Asymptotic Analysis of Some Stochastic Models from Population Dynamics and Population Genetics

by

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Graduate Department of Mathematics
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Abstract

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Near the beginning of the last century, R. A. Fisher and Sewall Wright devised an elegant, mathematically tractable model of gene reproduction and replacement that laid the foundation for contemporary population genetics. The Wright-Fisher model and its extensions have given biologists powerful tools of statistical inference that enabled the quantification of genetic drift and selection. Given the utility of these tools, we often forget that their model - for reasons of mathematical tractability - makes assumptions that are violated in many real-world populations. In particular, the classical models assume fixed population sizes, held constant by (unspecified) sampling mechanisms.

Here, we consider an alternative framework that merges Moran’s continuous time Markov chain model of allele frequencies in haploid populations of fixed size with the density dependent models of ecological competition of Lotka, Volterra, Gause, and Kolmogorov. This allows for haploid populations of stochastically varying – but bounded – size. Populations are kept finite by resource limitation. We show the existence of limits that naturally generalize the weak and strong selection regimes of classical population genetics, which allow the calculation of fixation times and probabilities, as well as the long-term stationary allele frequency distribution.
Acknowledgements

While any effort is inevitably shaped by every interaction, there are a few people to whom I am eternally grateful for the significant contributions they made to the writing of this dissertation and my overall intellectual development. First among them is Peter Abrams. To me he will always epitomize what a senior scientist should be. I will never forget that he gave me a second chance after I left a PhD in pure mathematics. I hope that I will follow his example providing essential guidance while encouraging students to find their own paths. I am equally indebted to Joe Repka, who has been my link to the mathematics department and has been consistently available for advice, comment, reading and critique of my writing, and without whom even submitting a thesis would be an impossibility. David Earn was a fantastic external examiner, and I’m deeply grateful for his careful reading of this thesis, and the many thoughtful suggestions he made for improving its content and readability.

Most of the questions posed and addressed here emerged from joint work with Christopher Quince, with whom I hope to have many more years of fruitful collaboration. Much of the rest emerged from conversations with Joshua Plotkin, in whose Mathematical Biology Group I was employed during a portion of the time this thesis was written. Both provided support both moral and financial, introduced me to a broad community of population geneticists and a host of fascinating problems, and constantly reminded me that a mathematical formalism is not an end in itself, but a means to obtain insight about the world around us.

My understanding and appreciation of mathematical population genetics has been deepened by many conversations with Warren Ewens, who provided invaluable mentorship, for which I am forever grateful.

My thanks also to Jeremy Quastel and Balig Virant for allowing me to participate in the Probability Seminar, for answering my innumerable naive questions, and for clarifying many misconceptions on my part.
Peter Ralph read and identified errors in earlier versions of Theorems 4.1 and 4.2.

Amaury Lambert provided many insightful comments on early drafts of Chapters 3 and 5.

Jesse Taylor pointed out that global weak convergence could be proven (as opposed to just convergence of finite dimensional distributions), which led to Corollary 4.3. Rick Durrett for showed me a draft of [39], which inspired considerable improvements to Theorems 4.2 and 4.2. Frank Ball introduced me to the notion of coupling and pointed me to [174].

Section 4.3.3 reproduces text and figures from [151] which was written in collaboration with Christopher Quince and Joshua B. Plotkin. All analytical results (and the errors therein) are my own contribution; I am grateful to Chris and Josh for helping me distill concrete biological insights out of an abstract formalism.

This project would have never been conceived, and I would likely never have met Peter Abrams, if I hadn’t first met Jonathan Dushoff and Lee Worden, who introduced me first to the field of mathematical biology and then to their supervisor, Simon Levin, who encouraged me to read and explore the field, and who directed me to Peter.

Finally, my sincerest thanks to Ida Bulat, who exhibited Buddha-like patience with my many, many requests, and to my dear friends Michael Buckley, Jeremy Draghi, Hayssam Hulays, Sergey Kryazhimskiy, Eden Legree, Jebney Lewis, Melanie Redman, Martin Reis, Phillip Smith, Alexander Stewart, and Katie Wood, who have all provided invaluable support, both moral and material, at important turns in the thinking, writing, and rewriting process.
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Chapter 1

Introduction: Two Streams of Mathematical Biology

I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics; for men thus endowed seem to have an extra sense.

– Charles Darwin

As we approach the centenary of modern mathematical biology, a retrospective look shows that there have been two streams of research that have dominated most of its development, both of which trace back to the very first efforts in the area. The first, originating in the work of Lotka [130] and Volterra [182, 183] and later Gause [65], is informed by ecology, and concerns itself with the dynamics of interacting populations of predators, prey, competitors, and mutualists, subject to resource limitation. Its principal mathematical tools have been ordinary, and later, partial differential equations and difference equations. Populations are typically modelled deterministically and treated as continuous quantities, rather than discrete individuals.

The second stream begins with the foundational work in population genetics by Haldane [71], Fisher [59], and Wright [186]. Concerned with the survival and increase in
frequency of rare mutations, their approach was stochastic, assuming discrete individuals and using Markov chains, including the Bienaymé–Galton–Watson process [184]. Whereas Lotka and Volterra and their successors were concerned with the mechanisms by which populations are regulated, the early population geneticists were content – for reasons of analytical tractability – to allow populations to either grow to infinity, or assume that they were held fixed in size by some unspecified sampling mechanism.

Beginning with Fisher [59], there has long been interest in understanding how incorporating more realistic population dynamics might complicate population genetics, usually by assuming that the total population size either varies deterministically (e.g., [52, 106, 147]), or alternates between a discrete set of values according to an a priori Markov chain (e.g., [111, 94, 32, 93, 92, 85]).

More recently, it has been acknowledged that such approaches are insufficient, and there is a need to more fully integrate the two streams of mathematical biology: to incorporate notions from ecology such as density dependence into population genetics, and to develop a stochastic, individual based approach to population dynamics [143, 48, 123, 90]. Some steps towards this path have already been taken, from the first, deterministic approach to density dependent population genetics [165, 28], to recent work incorporating density dependence into the Bienaymé–Galton–Watson process [121, 122]. In what follows, we present a complementary approach to incorporating density dependence into population genetics, taking Moran’s continuous time Markov formulation of population genetics [142] and Kurtz’s density-dependent population processes [116, 117, 118, 119] as a point of departure.

The balance of this chapter is a survey of the relevant concepts and models in mathematical biology that will be assumed in subsequent chapters, concluding with a summary of the results herein. Some of these results, along with a discussion of their biological significance, have appeared previously [148, 149, 150, 151]. In our previous publications, they were derived via heuristic singular perturbation methods. While the questions con-
sidered here were inspired by those previous studies, the proofs presented are novel and rigorous, and the models considered here substantially generalize the ones in those publications. Where relevant, we show how previous results may be obtained as special cases of those presented here.

Throughout, we assume familiarity with the language of measure-theoretic probability, stochastic processes and stochastic integration. We refer the uninitiated to Appendix A for a brief summary of the relevant definitions and results and some useful references.

