pi_n^k \) to one \( \Pi_n \).

The dynamics used in Section II are extended to include fluctuating selection, so \( s \) is now picked at random in each generation. To facilitate the calculations we assume dichotomous stochasticity, with \( s(t) \) either \( s_0 + \sigma \) or \( s_0 - \sigma \), both with probability \( 1/2 \). This is a useful minimal model for fluctuating selection (see [43], Appendix A) and one can quite easily extend the procedure presented here to similar scenarios.

The great advantage of this model is its amenability to direct numerical solution. In general the dimension of a Markov matrix for a model with fluctuating selection is \( NK \times NK \), where \( N \) is the number of individuals and \( K \) is the number of environmental (selection) states. Here, because the environment is picked at random in each generation
with no correlations, one can average over all states to obtain an \( N \times N \)-dimensional matrix. This task becomes even simpler when the noise is dichotomous.

The chance of the mutant type to capture any given slot out of the \( N \) open slots in the next haploid generation is

\[
\tilde{r}_\pm = \frac{n e^{\pm \sigma}}{n e^{\pm \sigma} + (N - n)},
\]

and this leads to a simple form for the transition probabilities,

\[
W_{n \rightarrow n+m} = \frac{1}{2} \binom{N}{n+m} \left[ r_+^{n+m}(1-r_+)^{N-n-m} + r_-^{n+m}(1-r_-)^{N-n-m} \right].
\]

Therefore, the BKE takes the form \( \Pi_n = W_{n,n+m} \Pi_{n+m} \), where \( W \) is the \((N-1) \times (N-1)\) Markov matrix whose \((n,n+m)\)-th element is given in (27). The elements of the vector

\[
f_n = W_{n \rightarrow N}
\]

are the chance of fixation in the next generation when the current mutant population is \( n \).

Therefore, one can solve the BKE with its boundary condition by inverting the Markov matrix \( W \) (minus the identity matrix \( 1 \)) and multiplying it by \( f_n \),

\[
\Pi = -(W - 1)^{-1} f.
\]

Throughout this paper we have employed this procedure to find direct numerical solutions for \( \Pi_n \), which are then compared with the outcomes of the various approximation techniques used.

V. THE WKB APPROACH AND A SCALABLE NUMERICAL TECHNIQUE

The direct numerical solution presented in the last section requires matrix inversion whose numerical complexity is \( \mathcal{O}(N^3) \). In this section we present the WKB approach for a system with fluctuating selection and adopt it as an alternative numerical technique. This new technique is scalable: it requires (up to) five independent steps of one-dimensional numerical integrations, so the numerical effort is essentially \( N \)-independent. Besides, the discussion here lays the groundwork for the derivation (in the next section) of analytical solutions by means of the WKB technique.

A. Fluctuating selection in logit space

For the sake of convenience, we define a new parameter, the logit function \( z \), whose relationship with the frequency \( x \) is given by

\[
z \equiv \ln \left( \frac{x}{1-x} \right), \quad \text{so} \quad x \equiv \frac{e^z}{e^z + 1}.
\]

Since \( z \) and \( x \) are simple functions of each other, we will switch between them often and in some cases will present mixed expressions that utilize both the variables. One can easily translate these expressions to those containing only \( x \) or only \( z \) using Eq. (30).
We define the effective selection, \( s_e(z) \), and the effective stochasticity, \( \sigma_e(z) \), as the mean and the standard deviation of \( \Delta z \) per generation. The two-destination approximation [Eq. (12)] is used to model the effect of drift. For a given value of \( s \) this implies

\[
x \to \frac{xe^s}{1 - x + xe^s} \pm \sqrt{\frac{x(1 - x)}{N}} = \frac{xe^s}{1 - x + xe^s} \left( 1 \pm \sqrt{\frac{A^2(1 - x)}{Nxe^{2s}}} \right)
\]

\[
1 - x \to \frac{1 - x}{1 - x + xe^s} \pm \sqrt{\frac{x(1 - x)}{N}} = \frac{1 - x}{1 - x + xe^s} \left( 1 \mp \sqrt{\frac{A^2x}{N(1 - x)}} \right),
\]

where

\[
A \equiv 1 - x + xe^s = 1 + \frac{e^{s + z}}{1 + e^z}.
\]

If \( N \) is taken to be a large parameter (larger than any other parameter in the problem, like \( A \) and so on), then to the leading order in \( N \) we have

\[
z \to z' = z + s + \ln \left( 1 \pm \sqrt{\frac{A^2(1 - x)}{Nxe^{2s}}} \right) - \ln \left( 1 \mp \sqrt{\frac{A^2x}{N(1 - x)}} \right) \approx z + s \pm \sqrt{\frac{A^2(1 - x)}{Nxe^{2s}}} + \sqrt{\frac{A^2x}{N(1 - x)}}.
\]

This simplifies to

\[
z \to z' \approx z + s \pm B(s),
\]

where

\[
B(s) = \frac{1 + \cosh(s + z)}{\sqrt{N} \cosh(z/2)}.
\]

Now let us consider the case of fluctuating selection. Since \( s \) may now take two values, \( s_0 + \sigma \) and \( s_0 - \sigma \), the four-destination BKE (equivalent to Eq. (13) above) is

\[
\Pi(z) = \frac{1}{4} \sum_{\zeta_1 = 1, -1} \sum_{\zeta_2 = 1, -1} \Pi[s_0 + \zeta_1 \sigma + \zeta_2 B(s_0 + \zeta_1 \sigma)].
\]

