Application of WKB and Fokker-Planck methods in analysing demographic stochasticity

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Abstract

In large but finite populations, weak demographic stochasticity due to random birth and death events can lead to population extinction. The process is analogous to the escaping problem of trapped particles under random forces. Methods widely used in studying such physical systems, for instance, Wentzel-Kramers-Brillouin (WKB) and Fokker-Planck methods, can be applied to solve similar biological problems. In this article, we review recent developments on the applications of WKB and Fokker-Planck methods to some typical stochastic population dynamical models, including the logistic growth, endemic SIR, predator-prey, and competitive Lotka-Volterra models. The mean extinction time strongly depends on the nature of the corresponding deterministic fixed point. For different types of fixed points, the extinction can be driven either by rare events or typical Gaussian fluctuations. In the former case, the large deviation function that governs the distribution of rare events can be well-approximated by the WKB method in the weak noise limit. In the later case, the Fokker-Planck approach is also appropriate.

Keywords Demographic stochasticity, Fokker-Planck equation, Mean extinction time, WKB
1 Introduction

Deterministic models based on rate equations have been playing a crucial role in analysing evolutionary population dynamics. The classic examples include the Hardy-Weinberg Law [Hardy, 1908, Weinberg, 1908], Fisher’s Fundamental Theorem of Natural Selection [Fisher, 1930], the Michaelis-Menten enzyme kinetics [Michaelis and Menten, 1913] (see Johnson and Goody [2011] for an English translation), the SIR epidemic model [Kermack and McKendrick, 1927], and the replicator equation in Evolutionary Game Theory [Taylor and Jonker, 1978]. These models have many convenient mathematical properties and they often very well capture the evolutionary dynamics in large populations. But deterministic models lose their power when confronted with biological systems that violate their fundamental assumptions, such as populations that are subject to substantial demographic stochasticity.

Demographic stochasticity is a form of population internal noise, caused by random independent events of birth and death of a finite number of individuals [Kendall, 1949, May, 1974]. It is in contrast to external disturbances, such as the fluctuations of environment parameters and natural catastrophes [Roughgarden, 1975, Lande, 1993]. Researchers have long been fascinated by the nature of demographic stochasticity and its impacts on population dynamics. One interesting property of finite population under the influence of demographic stochasticity is the possibility of extinction, which is not naturally predicted in deterministic rate equation models. Francis Galton proposed the famous problem of the extinction of family names already in 1873, which asks what proportion of the surnames will have become extinct after \( r \) generations in a large population, starting from the state that each adult man has a different family name (for reviews of the history see Kendall [1966]). But the correct answer to the problem was only given more than 50 years later by J.F. Steffensen, by first proving the criticality theorem of the Bienaymé-Galton-Watson branching process [Steffensen, 1930] (see a English translation by Guttorp [1995]).

In the last decades, facilitated with the development and application of various mathematical
tools and new modelling approaches, we were able to delve much deeper into the population dynamics under demographic fluctuations and to gain valuable knowledge. A number of such tools were originally developed for solving problems in statistical mechanics and quantum mechanics, such as the Fokker-Planck approximation and the Wentzel-Kramers-Brillouin (WKB) approximation methods. Taking advantage of the close analogy between biological systems and the corresponding physical systems, the methods developed for tackling physical problems can be transferred to answer biological questions. For example, the extinction of population from a steady state driven by weak noise is very similar to the escaping problem of particles in a trapping potential [Dykman et al., 1994]. Thanks to the successful transfer of knowledge, we know nowadays for example that for basic birth-death processes models of a single species with quasi-steady-state carrying capacity $K$, extinction happens on exponentially large time scales $-e^{K}$ as $K \to \infty$. If the population is more complex with more than one species interacting with each other, the extinction behaviour is determined by the nature of the deterministic fixed point.

In this paper, we do not attempt to provide a broad synthesis that covers all important developments in stochastic population dynamics, but to focus on basic and commonly used theoretical tools, namely, the WKB and Fokker-Planck approximation methods, inherited from quantum mechanics and statistical mechanics. For reviews of broader applications of statistical physics in evolutionary biology, see [Sella and Hirsh, 2005, Barton and Coe, 2009, de Vladar and Barton, 2011]. The special issue associated with Fisher et al. [2013] also provide interesting applications of statistical physics methods in studying various evolutionary biological problems. We review recent works on population extinction from a stable state driven by weak demographic stochasticity (intrinsic noise), where the environment is assumed to be stable. In summary, the nature of the stable states in the mean-field level determine the behaviour of the mean time to extinction. In systems with an attracting fixed point or limit cycle, extinction is caused by rare events, the diffusion approximation thus fails to give accurate estimations of the mean extinction time and the large deviation approach is required. For marginally stable states, extinction is driven by typical Gaussian fluctuations and the Fokker-Planck approximation is valid.