1.1 Density Dependence and the Lotka-Volterra-Gause Model

The notion of density dependence was first introduced by Verhulst [181], as a correction to the unrealistic exponential growth considered in Malthus’ An essay on the principle of population [134]. His logistic equation, familiar to any freshman student of calculus, captures the ecological notion of resource limitation in two simple parameters: if $X(t)$ is the number of individuals in of a population at time $t$, then

$$\dot{X} = rX \left(1 - \frac{X}{N}\right),$$  \hspace{1cm} (1.1)

where $r$ is the intrinsic growth rate of the population, the rate of growth in the absence of competition, and $N$ is the carrying capacity, the stable equilibrium the population will asymptotically approach, reflecting the saturation of resources by the population. The logistic equation is the foundation of mathematical ecology, and continues to be used extensively in the present. It is not uncommon to see the logistic equation in rescaled form: setting $Y(t) = \frac{X(t)}{N}$, we obtain an expression independent of $N$,

$$\dot{Y} = rY (1 - Y).$$  \hspace{1cm} (1.2)
Indeed, that the dynamics only depend on the rescaled variable may be taken as the definition of density-dependence.

Remark 1.1. In the theoretical ecology literature, the carrying capacity is frequently denoted by $K$, but to avoid confusion with the standard notation of population genetics, where $K$ is often used to denote the number of species, we use $N$. Given that we shall consider limits as $N \to \infty$, the choice of letters seems mathematically appropriate.

Verhulst’s logistic equation would eventually be generalized for the study of communities of organisms, consisting of predators and prey, competitors and mutualists, in the form of the Lotka-Volterra-Gause [130, 182, 183, 65] equations,

$$
\dot{Y}_i = \left( b_i + \sum_{j=1}^{K} a_{ij} Y_j \right) Y_i,
$$

(1.3)

describing the dynamics of a population of $K$ interacting species. Species $i$ has intrinsic growth rate $b_i$ and has interaction coefficient $a_{ij}$ with species $j$, leading to a net per capita individual growth rate

$$
f_i(Y) = b_i + \sum_{j=1}^{K} a_{ij} Y_j
$$

(1.4)

for all individuals of type $i$. Various ecological relationships can be captured by appropriate choices for the interaction coefficients, summarized in Table 1.1:

<table>
<thead>
<tr>
<th>Interaction</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predation/Parasitism</td>
<td>$a_{ij} &lt; 0$ and $a_{ji} &gt; 0$ or $a_{ij} &gt; 0$ and $a_{ji} &lt; 0$</td>
</tr>
<tr>
<td>Competition</td>
<td>$a_{ij} &lt; 0$ and $a_{ji} &lt; 0$</td>
</tr>
<tr>
<td>Mutualism</td>
<td>$a_{ij} &gt; 0$ and $a_{ji} &gt; 0$</td>
</tr>
</tbody>
</table>

Table 1.1: Ecological interactions and the corresponding conditions on interaction coefficients.

With their simplicity and versatility in describing community dynamics, the Lotka-Volterra-Gause equations have been employed frequently and investigated extensively (see e.g., [82] and references therein), although many natural questions regarding the
qualitative properties of the solutions remain unsolved \( e.g., \) necessary and sufficient conditions for the survival of species \( i \) remain unavailable for \( K > 3 \). They have been shown to give good fits in a few empirical studies of competition in microbial populations (see \( e.g., \) [65, 180, 152]), and as a result have become a standard model in theoretical population ecology.

For our purposes, the Lotka-Volterra-Gause equations are the prototypical model of species competing for limited resources, and we shall return to them throughout the following chapters. Nonetheless, they have distinct limitations, both biologically and mathematically: they are a drastically oversimplified model of interspecies interactions, whilst the set of equations of the form (1.3) is not structurally stable, so that even arbitrarily small nonlinear perturbations in individual growth rates can result in qualitatively different solutions [139].

1.1.1 Kolmogorov’s Population Equations and Competitive Dynamical Systems

Inspired by the work of Volterra, Kolmogorov [112] considered generalized equations for continuous population dynamics,

\[
\dot{Y}_i = f_i(Y)Y_i.
\]  

(1.5)

Following [169], we will refer to such equations as being of \textit{Kolmogorov} type. As with the Lotka-Volterra-Gause equations, \( f_i(Y) \) may be interpreted as the per capita growth rate of individuals of type \( i \).

Following [81, 172, 78, 79, 80], we have the following definitions:

**Definition 1.1.** 1.5 A dynamical system of Kolmogorov type is

(i) \textit{dissipative} if there is a compact set \( \mathcal{K} \) that uniformly attracts each compact set of initial values,
(ii) irreducible if the matrix \((\partial_j f_i)\) is irreducible for all \(\mathbf{x} \in \mathbb{R}_+^K\),

(iii) competitive if \(\frac{\partial f_i}{\partial x_j} \leq 0\) for all \(i \neq j\), and totally competitive if \(\frac{\partial f_i}{\partial x_j} < 0\) for all \(i \neq j\).

Each of these has a reasonable biological interpretation: the first requires that the population remain finite, the second that the population cannot be separated into distinct, non-interacting subpopulations (which could then be studied independently), and the third that individual growth rates decline in the presence of competitors. In what follows, we will limit our attention to Kolmogorov systems with all of these properties, as well as imposing the additional requirement that the dynamics have a source at the origin, so that populations will grow when started from small initial densities.

The family of dynamical systems of Kolmogorov type, unlike those satisfying the Lotka-Volterra-Gause equations, has the advantage of being topologically closed. Unfortunately, the search for meaningful results at this level of generality is somewhat Quixotic, as indicated by the following construction, due to Smale [172]:

**Example 1.1.** Let

\[
\Delta_0 = \left\{ \mathbf{x} \in \mathbb{R}^K : \sum_{i=1}^K x_i = 0 \right\}
\]  

(1.6)

and

\[
\Delta_1 = \left\{ \mathbf{x} \in \mathbb{R}_+^K : \sum_{i=1}^K x_i = 1 \right\},
\]

(1.7)

and let \(h_0 : \Delta_1 \to \Delta_0\) be any \(C^\infty\) map. Let \(h : \mathbb{R}_+^K \to \Delta_0\) be a \(C^\infty\) extension of \(h_0\) and let \(\beta : \mathbb{R} \to \mathbb{R}\) be a \(C^\infty\) function which is identically 1 in a neighbourhood of 1 and vanishes off of \((\frac{1}{2}, \frac{3}{2})\). Set

\[
f_i(\mathbf{x}) = 1 - \sum_{j=1}^K x_j + \eta \frac{1}{x_i} \beta \left( \sum_{j=1}^K x_j \right) \left( \prod_{j=1}^K x_j \right) h(\mathbf{x}).
\]

(1.8)

Then, for \(\eta > 0\) sufficiently small, the corresponding Kolmogorov population system is competitive. Moreover, \(\Delta_1\) is an attractor for all initial conditions in \(\mathbb{R}_+^K\), and, on \(\Delta_1\),
Chapter 1. Introduction

the dynamics are, up to a constant, those of \( \dot{Y} = h_0(Y) \) i.e., any dynamics are possible within a competitive dynamical system.