Accordingly,

\[
s_e(z) = \mathbb{E}[\Delta z] = s_0,
\]

and

\[
\sigma_e^2(z) = \frac{1}{4} \left\{ \sum_{\zeta_1 = 1, -1} \sum_{\zeta_2 = 1, -1} [s_0 + \zeta_1 \sigma + \zeta_2 B(s_0 + \zeta_1 \sigma)]^2 \right\} - s_0^2.
\]

From now on, we will employ an effective two-destination approximation, where \( z \to z + s_e \pm s_e \). As a result, the fundamental transcendental equation takes the form

\[
e^{q(z)s_e(z)} \cosh(q(z)s_e(z)) = 1.
\]

Since we will solve the equation in terms of the logit variable \( z \), the special solution for \( \Pi \) will be \( \Pi = e^{S(z)} \) where \( S(z) = \int q(z)dz \). In what follows we will use in some cases the solution \( q(n) = q(xN) \), and in these cases the change of variables in the integral yields \( S(n) = \int [q(n)/n]dn \).
B. A scalable numerical solution

Eq. (38) defines a simple numerical procedure that yields $S_n$ and $\Pi_n$. First we solve (38) to obtain $q(z)$ for each value of $z_n = \ln[n/(N - n)]$, from the minimal point $z_{\min} \approx -\ln N$ to the maximal point $z_{\max} \approx \ln N$. Summing $q$ over these $z$-values yields $S_n$ and the special solution for $\Pi_n$, and imposition of the boundary conditions yields the full solution.

However, the use of this technique necessitates a solution of $N$ transcendental equations of the form (38). Since zero is always a solution and we need the other, nontrivial solution, this task is complicated for a single $n$-value, and solving $N$ such equations requires considerable numerical effort.

To overcome this difficulty, one may utilize the approximate solutions presented in Section III. Once $\sigma_e(z)$ and $s_e(z)$ are given, via Eqs. (36) and (37), the value of $\hat{s} = s_e/\sigma_e$ yields a solution obtainable from Table I. In Figure 2 we present a few typical profiles of $q(z)$ versus $z$, between $z_{\min}$ and $z_{\max}$. In all cases $q(z)$ is small close to the extinction/fixation points, since the drift is strong in these regions so $\sigma_e$ increases while $s_e$ is kept fixed. In some cases the maximum value of $q$ lies in the small-$q$ sector [Fig. 2(e)-(f)], in some cases it is large enough to lie in the medium-$q$ sector [Fig. 2(c)-(d)], and in some cases it lies in the large-$q$ sector [Fig. 2(a)-(b)].

Our scalable numerical technique is easy to use. We will describe it for the most complicated case where $q(z)$ reaches the large-$q$ sector. Its adaptation to the other cases follows immediately.

First we identify the different regimes by solving for $z_1$ and $z_4$, the two points at which $|\hat{s}(z)| = 0.25$, and for $z_2(x)$
and $z_3(x)$, the two points at which $|\tilde{s}(z)| = 0.7$. In each regime we use the appropriate expression for $q(z)$ (note that $s_e = s_0$),

\begin{align*}
    z_{\text{min}} \leq z \leq z_1 : & \quad q_1(z) = \frac{-2s_0}{s_0^2 + \sigma_e^2}, \\
    z_1 \leq z \leq z_2 : & \quad q_2(z) = -\text{sign}(s_0) \frac{e^{3|s_0|/\sigma_e - 1.3}}{\sigma_e}, \\
    z_2 \leq z \leq z_3 : & \quad q_3(z) = \ln 2 \frac{1}{s_0 - \text{sign}(s_0)\sigma_e}, \\
    z_3 \leq z \leq z_4 : & \quad q_4(z) = -\text{sign}(s_0) \frac{e^{3|s_0|/\sigma_e - 1.3}}{\sigma_e}, \quad \text{and} \\
    z_4 \leq z \leq z_{\text{max}} : & \quad q_5(z) = \frac{-2s_0}{s_0^2 + \sigma_e^2}.
\end{align*}

This scheme, with five regions, is required only if the maximum value of $\tilde{s}$ is larger than 0.7. Otherwise, if the maximum value is between 0.25 and 0.7 then only three regions are required, and if the maximum value is smaller than 0.25 then only one region is needed.

Once the values of $z$ are found, the quantities $I_1$ to $I_5$ are defined as the integrals over $q(z)$ in the relevant regimes,

\begin{align*}
    I_1 &= \int_{-\infty}^{z_1} q_1(z) dz, \quad I_2 = \int_{z_1}^{z_2} q_2(z) dz, \quad \text{etc.} 
\end{align*}

In our numerical integrations we replaced $-\infty$ by $\kappa z_{\text{min}}$, where $\kappa$ is some large number, and correspondingly $+\infty$, at the right end of the integration that yields $I_5$, by $\kappa z_{\text{max}}$.