2 Extinction time of populations formed by a single species

2.1 The deterministic logistic growth model

One of the most widely applied population growth model of a single species is the logistic growth model, or the Verhulst model, named after Pierre-François Verhulst [Verhulst, 1838]. This model has been extensively used in modelling the saturation of population size due to resource limitations [Murray, 2007, McElreath and Boyd, 2008, Haefner, 2012], and formed the basis for several extended models that predicts more accurately the population growth in real biological systems, such as the Gompertz, Richards, Schnute, and Stannard models (for a review, see Tsoularis and Wallace [2002]).
The classic logistic model takes the form

$$\frac{dn}{dt} = rn \left(1 - \frac{n}{K}\right),$$

(1)

where $n$ represents population size, the positive constant $r$ defines the growth rate and $K$ is the carrying capacity. The unimpeded growth rate is modeled by the first term $rn$ and the second term captures the competition for resources, such as food or living space. The solution to the equation has the form of a logistic function

$$n(t) = \frac{Kn_0e^{rt}}{K + n_0 \left(e^{rt} - 1\right)},$$

(2)

where $n_0$ is the initial population size. Note that $\lim_{t \to \infty} n(t) = K$, and this limit is asymptotically reached as long as the initial population size is positive, and the extinction of the population will never happen.

2.2 Population dynamics under demographic stochasticity

When the typical size of the population is very large ($1/K \ll 1$), fluctuations in the observed number of individuals are typically small (Central Limit Theorem). In this case, the deterministic logistic growth model generally provides a good approximation to the population dynamics by predicting that the population will evolve towards and then persists at the stable stationary state where $n = K$. However, in the presence of the demographic noise, occasional large fluctuations can still induce extinction, making the stable states in the deterministic level metastable. In any finite population, extinction will occur as $t \to \infty$ with unit probability.

In an established population under logistic growth with a large carrying capacity, the population size fluctuates around $K$ due to random birth and death events, and typically the fluctuation is small in the large $K$ limit. But from time to time, a rare large fluctuation can happen, and it may lead to the extinction of the population. In such situations, it is interesting and often biologically important, to determine the most probable paths and the mean time to extinction, when starting from the stable population size. A rigorous approach for solving these problems in the weak noise limit is the large deviation theory [Touchette, 2009]. We use the logistic growth model to illustrate the main idea.

Let the function $T(n \to m)$ represent the probability of the transition $n \to m$ per unit time. For the logistic model $T(n \to n + 1) = \lambda_n = Bn$ describes the birth rate of the population, where $B$ is the per capita growth rate, and $T(n \to n - 1) = \mu_n = n + Bn^2 / K$ describes the death rate of the population, in which $K$ stands for the carrying capacity, the first term represents spontaneous death, and the second term represents death caused by competition. The function $P(n, t)$ is the probability density for the system to be in the state with the population of $n$ at the time $t$, obeying a Master equation

$$\frac{dP(n, t)}{dt} = \sum_m [T(m \to n, t)P(m, t) - T(n \to m, t)P(n, t)]$$

$$\quad = \mu_{n+1}P(n+1, t) + \lambda_{n-1}P(n-1, t) - (\mu_n + \lambda_n)P(n, t).$$

(3)
The initial condition $P(n, t = t_0) = \delta_{n, n(0)}$. Since $n = 0$ is an absorbing state, for $m > 0$, $T(0 \rightarrow m) = 0$, we have

$$\frac{d}{dt} P(n = 0, t) = \sum_{m>0} T(m \rightarrow 0)P(m, t). \hspace{1cm} (4)$$

The average $\bar{n} = \sum_n P(n, t)n$ satisfies a deterministic averaged (mean-field) rate equation

$$\frac{d\bar{n}}{dt} = (B - 1)\bar{n} - B\frac{\bar{n}^2}{K}, \hspace{1cm} (5)$$

where we neglect the number fluctuation $\bar{n}^2 = \bar{n}^2$ (mean-field). Eq. (5) has two fixed points: an attracting fixed point $\bar{n}_a = (B - 1)K/B$, provided $B > 1$; and a repelling fixed point $\bar{n}_e = 0$ (extinction point). In the presence of noise there is a quasi-stationary state for $B > 1$, in which the population fluctuates near $n_a$. However, the system eventually is going to reach $n = n_e = 0$ driven by rare events, where extinction happens. It is then important to estimate the extinction time.