Nonetheless, some general results can be obtained. Indeed, in Smale’s construction, the use of the simplex is in some sense generic: Hirsch [78, 79, 80] showed there is an invariant set \( C \), the carrying simplex, that is homeomorphic to the \((K - 1)\)-dimensional simplex \( \Delta_1 \), and is a global attractor of every point excluding the origin. This carrying simplex contains all of the asymptotic dynamics of the system.

In what follows, we will consider a class of stochastic processes that have competitive Kolmogorov systems as a functional Law of Large Numbers, specializing as needed to more specific models (in particular the Lotka-Volterra-Gause model) to obtain more precise results.

1.2 Classical Population Genetics

We now turn to the second stream, giving a brief introduction to the classical theory of population genetics. The literature is far too extensive to provide an exhaustive survey, so the discussion is limited to the handful of essential results necessary to provide the context for subsequent chapters. In particular, the discussion – and all results herein – are limited to panmictic populations of haploid individuals i.e., any individual can potentially interact with all other individuals, and reproduction is clonal, so that, absent mutation, offspring are identical to their parent. Somewhat egregiously, we omit the coalescent [108, 109] and subsequent developments in genealogical processes. See [53, 38, 49] for surveys of population genetics intended for a mathematical audience that address the coalescent, diploid populations, etc.
1.2.1 Wright-Fisher Model

The Wright-Fisher model [59, 186] is the foundational model in mathematical population genetics. While it seems surprising from our current perspective, at the beginning of the 20th century, Darwin’s theory of evolution seemed in peril, with its principal challenger being Mendel’s theory of inheritance [163, 53]. Like many so-called “gradualists”, Darwin believed that an individual’s traits were a blend of those of its parents. As his “saltationist” opponents pointed out, over time, random mating would lead to entirely uniform populations incapable of further adaptation. They further argued that the small changes proposed by Darwin would not under sufficient selection to change the composition of the population, and in any case could only produce difference in quantity, but not kind. After the immediate selective force ceased, they argued, reversion to the mean would return the population to its original state [163]

In contrast, the saltationists, informed by Mendel’s breeding experiments, argued that traits were inherited discretely through pairs of alleles, one from one each parent. They argued that natural selection, to the extent it acted at all, was primarily to emphasize pre-existing variants, or upon novel mutations that conveyed large benefits. Such a model maintained variation, but also encountered difficulty: without mutations that create “hopeful monsters” with sufficiently large fitness advantage, eventually all alleles would reach their Hardy-Weinberg equilibrium, and again, adaptation would cease. Wright and Fisher sought to merge of Darwinian evolution with Mendel’s discrete heredity in what we now refer to, following Huxley [84], as the Modern Synthesis: rare mutations give rise to new alleles encoding new traits which may or may not confer a selective advantage, which could in turn be small or large. Adaptation proceeds by the fixation of advantageous novel alleles, as new new traits displace existing ones. For this to occur, it is necessary that newly emerged advantageous alleles avoid stochastic extinction.

To demonstrate that this was possible, Wright and Fisher independently introduced their eponymous model. In its simplest form, the neutral model, we assume a panmictic
population consisting of \( N \) haploid individuals and discrete generations. That is, we assume that individuals reproduce clonally, and barring mutation, the offspring is genetically identical to the parent. Each individual has an *alleloype* (or *type* for brevity). When Wright and Fisher were devising their theory of heredity, DNA was yet to be discovered, but Mendel’s work gave a remarkably prescient picture of differing traits arising from the presence of different *alleles* at specific heritable loci. For simplicity, they assumed that genes at specific loci were inherited more or less independently, and focused on a single locus at which one of several distinct *alleles* might be present.

To model reproduction, they assumed that the \( n+1^{\text{st}} \) is formed by choosing \( N \) individuals to produce an offspring, uniformly at random *with replacement* from the \( n^{\text{th}} \) generation. Thus, in a population with \( K \) types, writing \( X_i^{(N)}(n) \) for the number of individuals of type \( i \) in the \( n^{\text{th}} \) generation, the Wright-Fisher model is a Markov chain with multinomial transition probabilities:

\[
\mathbb{P} \left\{ X_1^{(N)}(n+1) = j_1, \ldots, X_K^{(N)}(n+1) = j_K \mid X_1^{(N)}(n) = i_1, \ldots, X_K^{(N)}(n) = i_K \right\} = \frac{N!}{j_1! \cdots j_K!} \left( \frac{i_1}{N} \right)^{j_1} \cdots \left( \frac{i_K}{N} \right)^{j_K}. \tag{1.9}
\]

More generally, the model may be extended to include *mutation* by assuming that with probability \( \mu_{ij} \), the offspring of a parent of type \( i \) is of type \( j \), and *selection*, by assuming that individuals of type \( i \) are chosen with probability proportional to \( 1 + s_i \), the *relative fitness* of that type. The parameter \( s_i \) is referred to as the *selection coefficient*. In the absence of mutation, the Wright-Fisher model has \( K \) absorbing states, corresponding to \( X_i^{(N)}(n) = N \) and \( X_j^{(N)}(n) = 0 \) for all \( t \), for some \( i \); when the chain is in the \( i^{\text{th}} \) absorbing state, we say that type \( i \) has *fixed*.

There are myriad generalizations of the Wright-Fisher model, allowing for *e.g.*, diploid organisms, subdivided populations, multiple loci, *etc.* which have led to the development of a rich literature in population genetics, but the fundamental questions remain the
(i) In the absence of mutation, what is the probability that type $i$ eventually fixes? What is the expected absorption time, the first time the population is monomorphic (i.e., composed entirely of individuals of one type), and what is the expected time to fixation of type $i$, that is, the absorption time conditioned on the fixation of type $i$?

(ii) If mutation between types occurs, what is the stationary distribution of types?

For Wright and Fisher, the goal in answering the first question was to show that a single individual with even a vanishingly small fitness advantage – in the Wright-Fisher model, an unspecified trait that increased the individual’s probability of contributing to subsequent generations – had a non-zero probability of eventually fixing, and that the rate of fixation of advantageous alleles was sufficiently rapid that evolutionary processes could explain how observed diversity had arisen from simple organisms within the lifetime of the Earth.

A vast literature on fixation probabilities and times has since arisen, attempting to understand how complicated life-histories and ecological interactions will affect the process of adaptation. The question of which traits might arise remains a largely empirical one. Fixation probabilities, however, provide a quantitative measure of which traits we expect to survive, should they appear, and thereby a means to understand the trajectory of adaptation. An explicit expression for the fixation probability of a novel allele, based upon the traits it encodes, is an essential component of many theoretical approaches to predicting long-term evolution, such as the currently popular canonical equation of Adaptive Dynamics (see e.g., [31, 26, 25, 27]).

Answering the second question, regarding the stationary distribution, gives an understanding of how and when mutation and selection can maintain biological diversity and explain observed diversity, while simultaneously providing a means by which the
strength of selection and the population rate of mutation may be inferred from samples from a population assumed to be at equilibrium [102, 166, 76, 22, 30]. In particular, with models incorporating additional biological detail, inferred parameters can be compared with \textit{a priori} values obtained either from other summary statistics or \textit{in vitro} to compare models and reject hypotheses (\textit{e.g.,} [175, 64, 54].)