For any given value of $z$, $S(z)$ is the integral over $q(z)$ from $-\infty$ to $z$. To be precise,

\begin{align*}
    \text{if } z \leq z_1 : & \quad S(z) = \int_{-\infty}^{z} q_1(z) dz, \\
    \text{if } z_1 \leq z \leq z_2 : & \quad S(z) = I_1 + \int_{z_1}^{z} q_2(z) dz, \\
    \text{if } z_2 \leq z \leq z_3 : & \quad S(z) = I_1 + I_2 + \int_{z_2}^{z} q_3(z) dz, \quad \text{and so on.}
\end{align*}

Finally, the chance of ultimate fixation is given by

\begin{align*}
    \Pi(z(x)) &= \frac{e^{S(z)} - 1}{e^{S(z)} + 1}. 
\end{align*}

In the denominator above, the sum is taken over the number of $I_j$ present [depending on the number of regions in (39)].

All in all, this technique involves the numerical solution of at most five transcendental equations of the form $\tilde{s} = 0.25$ (or 0.7) and at most five numerical integrations over known functions. Typical results obtained using this scalable numerical technique are compared with the direct numerical (matrix inversion) results in Figure 3.

VI. ASYMPTOTIC MATCHING AND WKB: DERIVATION OF THE KNOWN DA SOLUTION

With the WKB procedure set up, the set of integrals defined in the last section, if solvable, provides an analytical expression for the chance of ultimate fixation. In this and in the next section we consider simple cases in which this analytical expression is attainable. In general, this depends on the existence of an intermediate regime where the effect
FIG. 3: The chance of ultimate fixation $\Pi_n$ is plotted against $n$ for a deleterious [panel (a)] and beneficial [panel (b)] mutant, using double logarithmic scales. The parameters are $N = 5000$, $\sigma = 0.3$ and $s_0 = \pm 0.1$. Blue circles represent the results of the direct numerical solution of the BKE, Eq. (29), while the dashed red line is the scalable numerical solution as described in this section (with $\kappa = 10$).

of drift is negligible. Such a regime always exists if $N$ is large enough and $\sigma > |s_0|$. When the system supports an intermediate regime, one may employ (as in [26 27]) a standard asymptotic matching procedure, where the solutions in the inner and the outer regimes are matched with the intermediate solution in the large-$N$ limit. Here we first quantify the conditions under which the intermediate regime exists, and then rederive the DA solution of [26 27]. In the succeeding sections we explain how to derive the same expressions and much better approximations using the WKB method.

A. The intermediate/middle regime at large $N$

When $q(x)$ is bounded and $N \to \infty$, the system admits an intermediate regime in which the drift is negligible. Eq. (37) implies that the drift is negligible with respect to $\sigma$ and $s_0$ when $B(s_0 \pm \sigma) \ll s_0 \pm \sigma$. The minimal value of $B$ appears at

$$z^* = 2 \cosh^{-1} \left( \frac{1}{2} \sqrt{9 \cosh^2(s) + 2 \cosh(s) - 7 + 3 \cosh(s) - 1} \right),$$

(43)

where $s$ can take the values $s_0 \pm \sigma$. So we have

$$B(z^*) = \frac{2 + 7s^2/2}{\sqrt{N}} + O(s^4) \approx \frac{2}{\sqrt{N}}.$$  

(44)

Therefore, when

$$\sqrt{N} \gg \frac{2}{(\sigma - |s_0|)},$$

(45)

the value of $q$ in the intermediate zone (far away from the extinction/fixation regimes) is independent of the drift. Since $s_0$ and $\sigma$ are $n$-independent, this implies that the value of $q$ in the intermediate zone does not depend on $z$ (or $x$ or $n$). For each system that satisfies (45) one expects a plateau in the $q$-$z$ diagram. Note that the value of $N$ above which the plateau appears scales like $4/(|s_0| - \sigma)^2$ and so it diverges as $\sigma \to |s_0|$.
The existence of an intermediate regime for large $N$ suggests an **asymptotic matching approach**: one can solve for the relevant quantity in the intermediate regime and match it to the solutions in the inner ($x \ll 1$) and the outer ($1 - x \ll 1$) regimes, where the system is close to fixation/extinction and the drift dominates its behavior. In the next subsection we review the results one obtains using the diffusion approximation, and then we show how to derive the same, and improved, results using WKB.

### B. Three frequency regimes and asymptotic matching: the diffusion approximation

In former studies [26, 27] a model with fluctuating selection has been solved by employing the diffusion approximation. In these studies, $\Pi_{n+m}$ was expanded to second order in $m$ (as in Eq. (7) above) and the relevant terms were collected to yield a differential equation for the chance of ultimate fixation as a function of $x$.

These works considered a Moran model, where the environment flips erratically between the two states $s_0 \pm \sigma$ and the persistence times are picked from an exponential distribution whose mean is $\tau$ generations, where a generation is defined as $N$ elementary birth-death events. In their regime of validity (when DA holds), these results hold also for our model, provided that one takes $\tau = 1$ and replaces $N$ by $2N$. (The strength of the drift is $V/N$, where $V$ is the variance of the number of offspring per individual. In Moran models the distribution of offspring per individual is geometric so $V = 2$, while in Wright-Fisher models the distribution is Poissonian and $V = 1$.)

Translating the expressions of [26, 27] to the Wright-Fisher language, the chance of ultimate fixation satisfies

$$
\left[\frac{1}{N} + \sigma^2 x(1-x)\right] \Pi'' + \left[2s_0 + \sigma^2(1 - 2x)\right] \Pi' = 0.
$$

(46)

Note that in the limit $\sigma \to 0$, Eq. (46) converges to Eq. (9). The boundary conditions are, as before, $\Pi(x = 0) = 0$ and $\Pi(x = 1) = 1$.