The commonly used methods for estimating the time until extinction includes the Fokker-Planck approximation (also called diffusion approximation in population genetics literature), and the Wentzel-Kramers-Brillouin (WKB) method. The former has a long history of application in studying biological population dynamics, going back to Fisher [1922], and was greatly promoted since the seminal work of Kimura [1964]. Nowadays it has become an indispensable topic in population genetics textbooks [Ewens, 2004, Svirezhev and Passekov, 2012]. But despite its honourable place in mathematical biology, the application of Fokker-Planck approximation is restricted to systems where the extinction is driven by typical Gaussian fluctuations (such as genetic drift), characterised by frequent but small jumps [Gardiner, 1985]. The WKB method was introduced into biology much later – the most works are published only in the last two decades. But the new methods has been gaining popularity steadily, because it generally makes more accurate predictions, and can be applied under much broader conditions. In the following we will first introduce the more general WKB method and then the classic Fokker-Planck approximation, in order to facilitate the comparison of the two methods later on.

### 2.2.1 Wentzel-Kramers-Brillouin (WKB) method

The Wentzel-Kramers-Brillouin (WKB) method was named after the three physicists Gregor Wentzel [Wentzel, 1926], Hendrik Kramers [Kramers, 1926] and Léon Brillouin [Brillouin, 1926]. It provides a systematic and controllable approximating method to calculate the mean extinction time in the small fluctuations limit. And it has been applied widely in studying different extinction problems, such as large fluctuations in numbers of molecules in chemical reactions [Dykman et al., 1994], the fixation of a strategy in evolutionary games [Black et al., 2012], and the extinction of epidemics [Chen et al., 2017].

In a finite population under logistic growth, once the stationary state is reached, the population size fluctuates around the metastable attractor $\bar{n}_s$. The characteristic scale of the fluctuations is
of the order of $1/\sqrt{K}$ (Central Limit Theorem). However, occasionally much larger fluctuations also happen that take the system far from the stable state [Dykman et al., 1994]. Such large fluctuations are rare events, and their probabilities form the tails of the quasi-stationary population state distribution. The mean extinction time $\tau$ (mean time to reach the absorbing state $n_e = 0$) is determined by this quasi-stationary distribution according to the Fermi’s golden rule:

$$\tau^{-1} = \sum_{n>0} T(n \rightarrow 0) P_{st}(n),$$

where the stationary distribution $P_{st}(n)$ satisfies

$$0 = \sum_m \left[ T(m \rightarrow n, t) P_{st}(m) - T(n \rightarrow m, t) P_{st}(n) \right].$$

In terms of the rescaled population size $x = n/K = ne$ with $\epsilon = 1/K$, $\lambda(x) = \lambda_n/K = Bx$, and $\mu(x) = \mu_n/K = x + Bx^2$. We look for the solution of Eq. (7) by proposing a large deviation form of the stationary distribution

$$P_{st}(x) = C \exp \left( -S_\epsilon/\epsilon \right)$$

with the WKB ansatz: $S_\epsilon = \sum_{i=0}^\infty \epsilon^i S_i$. Here $\epsilon \rightarrow 0$ (the weak-noise limit), characterising the noise level. An asymptotic expansion in small $\epsilon$ corresponds to a semiclassical approximation. In both quantum mechanics and statistical mechanics this is also known as a WKB expansion. In the former case, $\epsilon$ is the Planck constant $\hbar$, characterising quantum fluctuations; and in the later case, $\epsilon$ is the temperature, characterising thermal fluctuations. While in stochastic population dynamics, the small parameter $\epsilon$ is $1/K$, characterising population fluctuations.

Plugging Eq. (8) into Eq. (7) and expanding $S_\epsilon$ to $O(\epsilon)$, we obtain

$$S_0(x) = \int_0^x p(x') \, dx', \quad S_1(x) = \frac{1}{2} \ln[\mu(x)\lambda(x)]$$

where $p(x) = \ln \left[ \mu(x)/\lambda(x) \right] = \ln [(1 + Bx)/B]$. It is possible to construct an effective Hamiltonian such that the solution describes an optimal path which represents the ground (lowest-energy) state of the effective Hamiltonian:

$$H(x, p) = \lambda(x)(e^{p} - 1) + \mu(x)(e^{-p} - 1)$$

where the canonical momentum $p = \partial S_0/\partial x$.

We hence obtain the stationary distribution

$$P_{st}(x) = \frac{B - 1}{\sqrt{2\pi KBq^2(1 + Bq)}} e^{-KS_0(x)}$$

where

$$S_0(x) = 1 - B^{-1} - x + (x + B^{-1}) \ln(x + B^{-1}).$$
The leading-order WKB action $S_0$ describes an effective exponential barrier to extinction and the prefactor in Eq. (11) is determined by $S_1(x)$.