1.2.2 Neutrality, Strong vs. Weak Selection, and Kimura’s Diffusion

Unfortunately, even as simple a model as the Wright-Fisher model is analytically almost intractable, and much of the subsequent development of mathematical population genetics would have to wait for the introduction of approximating diffusions by Feller [55] and Kimura [98]. In order to obtain a diffusion approximation, we will assume that the mutation rate is \( \mathcal{O}\left(\frac{1}{N}\right) \) \textit{i.e.}, we will assume that there exist constants \( \theta_{ij} \), independent of \( N \), so that

\[
\mu_{ij} = \frac{\theta_{ij}}{N},
\]

(1.10)

This assumption is not unreasonable for a sufficiently small mutational target in a microbe with DNA chromosomes, or a higher eukaryote, where estimates of per base pair mutation rates vary on the order of \( 10^{-7} - 10^{-11} \), \textit{e.g.}, \( 5.4 \times 10^{-10} \) for \textit{Escherichia coli} [35]. Given typical gene lengths of order \( 10^2 - 10^3 \) [83], this assumption is valid for \( N \) of order \( 10^4 - 10^9 \). By contrast, population sizes were of the order of \( 5 \times 10^8 \) in Lenski’s \textit{E. coli} Long-term Experimental Evolution Project [126].

The (Nearly) Neutral Theory

Let \( X^{(N)}(n) = (X_1^{(N)}(n), \ldots, X_K^{(N)}(n)) \) (in general, we will write \( X \) for the vector with components \( X_i \)). If we assume that the selection coefficients, \( s_i \), are \( \mathcal{O}\left(\frac{1}{N}\right) \), then, the
vector of frequencies

\[ P^{(N)}(t) = \frac{1}{N} X^{(N)}([Nt]), \quad (1.11) \]

converges in distribution as \( N \to \infty \) to \( P(t) \), a diffusion process with infinitesimal generator

\[
(Gf)(p) = \sum_{i=1}^{K} \left( - \left( \sum_{j=1}^{K} \theta_{ij} \right) p_k + \sum_{j=1}^{K} \theta_{ji} p_j \right) (\partial_i f)(p) \\
+ \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i (\delta_{ij} - p_j) (\partial_i \partial_j f)(p). \quad (1.12)
\]

This diffusion process is commonly referred to as the Wright-Fisher diffusion or as Kimura’s diffusion. It was introduced in this form in [98], whilst convergence in distribution was proved in [51]. Using this diffusion process, it becomes possible to provide explicit, if asymptotic, answers to Wright and Fisher’s questions, at least in some cases (see e.g., [53]):

(i) Suppose that \( \mu_{ij} = 0 \) for all \( i, j \). Then, the states \( P(t) = e_i \) are absorbing for the diffusion process, and the absorption time

\[
T_{abs} = \inf \{ t > 0 : P(t) = e_i \text{ for some } i \} \quad (1.13)
\]

is a stopping time. Now, under the assumption of neutrality, \( P(t) \) is a martingale, and we can use the optional stopping theorem\(^2\) to conclude that

\[
p_i = \mathbb{E} [ P_i(T_{abs}) | P(0) = p ] = \mathbb{P} \{ P(T_{abs}) = e_i | P(0) = p \}. \quad (1.14)
\]

\(^1\)see A.4 for a discussion of infinitesimal generators and their uses.
\(^2\)see A.5 for a discussion of martingales, stopping times, and the optional stopping theorem.
Thus, if $h_i(p)$ is the fixation probability for type $i$ conditioned on $P(0) = p$, then

$$h_i(p) = p_i. \quad (1.15)$$

Moreover, the Dirichlet problems\(^3\) $G \phi(p) = -1$ and $G(h_i \phi)(p) = -h_i(p)$ can be solved to yield \([104, 103]\]

$$E[T_{\text{abs}}|P(0) = p] = \sum_{i=1}^{K} -(1 - p_i) \ln (1 - p_i) \quad (1.16)$$

and

$$E[T_{\text{abs}}|P_i(T_{\text{abs}}) = 1, |P(0) = p] = -(1 - p_i) \frac{p_i}{p_i} \ln (1 - p_i). \quad (1.17)$$

(ii) The Dirichlet problem, $G^* \phi(p) = 0$, for the adjoint

$$(G^* f)(p) = -\sum_{i=1}^{K} \partial_i \left[ \left( -\left( \sum_{j=1}^{K} \theta_{ij} \right) p_k + \sum_{j=1}^{K} \theta_{ji} p_j \right) f(p) \right]$$

$$+ \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} \partial_i \partial_j [p_i (\delta_{ij} - p_j) f(p)]. \quad (1.18)$$

can sometimes be solved to yield the *stationary distribution*,

$$\mathbb{P} \left\{ \lim_{t \to \infty} P(t) = p \right\}. \quad (1.19)$$

In particular, when $K = 2$, the stationary distribution for the Wright-Fisher diffusion with mutation is the *beta distribution* \([186]\):

$$\mathbb{P} \left\{ \lim_{t \to \infty} P(t) = (p, 1-p) \right\} = \frac{\Gamma(\theta_{12} + \theta_{21})}{\Gamma(\theta_{12})\Gamma(\theta_{21})} p^{\theta_{12}-1}(1-p)^{\theta_{21}-1}. \quad (1.20)$$

\(^3\)see A.4 for a discussion of Dirichlet problems for the generator and their application to exit probabilities and exit times.
If the mutation rates depend only on the parent type, so \( \theta_{ij} = \theta_i \) for all \( j \), \( G^* \phi(p) = 0 \), may be solved for arbitrary \( K \) to yield a Dirichlet distribution [185],

\[
\Gamma\left(\sum_{i=1}^{K} \theta_i\right) \prod_{i=1}^{K} p_i^{\theta_i-1}.
\] (1.21)

**Weak Selection**

If selection is weak,

\[
s_i = \frac{\alpha_i}{N},
\] (1.22)

then, proceeding as above, the limiting diffusion \( P(t) \) has infinitesimal generator

\[
(Gf)(p) = -\sum_{i=1}^{K} \left(-\left(\sum_{j=1}^{K} \theta_{ij}\right) p_k + \sum_{j=1}^{K} \theta_{ji} p_j + p_i \left(\alpha_i - \sum_{j=1}^{K} \alpha_j p_j\right)\right) (\partial_i f)(p)
\]

\[
+ \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i (\delta_{ij} - p_j) (\partial_i \partial_j f)(p). \] (1.23)

Here, however, fewer exact results are available, but we still have the following two results when \( K = 2 \),

(i) Suppose \( \mu_{12} = \mu_{21} = 0 \). Then [99] (see also [186, 60]),

\[
P\{P_1(T_{abs}) = 1|P_1(0) = p\} = \frac{1 - e^{-2(\alpha_1 - \alpha_2)p}}{1 - e^{-2(\alpha_1 - \alpha_2)}}
\]

\[
= p + (\alpha_1 - \alpha_2)p(1 - p) + \mathcal{O}((\alpha_1 - \alpha_2)^2). \] (1.24)

(ii) When mutation rates are non-zero, we have [186],

\[
P\left\{ \lim_{t \to \infty} P(t) = (p, 1 - p) \right\} \propto p^{\theta_{12}-1}(1 - p)^{\theta_{21}-1} e^{(\alpha_1 - \alpha_2)p}. \] (1.25)

**Remark 1.2.** The expressions given above are superficially different from those which commonly appear in population genetics, where the convention is to assume that \( \alpha_1 = \alpha \)
and \( \alpha_2 = 0 \).