Eq. (46) is a first-order linear differential equation and may be solved directly using an integrating factor, but the outcome is messy and hard to interpret. The strategy adopted in [26, 27] is based instead on asymptotic matching. The segment $0 \leq x \leq 1$ is divided into the following three parts:

- **The inner regime** (close to extinction), where $x \ll 1$ and $1 - x \approx 1$.

- **The middle (intermediate) regime**, where $x(1-x) \gg 1/N$. The drift term $1/N$ in (46) may be neglected in this regime. Unlike (45), here the width of the intermediate regime scales with $1/\sigma^2$, with no $s_0$-dependence. This happens since the treatment in [26, 27] assumes $s_0 \ll \sigma$.

- **The outer regime** (close to fixation) where $1 - x \ll 1$ and $x \approx 1$.

In each of these regimes Eq. (46) simplifies and may be solved explicitly, with solutions of the form $C_i + C_j \bar{\Pi}(x)$, where $C_i$ and $C_j$ are constants. These constants are determined by the requirement that the different solutions match each other when their regions of validity overlap. The inner solution matches the middle one when both $x \ll 1$ and $x \gg 1/N$ (i.e., when $Nx \gg 1$ but $x \ll 1$) and the middle matches the outer solution when $1 - x \ll 1$ while $1 - x \gg 1/N$.

The outcome of this procedure is demonstrated in Figure 4: the result of a numerical solution of the original, discrete BKE is compared with the expressions suggested in [26, 27].
FIG. 4: The numerical solution of the BKE [Eq. (29), with the transition probabilities in Eq. (27)] (solid blue line) is plotted against the solutions of Eq. (46) (dashed lines) in the inner (red), middle (green) and outer (cyan) regimes. The parameters are $N = 50000$, $s_0 = 0$ and $\sigma = 0.1$. Note the regions of overlap between the inner-middle and the middle-outer solutions.

VII. WKB APPROACH IN THE SMALL-$q$ SECTOR

Now we begin to derive the main analytical results of our work, by superimposing asymptotic matching on the WKB approach. We begin in the small-$q$ sector, by presenting our WKB technique in different $x$-regimes.

**In the middle/intermediate regime**, the drift is negligible and $q$ satisfies

$$e^{s_0 q_{\text{mid}}} \cosh(\sigma q_{\text{mid}}) = 1,$$

so

$$\Pi_{\text{mid}}(x) = C_3 + C_2 \left( \frac{x}{1-x} \right)^{q_{\text{mid}}}.$$  \hspace{1cm} (48)

If $q$ is also small, this implies

$$q_{\text{mid}} \approx -\frac{2s_0}{\sigma^2}.$$ \hspace{1cm} (49)

When $s_0 \ll \sigma$ (the approximation used in [26, 27]),

$$q_{\text{mid},1} \approx -\frac{2s_0}{\sigma^2}.$$ \hspace{1cm} (50)

**In the inner regime**, $x \ll 1$, so $z \approx \ln x$ is negative and large. In this limit, $\cosh(z/2) \approx 1/(2\sqrt{x})$ and $\cosh(s + z) \approx \exp(-s)/(2x)$. Accordingly [see Eq. (34)],

$$B(s) \approx \frac{2x + e^{-s}}{\sqrt{Nx}} \approx \frac{e^{-s}}{\sqrt{n}}.$$ \hspace{1cm} (51)

Plugging this into Eq. (37), we get

$$\sigma^2(n) = \sigma^2 + \frac{K(s_0)}{n},$$ \hspace{1cm} (52)

where

$$K(s_0) = e^{-2s_0} \cosh(2\sigma).$$ \hspace{1cm} (53)
Therefore, in the inner regime we can use
\[ q_{\text{in}} = -\frac{2s_0 n}{(s_0^2 + \sigma^2)n + K(s_0)} . \]  

In the outer regime we will use the symmetry relation
\[ \Pi(x|s_0) = 1 - \Pi(1 - x|-s_0) , \]  
which allows us to derive the outer and the inner solutions using the same formulas.

Armed with these expressions, we can now rederive the diffusion approximation, understand the assumptions on which it relies, and improve it in several ways.

A. Rederivation of past results obtained using the diffusion approximation

To rederive the results of [26, 27], we assume
\[ s_0 \ll \sigma \ll 1 \]  
so
\[ K(s_0) \approx 1 . \]  

In the middle regime this implies
\[ \Pi_{\text{mid}}(x) = C_3 + C_2 \left( \frac{x}{1 - x} \right)^{-2s_0/\sigma^2} . \]  

The inner solution becomes
\[ q_{\text{in}} = -\frac{2s_0}{\sigma^2 + 1/n} . \]  

Accordingly,
\[ S_{\text{in}}(n) = \int q_{\text{in}}(z) dz = \int q_{\text{in}}(n) \frac{dn}{n} = -\int dn \frac{2s_0}{\sigma^2 n + 1} = -\frac{2s_0}{\sigma^2} \ln(\sigma^2 n + 1) . \]

Adding \( \exp(S_{\text{in}}) \) to the constant solution and using the condition \( \Pi(x = 0) = 0 \), one finds in the inner regime (note \( n = Nx \))
\[ \Pi_{\text{in}}(x) = C_1 \left( 1 - e^{S(n)} \right) = C_1 \left[ 1 - (1 + Nx\sigma^2)^{-2s_0/\sigma^2} \right] . \]

Finally, in the outer regime we utilize the symmetry of the problem, \( \Pi(x|s_0) = 1 - \Pi(1 - x|-s_0) \), to obtain
\[ \Pi_{\text{out}} = 1 - C_4 \left\{ 1 - \left[ 1 + N(1 - x)\sigma^2 \right]^{-2s_0/\sigma^2} \right\} . \]

Eqs. (56), (59) and (60) are the same equations obtained using the diffusion approximation in [26, 27].