Using Eq. (6) we obtain the mean extinction time for the logistic growth model [Assaf and Meerson, 2010] for $1/K \ll x \ll 1/\sqrt{K}$

$$\tau = \sqrt{\frac{2\pi B}{N}} \frac{1}{(B-1)^2} e^{KS_0(0)}. \tag{13}$$

being exponentially large in $K$. The analytical result of the mean extinction time Eq. (13) shows excellent agreement with Monte Carlo simulations [Assaf and Meerson, 2017].

In this section we derived the mean extinction time of a population under logistic growth in a pedagogical way, for illustrating the basic concepts and techniques of the the WKB method. For more applications of the WKB methods in single species stochastic population models, Ovaskainen and Meerson [2010] provides an excellent overview. On the technical aspect, a comprehensive introduction to the path integral representation of master equations can be found in Weber and Frey [2017]. The recent review of Assaf and Meerson [2017] not only introduces the applications of the WKB method in studying population dynamics in well-mixed populations, but also includes the applications for populations on heterogeneous networks and spatial populations. The valuable extension to spatial settings opens the window to studying even more interesting problems, such as large fluctuations of the speed of biological invasions.

### 2.2.2 Fokker-Planck approximation method

The master equation, the exact formulation of the stochastic population dynamics, is in general difficult to solve. The WKB method provides a systematic and controllable way to approximately solve the master equation by utilising the small parameter $\epsilon = 1/K$. Another way of approximately solving the master equation is to start from a formal Kramers-Moyal expansion:

$$\frac{\partial P(X,t)}{\partial t} = \sum_{m=1}^{\infty} \frac{(-1)^m}{m!} \frac{\partial^m}{\partial X^m} \left[ a_m(X,t) P(X,t) \right], \tag{14}$$

where

$$a_m(X,t) = \int dY (Y - X)^m T(X \rightarrow Y). \tag{15}$$

Pawula Theorem states that the expansion in Eq. (14) may stop either up to the second term, or must contain an infinite number of terms. If the expansion stops after the second term, it is called the Fokker-Planck equation [Risken, 1996]. Van-Kampen made the Kramers-Moyal expansion controllable by introducing a small parameter that is the inverse of a system size $\Omega^{-1}$ [Gardiner, 1985]. In the context of population dynamics governed by the logistic growth function, $\Omega$ corresponds to the carrying capacity $K$, and the random variable $X$ in Eq. (14) corresponds to the population size $n$. Since we use the example of logistic growth through out
section 2, we will trade generality for consistency and use $K$ and $n$ in the following. In terms of the scaled variable $x = n/K$, $a_m \sim K^{1-m/2}$, the Kramers-Moyal expansion will stop at the second term when $K$ is large, and the system reduces to the Fokker-Planck equation. However, the Van-Kampen system size expansion should be used with caution. It may be valid only when $x$ is in the vicinity of its average. For the rare events driven by large fluctuations, the Fokker-Planck approximation may yield large errors.

For the logistic growth model, the system size is characterised by the carrying capacity $K$. In terms of rescaled variable $x = n/K$, the master equation (3) becomes

$$\frac{dP(x,t)}{dt} = K\mu(x + \delta x)P(x + \delta x, t) + K\lambda(x - \delta x)P(x - \delta x, t) - K(\mu(x) + \lambda(x))P(x, t)$$  \hspace{1cm} (16)

where $\delta x = 1/K$. Expanding Eq. (16) to $(\delta x)^2$, we obtain the Fokker-Planck equation

$$\frac{dP(x,t)}{dt} = \frac{1}{2K} \frac{\partial^2 (g^2 P)}{\partial x^2} - \frac{\partial (fP)}{\partial x},$$  \hspace{1cm} (17)

where $g^2 = \lambda + \mu = (B + 1)x + Bx^2$ and $f = \lambda - \mu = (B - 1)x - Bx^2$. In population genetics literature, the first term is often attributed to the effect of genetic drift, and the second term is attributed to directional selection [Kimura, 1964, Ewens, 2004]. A diffusive process described by a Fokker-Planck equation, can be equivalently described by a corresponding Langevin type stochastic differential equation [Gardiner, 1985]. For Eq. (17), the corresponding stochastic differential equation reads

$$dx = f(x,t) + K^{-1/2}g(x,t)dW(t),$$  \hspace{1cm} (18)

where $W(t)$ a Wiener process with $(W(t)W(t')) = \delta(t-t')$. Note that higher correlations functions of $W(t)$ vanish, reflecting that the stochastic process is diffusive and being consistent with the Fokker-Planck equation.