**Strong Selection**

In the *strong selection* regime, \( s_i = \mathcal{O}(1) \), and \( P_i^{(N)}(t) \) no longer converges weakly to a diffusion, but it can still be coupled\(^4\) over bounded time intervals to a diffusion process \( \tilde{P}_i^{(N)}(t) \) with generator

\[
\mathcal{G}^{(N)} f(p) = -\sum_{i=1}^{K} \left( -\left( \sum_{j=1}^{K} \theta_{ij} \right) p_k + \sum_{j=1}^{K} \theta_{ji} p_j + p_i \left( s_i - \sum_{j=1}^{K} s_j p_j \right) \right) (\partial_i f)(p)
+ \frac{1}{2N} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i (\delta_{ij} - p_j) (\partial_i \partial_j f)(p). \tag{1.26}
\]

such that for each fixed \( T > 0 \) there is a constant \( C_T > 0 \) such that [118]

\[
\lim_{N \to \infty} \mathbb{P} \left\{ \sup_{t \leq T} \left\| P^{(N)}(t) - \tilde{P}^{(N)}(t) \right\| > \frac{C_T \ln N}{N} \right\} = 0. \tag{1.27}
\]

While this does not necessarily justify the use of \( \tilde{P}_i^{(N)}(t) \) as an approximation to \( P_i^{(N)}(t) \) for all \( t \leq T_{\text{abs}} \), \( \tilde{P}_i^{(N)}(t) \) can nonetheless be used to obtain a very accurate approximation to the fixation probability when mutation rates are set to 0, which is, using the notation above [99] (see also [186, 60]),

\[
\mathbb{P} \{ P_1(T_{\text{abs}}) = 1 | P_1(0) = p \} = \frac{1 - e^{-2N(s_1-s_2)p}}{1 - e^{-2N(s_1-s_2)}}. \tag{1.28}
\]

In particular, assuming \( s_1 - s_2 > 0 \), if \( p = \frac{1}{N} \), as \( N \to \infty \) this approaches \( 1 - e^{-2(s_1-s_2)} = 2(s_1 - s_2) + \mathcal{O}(|s_1 - s_2|^2) \). The latter estimate was previously obtained by Haldane [71], who approximated the number of individuals of the novel type by a supercritical Bienaymé–Galton–Watson process, in which each in each generation, each individual produces offspring with numbers distributed according to a Poisson random variable

\(^4\)see A.2 for a discussion of coupling
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with rate $1 + (s_1 - s_2)$. In what follows, we will make use of such branching process approximations, which will be rigorously justified using a coupling argument.

1.2.3 The Neutral Theory of Molecular Evolution and the Neutralist/Selectionist Debate

Estimating substitution rates from hemoglobin, cytochrome c, and triosephosphate dehydrogenase, Kimura found them to be higher than would be plausible under selection, prompting him to speculate that genetic diversity was overwhelmingly the result of sampling effects among selectively neutral genes [100]. This hypothesis would be further developed (e.g., [107, 105]), and lead to the “neutralist/selectionist” debate as to whether natural selection or neutral genetic drift is the primary driver of evolution. This debate continues, as evidence has arisen for widespread selection on amino acids [138]. Further, the neutral theory substantially overestimates the observed diversity (see [114] and references therein), and evidence is lacking for the strong correlation between population sizes and genetic diversity, as would be expected in a neutral population [131]. While some hypotheses exist to explain the observed level of genetic diversity (e.g., the nearly neutral theory [146] or genetic hitchhiking [69]), it remains an interesting an important question to determine mechanisms that give rise to the observed, intermediate level of diversity.

1.2.4 Moran’s Model

In [142], Moran introduced an alternative formulation for mathematical population genetics, which, although largely neglected by biologists, is in many ways preferable to the Wright-Fisher model for the purposes of mathematical analysis. Moran’s formulation is a continuous time Markov chain, in which individuals of type $i$ reproduce and replace
individuals of type \( j \) with intensity

\[
\left( 1 - \sum_{j \neq i} \mu_{ij} \right) \beta_i X_i^{(N)}(t) + \sum_{j \neq i} \mu_{ji} \beta_j X_j^{(N)}(t) \left( \frac{X_j^{(N)}(t)}{N} \right),
\]

i.e., individuals of type \( i \) produce offspring at rate \( \beta_i \), and these offspring are of type \( j \neq i \) with probability \( \mu_{ij} \). Each offspring replaces an individual chosen uniformly at random from the population, insuring the population size remains fixed at \( N \).

In addition to being a more biologically appropriate model for, e.g., microorganisms, which tend to have overlapping generations and reproduce by binary fission, the Moran model has the advantage of being analytically tractable without recourse to the diffusion approximation. For example, when \( K = 2 \) and \( \mu_{12} = \mu_{21} = 0 \), adopting the notation from the previous section, we have \[142\]

\[
P\left\{ X_1^{(N)}(T_{\text{abs}}) = N \mid X_1^{(N)}(0) = n \right\} = \frac{1 - \left( \frac{\beta_2}{\beta_1} \right)^n}{1 - \left( \frac{\beta_2}{\beta_1} \right)}.
\]

\[1.30\]

\( N.B. \) For the (discrete) Moran model, we take the time to first absorption (i.e., fixation or extinction of type 1) to be

\[
T_{\text{abs}} = \inf \left\{ t \geq 0 : X_1^{(N)}(t) \in \{0, N\} \right\}.
\]

\[1.31\]

In the weak selection regime, the Moran model and the Wright-Fisher model are asymptotically equivalent: if we let \( \beta_i = 1 + s_i \) and \( N_e = \frac{N}{2} \), and assume that \( \theta_{ij} = 2N_e \mu_{ij} \) and \( \alpha_i = 2N_e s_i \), then \( \frac{1}{N} X^{(N)}(N_e t) \) converges in distribution to \( P(t) \), the same diffusion as for the Wright-Fisher model, with generator \(1.12\). \( N_e \) is referred to as the effective population size for the Moran model. For appropriate choices of \( N_e \), a wide array of population genetic models converge to Kimura’s diffusion \[141, 170\].

We shall use Moran’s model as a point of departure for a modelling framework that in-
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integrates Kolmogorov’s approach to population dynamics with population genetics, modelling allele frequencies via continuous time Markov processes. Unlike Moran, we decouple birth and death events, but allow their rates to depend on the number and type of all individuals composing the population.