This derivation of the DA result assumes \( s_0 \ll \sigma \). Due to this assumption the results depend solely on \( 2s_0/\sigma_c^2 \), which is the single parameter that is involved in a standard diffusion equation of the canonical form \( E(\Delta z)\Pi' + \text{Var}(\Delta z)\Pi''/2 = 0 \). Since \( \sigma \leq \sigma_c \), this assumption implies that the system is deep inside the small-\( q \) sector for every \( x \) (or \( z \)). However, the requirement for the small-\( q \) sector, \( s_e/\sigma_c < 0.25 \), say, is much weaker than \( s_0 \ll \sigma \), and in the next subsection we will show how to derive a better approximation in this sector.

B. Improved small-\( q \) approximation

To obtain better expressions we relinquish the assumption \( s_0 \ll \sigma \ll 1 \), so that in the inner regime one needs to use Eq. (54) for \( q \) [instead of Eq. (57)]. Integrating over \( dz = dn/n \) we get
\[ S_{\text{in}}(x) = q_{\text{mid}} \ln(1 + QNx) , \]
where \( q_{\text{mid}} \) was defined in \( 49 \) and \( Q \equiv (s_0^2 + \sigma^2)/K = (s_0^2 + \sigma^2)/[\exp(-2s_0) \cosh(2\sigma)] \). The inner solution thus takes the form

\[
\Pi_{\text{in}}(x) = C_1 \left[ 1 - (1 + QNx)^{q_{\text{mid}}} \right].
\] (62)

The symmetry relation \( 55 \) implies

\[
\Pi_{\text{out}}(x) = 1 - C_4 \left\{ 1 - \left[ 1 + \tilde{Q}(1-x) \right]^{-q_{\text{mid}}} \right\}.
\] (63)

where \( \tilde{Q} \equiv Q(-s_0) = (s_0^2 + \sigma^2)/[\exp(2s_0) \cosh(2\sigma)] \). The middle solution is, like Eq. \( 56 \) but without the \( s_0 \ll \sigma \) restriction,

\[
\Pi_{\text{mid}}(x) = C_3 + C_2 \left( \frac{x}{1-x} \right)^{q_{\text{mid}}}. \] (64)

Matching the inner and the middle solutions in the region \( 1/N \ll x \ll 1 \), and the middle and the outer solutions in the region \( 1/N \ll 1-x \ll 1 \), we get

\[
C_1 - C_1(QNx)^{q_{\text{mid}}} = C_3 + C_2 x^{q_{\text{mid}}} \quad \text{and} \quad C_3 + C_2(1-x)^{-q_{\text{mid}}} = 1 - C_4 + C_4 \left[ \tilde{Q}(1-x) \right]^{-q_{\text{mid}}}. \] (65)

This gives

\[
C_1 = C_3 = \frac{1}{1 - \left( N^2 \tilde{Q} \right)^{q_{\text{mid}}}}, \quad C_2 = \frac{(NQ)^{q_{\text{mid}}}}{N^2 \tilde{Q}^{q_{\text{mid}}}} - 1 \quad \text{and} \quad C_4 = \frac{\left( N^2 Q \tilde{Q} \right)^{q_{\text{mid}}}}{N^2 \tilde{Q}^{q_{\text{mid}}}} - 1. \] (66)

Figure 5 compares the results of the direct numerical solution of the BKE with the analytical expressions of the diffusion approximation and the improved small-\( q \) approximation, in all the three regimes, for beneficial (positive \( s_0 \)) and deleterious (negative \( s_0 \)) mutants. Clearly, the improved small-\( q \) approximation does a much better job of reproducing the numerical result.

The asymptotic matching approach relies on \( N \) being large. The larger the value of \( N \), the wider is the intermediate regime where the drift is negligible, and wider correspondingly is the overlap between this regime and the inner/outer regimes. One therefore expects the analytical expressions to fit the numerical results better as \( N \) increases, and this is indeed what happens, as demonstrated in Figure 6.

Unlike DA, which depends on the ratio between the mean and the variance of \( \Delta z \), in the small-\( q \) approximation the important parameter is the ratio between the mean and the second moment. As explained in Section II B the procedure that yields the diffusion approximation does not allow one to distinguish between the variance and the second moment, since the justification of the continuum approximation requires the mean to be negligible with respect to the second moment. Here, the use of the WKB approach makes it clear that it is the second moment, and not the variance, that is the correct coefficient of the \( \Pi'' \) term in the small-\( q \) sector.