The stationary distribution of Eq. (17) reads [Gardiner, 1985]

$$P_{st}(x) \propto e^{-K S_{FP}(x)},$$  \hspace{1cm} (19)

where $0 < x < x_s = \bar{n}/K$ and the effective potential

$$S_{FP}(x) = \int_x^{x_s} dy \frac{2f(y)}{g^2(y)} = 2 \left[x - 1 + B^{-1} - 2 \ln \left(\frac{1 + B + Bx}{2B}\right)\right].$$  \hspace{1cm} (20)

In the vicinity of the stable point (attracting fixed point in the deterministic level) $x_s = (B - 1)/B$, $S_0(x) \approx S_{FP}(x) \approx (x - x_s)^2 \ll 1$, leading to the Gaussian fluctuation. A comparison between $S_0(x)$ and $S_{FP}(x)$ under different $x$ values is shown in Fig. 1. Near the stable fixed point, fluctuations are Gaussian, and hence the stochastic processes can be well-approximated by the Fokker-Planck equation. But if we are interested in rare events driven by large fluctuations, for example the extinction event, the Fokker-Planck approximation becomes invalid. As is shown in the previous section, the mean extinction time is determined by the effective potential $S_{FP}$ at $x = 0$ which is far from $x_s$ for $B \neq 1$.  

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Figure 1: Comparison between $S_0(x)$ in Eq. (12) and $S_{FP}(x)$ in Eq. (20) for $B = 10$.

Compare the effective potential given by the WKB approximation

$$S_0(0) = 1 - B^{-1} + B^{-1} \ln B^{-1},$$

and the corresponding result given by Fokker-Planck approximation

$$S_{FP}(0) = 2 \left\{-1 + B^{-1} - 2 \ln [(1 + B)/2B]\right\},$$

we can see that although Fokker-Planck approximation predicts the correct behaviour of the mean extinction time, namely, $\tau \sim e^{cK}$, it yields an error that is exponentially large in $K$ [Doering et al., 2005, Bressloff and Newby, 2014]. Only in the special case when $B \to 1$, $S_0(0) - S_{FP}(0) = o((B - 1)^2)$ can be neglected. In this limit, $x_s \to 0$, and hence the extinction is a typical event driven by Gaussian fluctuations. In summary, the Fokker-Planck approximation is valid only under the special case if $B \to 1$ and extinction is driven by typical Gaussian fluctuations, but if extinction is caused by rare events when $B > 1$, the Fokker-Planck approximation fails to give accurate estimations of the mean time to extinction.

The difference range of applications between the WKB methods and the Fokker-Planck approximation arise from the fundamental difference between the Master equation and the Fokker-Planck equation. A diffusion process characterised by the Fokker-Planck equation can always be approximated by a jump process described by the Master equation, while the reverse is true only under the conditions that the jumps must be frequent and the step sizes of such jumps must be small comparing to the time and length scales of observables [Gardiner, 1985].

3 Extinction time of populations of two interacting species

In populations of two interacting species (e.g. predator and prey) or two different types of individuals (e.g. susceptible and infected), the equilibrium state predicted by the deterministic rate functions can either be a stable fixed point, a stable limit cycle, marginal stable cycles, or no attractor at all. In general, for an attracting fixed point or a stable limit cycle, the extinction
from a stable quasi-stationary coexistence state is a rare event driven by large fluctuations, and
the mean extinction time will be exponentially large in population size. In this situation the
Fokker-Planck approximation is invalid, whereas the WKB approximation method can provide
fully controlled weak noise expansion. However if the coexistence state is marginally stable,
then the extinction event is a diffusion process driven by typical fluctuations but not a jump.
In this case the Fokker-Plank approximation is also valid and the mean extinction time grows
algebraically with the initial population size. We discuss the different cases separately in the
following.

3.1 Extinction from an attracting fixed point

As an example of multi-species stochastic systems with an attracting fixed point, we consider
the endemic SIR model. The SIR model describes the spread of a disease in a population, with
susceptible ($S$), infected ($I$) and recovered ($R$) individuals. Assuming that $N$ is the total popula-
tion size at equilibrium, individuals are born (as susceptible) at rate $\mu N$. Susceptible, infected,
and recovered individuals die at rate $\mu S$, $\mu I$, and $\mu R$, respectively. Susceptible individuals
become infected at rate $(\beta/N)SI$, and infected individuals recover at rate $\gamma I$. The corresponding
deterministic rate equations for the SIR model is:

\[
\begin{align*}
\frac{dS}{dt} &= \mu N - \mu S - (\beta/N)SI, \\
\frac{dI}{dt} &= -\mu I - \gamma I + (\beta/N)SI, \\
\frac{dR}{dt} &= -\mu R + \gamma I.
\end{align*}
\]