1.2.5 Cannings’ Models and Neutrality

We conclude our brief survey of mathematical population genetics with Cannings’ models [24]. There have been a number of different notions of neutrality that have arisen in the population genetic literature, usually in the context of diffusion limits, not all of which are interchangeable, which has led to occasional confusion [162]. As we will have need of a suitable null model in later chapters, we wish to fix one notion of neutrality. Perhaps the most robust of these are the exchangeable models proposed by Cannings. Recall that a random vector \((v_1, \ldots, v_N)\) is exchangeable if \((v_{\sigma(1)}, \ldots, v_{\sigma(N)})\) has the same distribution as \((v_1, \ldots, v_N)\) for all permutations \(\sigma\) of \(\{1, \ldots, N\}\) i.e., relabelling the components leaves the underlying random vector unchanged. Suppose we have a haploid population of \(N\) panmictic individuals with discrete generations. Label the individuals in the \(n^{th}\) generation by \(1, \ldots, N\), and write \(v_i(n)\) for the number of offspring of the \(i^{th}\) individual in the \(n + 1^{st}\) generation; by assumption, \(v_i(n) \in \mathbb{N}_0 := \{0, 1, 2, \ldots\}\) and

\[
\sum_{i=1}^{N} v_i(n) = N. \tag{1.32}
\]

for all \(n \geq 0\). This describes a Cannings’ Model if \((v_1(n), \ldots, v_N(n))\) is an exchangeable random vector for all \(n\), and, moreover, \(\{(v_1(n), \ldots, v_N(n)) : n \in \mathbb{N}_0\}\) are identically and independently distributed. For example, the Wright-Fisher model is the Cannings’ model for which \((v_1(n), \ldots, v_N(n))\) is multinomial distributed with \(N\) trials, each with probability of success \(\frac{1}{N}\).

All individuals in a Cannings’ model are effectively interchangeable, and if individuals
are assigned types, those types are merely labels, and have no effect on the change in allele frequency. Cannings’ models thus provide a suitable mathematical definition for a neutral population.

Suppose that we have a Cannings’ model with $K$ types, and, as before, let $X_i^{(N)}(n)$ be the number of individuals of type $i$ in the $n^{th}$ generation and let

$$X^{(N)}(n) = (X_i^{(N)}(n), \ldots, X_i^{(N)}(n)). \quad (1.33)$$

Let $c_N$ be the probability that two individuals independently sampled uniformly from generation $n + 1$ have the same parent in generation $n$, so

$$c_N = \frac{\mathbb{E}[v_1(n)(v_1(n) - 1)]}{N - 1}. \quad (1.34)$$

Recently, M"ohle [141] showed that, provided

$$\frac{\mathbb{E}[v_1(n)(v_1(n) - 1)v_2(n)(v_2(n) - 1)]}{N^2c_N} \rightarrow 0 \quad (1.35)$$

as $N \rightarrow \infty$, then $X^{(N)}\left(\left\lfloor \frac{t}{c_N} \right\rfloor\right)$ converges to a diffusion satisfying Kimura’s generator

$$(Gf)(p) = \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i (\delta_{ij} - p_j) (\partial_i \partial_j f)(p). \quad (1.36)$$

In Chapter 4, we will follow Cannings’ example, and use exchangeable processes as a point of departure for analyzing processes in the weak selection regime.

### 1.3 Outline of Thesis

Our goal is the development of a mathematical formalism that is sufficiently simple so as to be analytically tractable, and amenable to the exact computation of fixation prob-
abilities, fixation times, and stationary allele frequencies, while remaining rich enough
to encompass diverse ecological dynamics. This thesis is an effort in this direction. In
particular, we will develop a class of models which we call density-dependent birth-death-
mutation processes, such that

- selection is at the level of individuals that reproduce and die, rather than abstracted
genes,

- rather than imposing fixed, deterministically varying, or exogenously determined
  population sizes or compositions, we will insist that the total population number
  varies with the population dynamics, in the same stochastic events that cause allele
  numbers to vary,

- populations will be regulated by density dependent competition for limited re-
  sources rather than being “sampled” by unspecified external mechanisms.

- rather than assuming a priori selection coefficients (constant or time-varying), we
  allow the selection coefficients to emerge mechanistically from the population dy-
  namics, and seek to interpret them in terms of life-history strategies.

The lack of fixed population sizes is a particularly important feature of the pop-
ulation models considered in this thesis. At the risk of stating the obvious, natural
populations are not fixed, but are subject to internally generated demographic stochasticity and exogenous environmental stochasticity. There has been long and sustained
interest in determining the effects of variable population size on the probability of allele
fixation (e.g., [59, 111, 52, 94, 101, 106, 147, 154, 160, 23, 121, 122, 153, 45, 124], among
many others). Here, we provide a general framework for investigating the effects of de-
omorphic stochasticity which allows us to consider diverse community dynamics, and
thus provides a first step towards the generalized theory of coevolution that incorporates
complex, multi-trophic interactions that some have called community genetics [6, 7, 143].
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We take philosophical guidance from Nisbet and Gurney [144], and focus on obtaining a robust approach to demographic stochasticity, into which environmental stochasticity can later be incorporated. While it is beyond the scope of this thesis, we propose that the problem of intermediate diversity that drives some of the neutralist/selectionist debate might in part be explained by ecological mechanisms of coexistence, that arise when multiple species interact with nonlinear birth and death rates (e.g., [9, 139, 10]) and varying population sizes. This is a question to which we intend to return; the results here are a foundation for that effort.

Density-dependent birth-death-mutation processes are a hybrid of multi-type birth and death processes (so that rates are proportional to the number of individuals; we do not, however, assume binary reproduction) and the density-dependent population processes considered by Thomas Kurtz ([116, 117, 118, 119], see also [50]), modified to allow weak mutation. In those papers, Kurtz derived a functional law of large numbers and central limit theorem valid for times less than a fixed $T$ that is independent of $N$. Unfortunately, Kurtz’s results on density dependent population processes are not directly useful in finding the probability of the extinction/fixation events that drive adaptive evolution. In what follows, we identify and prove convergence for the limits and appropriate to population genetics.

As in classical population genetics, we will derive our results as a parameter, $N$, tends to infinity. Unlike the classical theory, $N$ is not a number of individuals at which the population is fixed, but rather an analogue of the carrying capacity in the logistic equation,

$$
\dot{X} = rX \left(1 - \frac{X}{N} \right),
$$

which measures the strength of interaction between individuals and is proportional to the equilibrium population size, where net per-capita growth rates drop to zero. This system size, $N$, will be interpreted slightly differently in different models. In a Gause-Lotka-Volterra model, it is an abstract measure of the number of individuals an environment
can sustain. In an explicit resource model \( e.g., \) of a chemostat, it might measure the volume of the reaction vessel. In the epidemic models contained herein, it is proportional to the number of uninfected hosts. It is important to realize that we do not require that the total number of individuals of all types sum to \( N \). Instead, we will consider individuals to be common or rare when their numbers are \( \mathcal{O}(N) \), or asymptotically smaller than \( N \), respectively, and allow those numbers to vary stochastically.