An important quantity is the chance of a single mutant to reach fixation, \( \Pi(x = 1/N) \). Eqs. (62) and (66) yield

\[
\Pi(1/N) = \frac{1 - \left[ 1 + \frac{e^{x_0}(s_0^2 + \sigma^2)}{\cosh(2\sigma)} \right]^{-\frac{x_0}{s_0^2 + \sigma^2}}}{1 - \left[ \frac{N(s_0^2 + \sigma^2)}{\cosh(2\sigma)} \right]^{-\frac{x_0}{s_0^2 + \sigma^2}}}. \] (67)

It is interesting to examine the \( N \)-dependence of this expression. When \( q_{\text{mid}} \) is negative (i.e. for a beneficial mutant, with \( s_0 > 0 \)), the \( N \)-dependent term in the denominator disappears when \( N \to \infty \), and the chance of fixation becomes
$N$-independent. This implies that above some critical abundance, say $n_c$, the chance of fixation is nearly one. As explained in the companion letter [47],

$$n_c = \frac{e^{\frac{s^2 + \sigma^2}{s_0^2}} - 1}{s_0^2 + \sigma^2}. \quad (68)$$

On the other hand, when $q_{\text{mid}}$ is positive (i.e. for a deleterious mutant, with $s_0 < 0$), the chance of fixation decays to zero when $N \to \infty$. When selection is fixed [Eq. (10)] this decay is exponential, but in our case the decay of $\Pi$ is only as a power law in $N$, $\Pi \sim N^{-2q_{\text{mid}}}$. This happens because selection may change sign: although $s_0 < 0$, as long as $\sigma > |s_0|$ there are periods when $s = s_0 + \sigma > 0$. Accordingly, the mutant may reach fixation due to an improbable series of good years. The length of such a series that leads to fixation is logarithmic in $N$, so its probability decays like a power law [43]. On the other hand, when $\sigma < |s_0|$ the mutant can win only due to the drift (as it needs a rare series of binomial trials in which its actual abundance grows despite the expected abundance decrease), and then the chance of fixation decays exponentially with $N$.

FIG. 5: Chance of fixation as found from the numerical solution of the BKE (solid black line), from the diffusion approximation (dashed dotted lines), and from the improved small-$q$ approximation (dashed lines), for negative (left) and positive (right) values of $s_0$. In the case of the diffusion and the improved small-$q$ curves, the red curves are those for the inner region, the green ones are for the middle region, and the blue ones are for the outer region.

VIII. BEYOND THE SMALL-$q$ SECTOR: A SEMI-DIFFUSIVE APPROACH

In the last section we obtained analytical expressions for $\Pi$ in the small-$q$ sector, i.e, when $|\tilde{s}| = |s_e/\sigma_e| < 0.25$ for all values of $z$ (or $x$). In this section we aim to expand our analytical technique to the case where this condition is not satisfied. We assume that $N$ is large enough such that the intermediate regime, in which the drift is negligible, exists (see Section VIA above). In general, since $\sigma_e$ increases towards the extinction/fixation points, we expect that $|\tilde{s}| > 0.25$ in this intermediate regime, while in the inner and the outer regimes the small-$q$ approximation still holds. Accordingly, in the intermediate regime we still have

$$\Pi_{\text{mid}}(x) = C_3 + C_2 \left( \frac{x}{1 - x} \right)^{q_{\text{mid}}}, \quad (69)$$
FIG. 6: The performance of DA improves as $N$ increases. Here the direct numerical results (solid black) are compared with the inner (dashed red), middle (dashed green), and outer (dashed blue) solutions of the improved small-$q$ approximation for different values of $N$. While for $N = 1000$ the improved small-$q$ curves perform poorly, they fit the numerical curve very well when $N = 10000$.

but now $q_{\text{mid}}$ is obtained from the fundamental transcendental equation $\exp(q s_0) \cosh(q \sigma) = 1$, and we do not assume [as in Eq. (49)] that $q$ is small.

In the inner and outer regimes $\sigma_e$ is larger, so one may try to employ the small-$q$ solutions obtained in the last section, with minimal modification to ensure that their large-$n$ limit matches the solution in the intermediate regime. Thus we suggest the approximation

$$q_{\text{fin}} = \frac{-2 s_0 n}{K(s_0) - \frac{2 s_0 n}{q_{\text{mid}}}}$$

with $K(s_0)$ defined in Eq. (53). Eq. (70) converges to $q_{\text{mid}}$ when $n$ is large and to $-2 s_0 n / K(s_0)$ when $n$ is small.

The rest of the calculation proceeds along the lines of the last section, and the results turn out to be exactly those obtained in Eq. (66), with the substitutions

$$Q \rightarrow -\frac{2 s_0}{K(s_0) q_{\text{mid}}}$$

and

$$\tilde{Q} \rightarrow -\frac{2 s_0}{K(-s_0) q_{\text{mid}}}.$$  

Figure 7 shows a comparison between the numerical solution of the BKE (solid black curve), and the semi-analytical curves in the different regimes.

IX. DISCUSSION

The analysis of competition between different types (strains, alleles, species) lies at the heart of the theory of population genetics, ecology and evolution. The quantity we have considered here, the chance of ultimate fixation, together with other quantities like the mean time to absorption (either fixation or loss), determines the genetic polymorphism in a population and the divergence rate between populations [2], marks the transition between the successive fixation and clonal interference phases of evolutionary dynamics [18], and controls the species richness in ecological communities [19]. Given the increasing recognition of the importance of environmentally-induced selection fluctuations in the wild [11–20], many studies have focused on the calculation of these quantities in a varying environment.