According to this formulation, the $R$ individuals obtain lifelong immunity and will never become
$S$ or $I$ again, its dynamics is thus decoupled from that of the other two subpopulations. For
simplicity, we will ignore the $R$ individuals, and focus on the population dynamics of only $S$ and
$I$ individuals. By setting $\mu I + \gamma = \Gamma$, which measures the effective death rate of the infected, we
obtain the corresponding SI model:

\[
\begin{align*}
\frac{dS}{dt} &= \mu N - \mu S - (\beta/N)SI, \\
\frac{dI}{dt} &= -\Gamma I + (\beta/N)SI.
\end{align*}
\]

For a sufficiently high infection rate, $\beta > \Gamma$, there is an attracting fixed point $\bar{S} = N\Gamma/\beta$, $\bar{I} = \mu(\beta - \Gamma)N/(|\beta\Gamma|)$, corresponding to an endemic state, and an unstable fixed point $S = N$, $I = 0$,
describing an uninfected steady-state population.

Accounting for the demographic stochasticity and random contacts between the susceptible and
infected, the master equation for the probability $P(n, m, t)$ of finding $n$ susceptible and $m$ infected
individuals at time \( t \) reads

\[
\frac{dP(n,m,t)}{dt} = \mu \left[ N(P(n-1,m) - P(n,m)) + (n+1)P(n+1,m) - nP(n,m) \right] \\
+ \Gamma \left[ (m+1)P(n,m+1) - mP(n,m) \right] \\
+ (\beta/N) [(n+1)(m-1)P(n+1,m-1) - nmP(n,m)].
\] (25)

For a finite population, the extinction of the disease starting from the quasi-stationary endemic state, occurs in a finite time due to rare events. It therefore is interesting to find out the mean time it takes for the \( I \) subpopulation to go extinct. For weak fluctuations \( 1/N \ll 1 \), a long lived quasi-stationary distribution has a Gaussian peak around the stable state of the deterministic model. The Fokker-Planck approximation to the master equation can accurately describe small deviations from the stable state, but it fails to describe the probability of large fluctuations.

Similar to the one species case, the problem can be reduced to the dynamics of an effective classical Hamiltonian system by the WKB approximation. The demographic stochasticity induced extinction of the disease proceeds along the optimal path: a particular trajectory in the phase space. The effective classical Hamiltonian of the SI model is [Kamenev and Meerson, 2008]:

\[
H = \mu(p_S - 1)(N - S) - \Gamma(p_I - 1)I - (\beta/N)(p_S - p_I)p_I S I,
\] (26)

where \( p_S \) and \( p_I \) are the canonical momenta, and \( S = -\partial_{p_S} S \) and \( I = -\partial_{p_I} S \). The phase space defined by the Hamiltonian (26), provides an important tool to study the extinction dynamics. All the mean-field trajectories, described by Eqs. (24) are located in the zero energy \( H = 0 \) plane \( p_S = p_I = 1 \). As illustrated in Fig. 2, the attracting fixed point of the mean-field theory becomes a hyperbolic point \( \bar{A} = [\bar{S},\bar{I},1,1] \) in this phase space. There are two more zero-energy fixed points in the system: the point \( \bar{C} = [N,0,1,1] \) that is present in the mean-field description, and the emergent fixed point \( \bar{B} = [N,0,1,\Gamma/\beta] \) due to the presence of fluctuations. Both of them are hyperbolic and describe extinction of the disease.

The optimal path (instanton) that brings the system from the stable endemic state to the extinction of the disease, is given by the trajectory that minimises the action \( S \). The optimal path must be a zero-energy trajectory. It turns out that there is no trajectory going directly from \( \bar{A} \) to \( \bar{C} \) (see Fig. 2), instead, the fluctuational extinction point \( \bar{B} \) plays a crucial role in the disease extinction.

The mean extinction time of the disease \( \tau \) is exponentially large in \( N \gg 1 \) and

\[
\tau \sim e^{S_0},
\] (27)

where the effective potential

\[
S_0 = \int_{-\infty}^{\infty} (p_S \dot{S} + p_I \dot{I}) \, dt,
\] (28)

and the integration is evaluated along the optimal path going from \( \bar{A} \) to \( \bar{C} \).
For populations of more than one species interacting with each other, the analytical form of the mean extinction time is not available [Assaf and Meerson, 2017], and the optimal path can be computed only numerically. It is worth mentioning that, for extinction from a deterministically stable limit cycle driven by large fluctuations, the corresponding mean extinction time is also exponentially large in the population size $N$ [Smith and Meerson, 2016].