In Chapter 2, we formally define density-dependent birth-death-mutation processes and prove a functional law of large numbers. This tells us that in the limit of large \( N \), common types \( (i.e., \) those with initial numbers proportional to \( N \)) behave essentially deterministically – if there are sufficiently many individuals of a given type, the fluctuations are effectively “averaged out”. More precisely, there exists a dynamical system of Kolmogorov type,

\[
\dot{Y} = F(Y)
\]

such that for times \( t < C \ln N \), for a constant \( C \) depending on the vector field \( F \), the number of individuals of type \( i \) is \( NY_i(t) + \mathcal{O}(N^r) \) for some \( \frac{1}{2} < r < 1 \).

We are thus left with considering two situations: as in classical population genetics, we will be concerned with the ability of rare types \( (i.e., \) those with initial numbers \( \ll N \)) to become common. Further, we will be interested in the long-term dynamics, when our functional law of large numbers no longer applies. We note that for \( N \) large, \( Y \) will come arbitrarily close to its asymptotic attractor, which will be integral to understanding the stochastic dynamics. Unfortunately, disparate topological classes will have to be analyzed by qualitatively different means, and Smale’s construction shows that this analysis can never be exhaustive. Instead, we focus on two cases which are most naturally analogous to the strong and weak selection regimes of population genetics, and which encompass many results of classical population genetics, which we may obtain as simple corollaries. More importantly, our approach leads to many novel results.
Chapter 3 discusses fixation times and fixation probabilities in the strong selection regime. Here, this is equivalent to $\dot{Y} = F(Y)$ having a unique, globally stable axial fixed point, which without loss of generality we take to be $x^{*1} = x_{1}^{*1}e_{1}$. Under this assumption, without mutation, if the number of individuals of the advantageous type 1 reaches $\varepsilon N$, i.e., if type 1 becomes common, then it will eventually fix with probability approaching 1 as $N \to \infty$. (more precisely, the probability that type 1 fails to fix decays exponentially in $N$). We thus consider the problem of fixation of a small number of novel individuals (usually, but not necessarily, assumed to be one) invading a community of resident species which are assumed much more numerous. We compute the probability of hitting $\varepsilon N$, which we show is a function of the average birth rate and death rate of type 1, into which all other types only enter via the functional Law of Large Numbers. We also derive an expression the expected time to fixation for type 1. Analogously to Haldane’s branching process approximation [71], these results are obtained using a coupling to a time-inhomogeneous Markov branching processes; the asymptotic probability of hitting $\varepsilon N$ is then the probability that the coupled branching process grows indefinitely.

In Chapter 4 we consider a generalization of the weak-selection regime, which here is the degenerate case when the set of interior fixed points of $\dot{Y} = F(Y)$ is a is globally asymptotically stable embedded submanifold of $\mathbb{R}^K_+$ (recall, $K$ is the number of distinct types). We show that suitably modified and rescaled, the density of types converges in distribution (i.e., the corresponding probability measures on Skorokhod space $\mathbb{D}_{\mathbb{R}^K_+}[0,\infty)$ converge in the weak topology) to a diffusion on that manifold. We show that the diffusion limit we obtain reduces to Kimura’s diffusion when the initial birth-death-mutation process is exchangeable, and consider a number of departures from exchangeability in which a diffusion limit is still available. These encompass, generalize, and provide rigorous justification for a number of previously considered population genetic models (e.g., Gillespie’s models of fecundity variance polymorphism [66, 67, 68, 61]) while providing an explicit

\footnote{see A.3 for the definition of Skorokhod space $\mathbb{D}$.}
population genetic formulation of more ecological notions such as r vs. K selection [132, 155, 156] and resource ratio theory [133, 178, 179]. We then consider what we call the Generalized Moran model, which we use to consider a fecundity-mortality tradeoff as a simple example of a life-history strategy. When the number of species, K, is equal to two, we use the diffusion approximation to the Generalized Moran model to obtain analytical expressions for the fixation probabilities and expected time to fixation, and if mutation is allowed, the quasi-stationary distribution of allele frequencies. Using these, we find selection favouring reduced fecundity, and interestingly, that the stationary allele frequency distribution is indistinguishable from that for the Wright-Fisher model, so that inference techniques based upon the allele frequency distribution may not be adequate to distinguish between different hypotheses.

Chapter 5 demonstrates the versatility of the methods developed in Chapter 3 and Chapter 4, by applying them to an example of epidemiological interest, the evolution of virulence in the SIR (Susceptible-Infective-Recovered) model with demography. We consider a two-strain epidemic, where the pathogens convey cross-immunity and thus compete for hosts. We consider the fixation probability for a novel strain invading a population of hosts in which a “wild-type” strain has reached endemic equilibrium, and show this can be simply expressed as the ratio of the two strains’ basic reproductive numbers. The basic reproductive number, the expected number of new infections caused by a single infected individual entering a population of susceptibles, has long been used in mathematical epidemiology to characterize the deterministic evolutionary dynamics of pathogens [127, 2, 3, 20, 136, 110, 137]). Finally, we look at the weakly selected two-strain epidemic, which provides an interesting co-dimension two application of the results of Chapter 4, and also suggests that stochasticity in viral evolution may give new life to the currently out-of-favour notion of selection for reduced virulence.

Finally, we conclude with a discussion of future work.
Chapter 2

Density Dependent

Birth-Death-Mutation Processes

In this chapter, we introduce the primary object of this study, density dependent birth-death mutation processes. These are a class of continuous time Markov jump processes generalizing the models considered by Wright, Fisher and Moran, such that their functional Law of Large Numbers gives rise to a competitive Kolmogorov dynamical system. We begin by recalling a broader class of processes, the density dependent population processes that were introduced by T. G. Kurtz ([116, 117, 118, 119], see also [50]) to describe families of jump Markov processes arising in chemistry, population dynamics and population genetics. We introduce a slight generalization of Kurtz’s density dependent population processes that allows us to consider $O\left(\frac{1}{N}\right)$ effects like mutation. We then derive a simple extension of the functional Law of Large Numbers for these processes, Proposition 2.1, which shows that, provided the initial number of individuals of type $i$ is $O(N)$, then the rescaled process $N^{-1}X_i^{(N)}(t)$ is approximately deterministic. This was originally proved by Kurtz [116] for times $t \in [0, T]$ for a fixed $T > 0$, independent of $N$. Because we wish to consider extinction and fixation, we require a result valid for times that scale with $N$, and an estimate of the error in our approximation, hence Proposition
2.1, which uses a different method of proof from [116].

This result shapes our overall strategy: from it, we know that once the population exceeds $\varepsilon N$ for any $\varepsilon > 0$ independent of $N$, it can be approximated by a deterministic process, for a time span sufficiently long that both the original process and the functional Law of Large Numbers approximation are in a $o(1)$-neighbourhood of the attractor of the deterministic dynamics. Thus, we need only answer two questions: what are the dynamics when the number of individuals is $o(N)$, and, what happens when the stochastic process is started near the asymptotic attractor. Chapter 3 addresses the former question.

Unfortunately, Smale’s construction (Example 1.1) shows that a complete answer to the latter question is impossible, as essentially arbitrary asymptotic dynamics are possible. We thus proceed by identifying two asymptotic regimes, the strong and weak selection regimes that generalize the eponymous regimes from classical population genetics. In the strong selection regime, there is a single type that is guaranteed to fix in the deterministic limit; in this case, fixation is equivalent to the selected type reaching $\varepsilon N$ before going extinct, and thus is completely understood by the results in Chapter 3. The weak selection regime corresponds to the existence of a manifold of fixed points at which deterministic coexistence is possible, and is the subject of Chapter 4.