The diffusion approximation, which shows a remarkably good performance when applied to systems under fixed selection, has a rather narrow range of applicability for systems with fluctuating selection. Here we have shown how to
FIG. 7: Chance of fixation as found from the direct numerical solution of the BKE (solid black curve), and using our analytical approximation for the regimes where $q$ is not small (dashed curves), for a beneficial (left panel) and a deleterious (right panel) mutant. The inner (red), middle (green) and outer (blue) solutions cover the numerical answer quite well and show good overlap. In both cases $|\tilde{s}| \approx 0.35$, so the small-$q$ approximation does not work.

extend the analytical results to a much wider part of the regime $\sigma > |s_0|$. This analysis is based on three steps. First, the controlling-factor WKB scheme allows us to focus on a single parameter, $q = S'$, which determines the nontrivial solution of $\Pi$. Second, the two-destination approximation reduces the problem to the analysis of a relatively simple transcendental equation whose approximate solutions are presented in Section III. Third, when $N$ is large enough and the intermediate regime exists, we employ the asymptotic matching technique, solved in the inner, outer and middle regimes, and match the outcomes in the regions of overlap.

Each of these three steps must be examined in itself. The third step, asymptotic matching, is a well-established and trusted technique, and it is known that the corrections scale as powers of the small parameter $1/N$. The controlling-factor WKB method neglects physical optics corrections; our preliminary calculations (not included in this paper) suggest that the related corrections disappear like inverse powers of $N$ as well. The two-destination approximation is more subtle, as it neglects long jumps and puts a limit on the applicability of the technique presented here. The replacement of all possible jumps by two destinations, $s_e + \sigma_e$ and $s_e - \sigma_e$, implies that once $\sigma_e$ becomes smaller than $|s_e|$, the jumps become unidirectional and the system flows deterministically to either fixation or extinction, whereas in practice rare long jumps may still lead to a different result. Because of this fact our approximation breaks down as $\sigma \to |s_0|$, where the relative importance of these long jumps increases. To overcome this difficulty, one may either abandon the two-destination approximation (in which case a more complicated transcendental equation appears), or devise an alternative two-destination scheme in which long jumps are taken into account while keeping the same mean and variance as $s_e$ and $\sigma_e^2$, respectively. We intend to employ such a strategy in a forthcoming work to address analytically the cases where $\sigma$ is close to, or even smaller than, $|s_0|$.

In the small-$q$ sector, when for any $z$ the ratio $|\tilde{s}| = |s_e/\sigma_e|$ is smaller than 0.25, we provide in Section VII a complete asymptotic matching solution. The main novelty in this solution, with respect to the standard diffusion approximation, is the replacement of the parameter $s_0/\text{Var}[\Delta z]$ by the ratio of $s_0$ and the second moment of $\Delta z$, $s_0/E[(\Delta z)^2]$. Note that the use of the variance is not a necessary part of the DA formalism; as explained in Section II when the assumptions behind DA hold, the difference between the second moment and the variance is negligible,
so each of them may serve equally well as the coefficient of the stochastic term $\Pi''$. The variance is frequently used in the literature [8], since intuitively one expects the strength of the stochasticity to be proportional to the variance – a parameter that reflects how much the jumps are scattered around their mean – and not by the second moment which partially includes the deterministic bias. However, as we have seen here, in our case the WKB analysis promotes the use of the second moment, and indeed the expressions obtained for $\Pi$ in the small-$q$ approximation fit the results much better than the variance-based DA expression.

When $q$ in the intermediate regime is not small, as in the case discussed in Section VIII, the application of the asymptotic matching approach becomes more complicated. Deep in the inner and outer regimes the strength of the drift is strong and the solution belongs to the small-$q$ sector, whereas in the middle regime it must approach other values. Here we presented a simple ad hoc solution to this problem by devising an expression that converges to the appropriate limit on both sides, neglecting possible mismatches between these two ends. Better approximations may be based on more detailed matching techniques in which the number of different regions increases.

In this work and in the companion letter [47] we have considered only dynamics that have no attractive fixed points except the absorbing states at extinction and fixation. When the system admits an attractive fixed point at finite $x$, either because of density-dependent feedback or due to stochasticity-induced stable coexistence [50]-[52], the chance of invasion or establishment becomes a very important quantity. The properties of the chance of invasion in this case may differ significantly from those of the chance of fixation; for example, the chance of invasion may be quite large despite the chance of fixation being very small, meaning that the system supports the long-lasting transient existence of ultimately-extinct species [27]. Still, as a technical problem, the calculation of this quantity, the chance of invasion, is very similar to the calculation of $\Pi$ as detailed here. We intend to exploit this feature in future work.
Appendix A: The assumptions behind the diffusion approximation for populations under fixed selection

The derivation of the diffusion approximation for random walks and other stochastic processes, either through the Kramers-Moyal expansion or via van Kampen’s $\Omega$-expansion, is an established procedure [3]. In section II we applied a Kramers-Moyal-type expansion to Eq. (5); here we would like to clarify the conditions for its validity by monitoring carefully the neglected higher-order terms.