### 3.2 Extinction from marginally stable equilibrium states

If the extinction is not driven by rare events, it can occur much more quickly. As we will see, the mean extinction time may have a power-law dependence on the population size in the predator-prey and competitive Lotka-Volterra models. In these models, since extinction is driven by Gaussian fluctuations, the Fokker-Planck approximation can be applied.

We first take the classic Lotka-Volterra predator-prey model as an example. Use the continuous variables $q_1$ and $q_2$ to represent the predator and prey populations, the deterministic rate equations are:

\[
\begin{align*}
\frac{dq_1}{dt} &= -\sigma q_1 + \lambda q_1 q_2, \\
\frac{dq_2}{dt} &= \mu q_2 - \lambda q_1 q_2,
\end{align*}
\] (29)

where $\sigma$ represents the death rate of the predator, $\mu$ represents the birth rate of the prey, and $\lambda$ is the rate of interaction between a predator and a prey. Note that this formulation assumes that the preys have no intrinsic death, their population will grow exponentially without the presence of the predator. There are three fixed points: $(q_1, q_2) = (0, 0), (0, \infty)$, and $(\mu/\lambda, \sigma/\lambda)$. The first one corresponds to the case where both species are extinct. The second one describes the population explosion of the prey due to the extinction of the predator. The third one represents the steady
state where the predator and the prey coexist at the population size $N_1 = \mu / \lambda$ and $N_2 = \sigma / \lambda$, respectively.

A particular feature of the Lotka-Volterra model is that there is an “accidental” conserved quantity:

$$ G = \lambda q_1 - \mu - \mu \ln(q_1 \lambda / \mu) + \lambda q_2 - \sigma - \sigma \ln(q_2 \lambda / \sigma), \quad (30) $$

where $G = 0$ corresponds to the coexistence fixed point, and $G > 0$ corresponds to larger amplitude cycles [Parker and Kamenev, 2009]. An illustration of orbits at different $G$ values is shown in Fig. 3. For a given initial condition, the predator and prey populations cycle along a closed orbit.

The existence of an “accidental” conserved quantity $G$ not only leads to closed orbits, but also makes them marginally stable. Population fluctuations due to demographic noise are isotropic in the space $(q_1, q_2)$, leading to slow diffusion between the mean-field orbits. Even large deviations from a mean-field orbit, such as extinction, can be seen as the accumulation of many small step fluctuations in the radial direction. This is in contrast with the systems with a stable fixed point or limit cycle, such as the endemic SIR model discussed in the previous section. In those systems, large deviations proceed only along very special optimal paths in the phage space [Dykman et al., 1994, Elgart and Kamenev, 2004, Kamenev and Meerson, 2008]. Consequently, the mean extinction time in marginally stable systems such as the predator-prey model has a power law dependence on the sizes of the two populations.
In the presence demographic noises, the corresponding master equation is
\[
\frac{dP(m,n,t)}{dt} = \sigma \left[ (m+1)P(m+1,n) - mP(m,n) \right] + \mu (n-1)P(m,n-1) - nP(m,n) + \lambda \left[ (m+1)(m-1)P(m-1,n+1) - nP(m,n) \right],
\]
(31)
where \( P(m,n,t) \) is the probability of the system having \( m \) predators and \( n \) prey at time \( t \).

Since extinction in this case is driven by Gaussian fluctuations rather than large jumps, the Fokker-Planck approximation can be appropriately applied. \( G \) can be identified as a “slow” dynamic variable that is responsible for the long time behaviour of the system. In the presence of demographic stochasticity, after averaging out the “fast” variable (angles in \( (q_1, q_2) \) space), one can obtain a one-dimensional Fokker-Planck equation on the probability distribution of \( G \). Solving the mean first passage time of this one-dimensional problem gives that the mean extinction time \( \tau \sim N_1^{3/2}/N_2^{1/2} \) with \( N_1 \leq N_2 \) [Parker and Kamenev, 2009].