We consider a Wright-Fisher (non-overlapping-generation) dynamics under fixed selection. As stated in Eq. (7), the assumed smoothness of $\Pi_n$ over the integers $n$ allows one to approximate $\Pi_{n+m} = \Pi(x + m/N)$, where $x = n/N$, as

$$\Pi(x + m/N) = \Pi(x) + \frac{m}{N} \Pi'(x) + \frac{m^2}{2N^2} \Pi''(x) + \frac{m^3}{6N^3} \Pi'''(x) + \text{higher order terms},$$

(A1)

where primes denote derivatives with respect to $x$. As stated in Eq. (2), the transition probability $W_{n\rightarrow n+m}$ to go from a population of size $n$ to a population of size $n+m$ (where $n+m$ may range from 0 to $N$) in a single step is

$$W_{n\rightarrow n+m} = \left( \frac{N}{n+m} \right)^{n+m} (1-r)^{N-n-m},$$

(A2)

where [see Eq. (1)] $r$ is the probability of the mutant type to capture any given slot out of the $N$ open slots in each generation, namely

$$r = \frac{xe^s}{xe^s + (1-x)}.$$

(A3)

The first three moments of the change in population ($m$) are therefore:

$$\bar{m} = \sum_{m=-n}^{N-n} m W_{n\rightarrow n+m} = N(r-x)$$

$$= Nsx(1-x) + \frac{Ns^2x(1-x)}{2} + O(s^3),$$

$$\bar{m}^2 = \sum_{m=-n}^{N-n} m^2 W_{n\rightarrow n+m} = N^2(r-x)^2 + Nr(1-r)$$

$$= Nx(1-x) + Nsx(1-x)(1-2x) + \frac{Ns^2x(1-x)[1+2x(1-x)(N-3)]}{2} + O(s^3),$$

(A4)

$$\bar{m}^3 = \sum_{m=-n}^{N-n} m^3 W_{n\rightarrow n+m} = N^3(r-x)^3 + 3rN^2(r-x)(1-r) + Nr(1-r)(1-2r)$$

$$= Nx(1-x)(1-2x) + Nsx(1-x)[1+3x(1-x)(N-2)] + \frac{Ns^2x(1-x)(1-2x)(1+3x(1-x)(3N-4))}{2} + O(s^3).$$

Here note that, for any $i$, the highest power of $N$ in the $O(s^3)$ terms in $\bar{m}^i$ is $i$, so if we wish to look at only the highest-magnitude terms, we can forget all the other terms hidden in $O(s^3)$ and consider only the $N^i s^3$ terms. (This statement assumes that $N$ is large and $s$ is small, in some way; these notions will be made precise below.)
Putting in Eqs. (A1) and (A4) in the Backward Kolmogorov Equation [Eq. (5)], we get

\[ 0 = \frac{\overline{m}}{N} \Pi' + \frac{m^2}{2N^2} \Pi'' + \frac{m^3}{6N^3} \Pi''' + \ldots \]

\[
= \left\{ sx(1 - x) + \frac{s^2x(1 - x)}{2} + A(x)s^3 \right\} \Pi' \\
+ \left\{ \frac{x(1 - x)}{2N} + \frac{sx(1 - x)(1 - 2x)}{2N} + \frac{s^2x(1 - x)[1 + 2x(1 - x)(N - 3)]}{4N} + B(x)s^3 \right\} \Pi'' \\
+ \left\{ \frac{x(1 - x)(1 - 2x)}{6N^2} + \frac{sx(1 - x)[1 + 3x(1 - x)(N - 2)]}{6N^2} + \frac{s^2x(1 - x)(1 - 2x)(1 + 3x(1 - x)(3N - 4))}{12N^2} + C(x)s^3 \right\} \Pi''' \\
+ \ldots,
\]

where \( A(x), B(x), C(x), \) etc., are functions only of \( x, \) not of \( N. \) This is because, as explained above, the largest coefficient of \( s^3 \) (and \( s^4, s^5, \) etc.) in \( \overline{m}^i \) is proportional to \( N^i, \) so division of \( \overline{m}^i \) by \( N^i \) makes the \( N\)-dependence in these terms disappear. We have ignored the other, smaller-magnitude, terms.

\( N \) is by assumption a large number, \( N \gg 1. \) In order to reduce Eq. (A5) to the diffusion equation, which in the current context takes the form [1, 2, 46]

\[ \Pi'' + 2Ns\Pi' = 0, \] (A6)

the only other assumption needed is \( s \) being small enough such that

\[ Ns^2 \ll 1. \] (A7)

With this assumption, checking Eq. (A5) term-by-term, it becomes clear that the dominant terms are

\[ 0 = sx(1 - x)\Pi' + \frac{x(1 - x)}{2N}\Pi'', \] (A8)

which is the same as Eq. (A6).

Under the above assumption, the second moment of \( m \) reduces to its variance. This is seen on calculating the variance explicitly,

\[ \text{Var}(m) = \overline{m^2} - \overline{m}^2 = Nr(1 - r) \]

\[ = Nx(1 - x) + Nsx(1 - x)(1 - 2x) + \frac{Ns^2x(1 - x)[1 - 6x(1 - x)]}{2} + O(s^3). \] (A9)

Comparison of this with Eq. (A4) shows that \( \text{Var}(m) \) and \( \overline{m}^2 \) differ only in the \( s^2 \) terms (and those with higher powers of \( s \)), which are smaller than \( \overline{m}^2 \) precisely by a factor of \( Ns^2 \ll 1. \)

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