In the previous example of the predator-prey Lotka-Volterra model, overcrowding and intra-specific competition are not considered. The death of prey is solely caused by predation, and the per capita reproduction rate of predators only depends on the abundance of prey. These paradise-like conditions are seldom met in real biological systems. Instead, competition is the norm and battles over resources for survival and reproduction can often be fierce and unforgiving. The competitive Lokta-Volterra model captures the self-limiting behaviour of the population growth. The corresponding deterministic rate equations are:
\[
\frac{dx}{dt} = r_1 x (1 - x - \alpha y),
\]
(32)
\[
\frac{dy}{dt} = r_2 y (1 - y - \alpha x),
\]
(33)
where \( x = n_1/K_1, y = n_2/K_2 \) are rescaled population size, in which \( n_1 \) and \( n_2 \) are the population size of each of the competing species, \( K_i \) is the carrying capacity for each of them, \( r_1 \) and \( r_2 \) are the intrinsic optimal growth rate of the two species when competition is absent, and \( \alpha \in [0,1] \) is the competition coefficient between the two species. In the limiting case when \( \alpha = 0 \), the growth of the two species are independent of each other. When \( 0 < \alpha < 1 \), there is an attracting fixed point \( x^*_1 = y^*_2 = 1/(1 + \alpha) \) where the two species coexist. If \( \alpha = 1 \), the two species are competitively identical. Considering that they have the same carrying capacity \( K_1 = K_2 = K \), the only difference is that one species reproduces faster and dies sooner than the other. This leads to the degenerate case where there is a line of fixed points corresponding to the marginally stable coexistence of the two species with the ratio of populations determined uniquely by the initial conditions. In the degenerate case, the Fokker-Planck approximation can be applied. The corresponding Fokker-Planck equation is equivalent to stochastic differential equations of \( x(t) \) and \( y(t) \), which can be reduced to one-dimension by introducing \( z(t) = x(t) - y(t) \):
\[
dz = \nu(z) + \sqrt{2D(z)}dW(t).
\]
(34)
Here \( W(t) \) is a Wiener process. By determining the drift \( \nu(z) \) and the diffusion \( D(z) \) terms, the mean time to extinction of one or the other species \( \tau \sim K \) [Lin et al., 2012].
4 Discussion

In this article we review the problem of population extinction due to demographic stochasticity, using the WKB approximation and the Fokker-Planck approximation methods. We emphasize the conditions under which each method can be appropriately applied: the Fokker-Planck approximation is only valid in estimating the mean extinction time if the extinction is driven by Gaussian fluctuations, whereas the WKB approximation is more reliable and can handle extinction events driven by large jumps. Besides these two methods, there are also many other novel approaches for quantifying the influence of demographic stochasticity, which we did not include in this review. For example, the average shift of a Lyapunov function can be used to indicate the stability of the system [Claussen and Traulsen, 2008, Zheng et al., 2017]: being stable under the demographic stochasticity if \( \langle \Delta H \rangle < 0 \), while being unstable if \( \langle \Delta H \rangle > 0 \), in which \( H \) is a Lyapunov function.

We focused on the effect of weak demographic stochasticity on population extinction, in particular, the mean extinction time in populations with one species or two interacting species. Noise can strongly modify the behaviour of nonlinear dynamical systems [Longtin, 2003, Anishchenko et al., 2007], especially in small populations [Lande, 1998]. On the one hand, demographic stochasticity can facilitate the long-term coexistence of different species or individuals of different strategies within the same species [Calsbeek et al., 2002, Claussen and Traulsen, 2008, Okuyama, 2015, Zheng et al., 2017], but on the other hand, it can also disrupt cyclic host-parasite coevolution and lead to fast fixation of alleles [Gokhale et al., 2013]. In conservation biology, demographic stochasticity can be used for determining the minimum population sizes for protecting endangered species from extinction [Shaffer, 1981], and detecting early warning signals of drastic ecosystem regime shifts [Fung et al., 2013]. In evolutionary games, the maintenance of cooperation against the invasion of defectors is shown to be also facilitated by demographic noise [Huang et al., 2015, Constable et al., 2016]. Moreover, demographic stochasticity often interacts with other driving forces of biological population dynamics, such as natural selection, sexual selection and environmental fluctuations.

Beyond the direct applications, theoretical studies of demographic stochasticity can lead to thought-provoking implications and thus inspire future investigations and interdisciplinary collaborations across many branches of evolutionary biology. For example, the finding of a faster life-cycle is more prone to extinction than a slower life-cycle [Lin et al., 2012] links naturally to life-history evolution. It may contribute to explaining the emergence and maintenance of life-history patterns featured with extremely slow reproduction and extremely slow (even negative) aging among the great diversity of life-history patterns across the tree of life [Baudisch and Vaupel, 2012, Jones et al., 2014].

Through this review, we hope to present a glimpse into the vast potential of applying methods developed in statistical physics and quantum mechanics in solving biological problems, and we would like to encourage further exchange of knowledge and collaboration between physicists and biologists, for developing novel approaches in modelling biological evolution.
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