Finally, we conclude the chapter by considering sufficient conditions for being in these two regimes in the Lotka-Volterra-Gause equations.

### 2.1 Density Dependent Population Processes

Consider a population consisting of a finite number of discrete individuals. Each individual has a type, which is indexed by an integer in the set $\{1, \ldots, K\}$. All individuals of a given type are identical.
Denote the number of individuals of type \( i \in \{1, \ldots, K \} \) at time \( t \) by \( X_i^{(N)}(t) \) and let

\[
X^{(N)}(t) = \left( X_1^{(N)}(t), \ldots, X_K^{(N)}(t) \right). \tag{2.1}
\]

**Definition 2.1.** Let \( \{\lambda_n^{(N)}(x)\}_{n \in \mathbb{Z}^K} \) be a collection of non-negative functions defined on a subset \( E \subseteq \mathbb{R}^K \). Set

\[
E^{(N)} := E \cap \{ N^{-1}k : k \in \mathbb{Z}^K \}, \tag{2.2}
\]

and assume that \( x \in E^{(N)} \) and \( \lambda_n^{(N)}(x) > 0 \) imply \( x + N^{-1}n \in E^{(N)} \). The *density dependent family* corresponding to the \( \lambda_n^{(N)}(x) \) is a sequence \( \{X^{(N)}\} \) of jump Markov processes such that \( X^{(N)} \) has state space \( E^{(N)} \) and intensities

\[
q_{x,x'}^{(N)} = N\lambda_{N(x' - x)}^{(N)}(x), \quad x, x' \in E^{(N)}. \tag{2.3}
\]

**Remark 2.1.** As we discussed in the Introduction, the index \( N \), sometimes referred to as the “system size”, plays the role of the fixed population size \( N \) in the Wright-Fisher and Moran models, and of the carrying capacity \( N \) in Verhulst’s logistic equation (1.1). It should not, however, be thought of as a fixed population size – we allow the total number of individuals to vary stochastically, but, under our assumption of density dependence, after a transient phase, the total number of individuals will fluctuate about an “asymptotic equilibrium” value that is proportional to \( N \).

**Remark 2.2.** The class of density dependent population processes includes examples which would not be considered density dependent in the ecologist’s sense. For example, the simple birth-death process with rates

\[
q_{x,x+1}^{(N)} = \beta x, \quad q_{x,x-1}^{(N)} = \delta x \tag{2.4}
\]
corresponds to the density dependent family

$$
\lambda_1^{(N)}(x) = \beta x, \quad \lambda_{-1}^{(N)}(x) = \delta x.
$$

However, if $\beta > \delta$, then this process will grow without bound with probability $\frac{\delta}{\beta}$ [96]. To exclude this, and similar examples, we introduce a narrower class of density dependent birth-death-mutation processes in the next section. Nonetheless, whenever possible, we will prove results at the level of generality of density dependent population processes, specializing to the latter class as necessary to obtain more refined results.

### 2.1.1 Stochastic Differential Equation Representation

Henceforth, we adopt the following assumptions

**Assumption 2.1.** For all compact sets $\mathcal{K} \subset \mathbb{R}^K_+$,

$$
\sum_{n \in \mathbb{Z}^K} \|n\|_2 \sup_{x \in \mathcal{K}} \lambda_n^{(N)}(x) < \infty \quad \text{and} \quad \sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \sup_{x \in \mathcal{K}} \|\lambda_n^{(N)}(x) - \lambda_n(x)\| < \infty. \quad (2.6)
$$

**Assumption 2.2.** There exist functions $\{\lambda_n(x)\}_{n \in \mathbb{Z}^K}$ such that for all compact sets $\mathcal{K} \subset \mathbb{R}^K_+$,

$$
\lim_{N \to \infty} \sum_{n \in \mathbb{Z}^K} \|n\|_2 \sup_{x \in \mathcal{K}} \|\lambda_n^{(N)}(x) - \lambda_n(x)\| = 0 \quad (2.7)
$$

and

$$
\lim_{N \to \infty} N \sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \sup_{x \in \mathcal{K}} \|\lambda_n^{(N)}(x) - \lambda_n(x)\| < \infty. \quad (2.8)
$$

**Remark 2.3.** Assumption 2.1 guarantees that the jumps in $X^{(N)}(t)$ have finite mean and variance for all $N$. For our purposes, this will mean that the total number of offspring per individual, per reproductive event, has finite mean and variance – an eminently plausible assumption for natural populations (although, see e.g., [42] for a discussion of the biological applicability of models in which variance in individual reproductive output
tends to infinity with population size).

Remark 2.4. Assumption 2.2, together with the functional form of the transition rates \( \lambda^{(N)}(x) \), Equation 2.3, combine to give us a notion of density dependence: like the logistic equation, (1.1), the number of individuals of each type only appear in the rates rescaled by the system size \( N \) – we could have equally well expressed the rates in terms of the rescaled process \( Y^{(N)}(t) = N^{-1}X^{(N)}(t) \). Assumption 2.2 requires that those transition rates approach a finite limit as \( N \to \infty \); in particular, we require that the rates converge in such a way that the mean and variance of the jump sizes also converge to finite limits, which is a minimal requirement for a biologically meaningful limit. As we saw previously, this notion of density-dependence is weaker than that of the logistic equation, as it does not guarantee that populations approach a finite equilibrium density. We will discuss the appropriate additional assumptions to guarantee finiteness below.

We then have the following representation of the process \( X^{(N)} \): let \( H^{(N)}_n(t) \) be a counting process\(^1\) with intensity \( \lambda^{(N)}_n(X^{(N)}(t)) \geq 0 \), and compensated process

\[
\tilde{H}^{(N)}_n(t) = H^{(N)}_n(t) - \int_0^t \lambda^{(N)}_n(X^{(N)}(s-)) \, ds
\]  

(2.9)

is a square-integrable local martingale with quadratic variation process\(^2\)

\[
[H^{(N)}_n](t) = H^{(N)}_n(t).
\]  

(2.10)

We assume that the processes \( H^{(N)}_n(t) \) are orthogonal, so

\[
[H^{(N)}_n, H^{(N)}_m](t) = 0 \quad \text{for } n \neq m.
\]  

(2.11)

\(^1\)see A.8 for a discussion of counting processes.

\(^2\)see A.6 for the definition of the quadratic variation and covariation processes.
We can then write
\[
X^{(N)}(t) = X^{(N)}(0) + \sum_{n \in \mathbb{Z}^K} H_n^{(N)}(t),
\]
(2.12)

It will be convenient to decompose the semimartingale \( X^{(N)}(t) \) into finite-variation and local martingale components\(^3\),
\[
X^{(N)}(t) = X^{(N)}(0) + \int_{0+}^t N F^{(N)} \left( \frac{X^{(N)}(s)}{N} \right) \, ds + M^{(N)}(t)
\]
(2.13)
where
\[
F^{(N)}(x) = \sum_{n \in \mathbb{Z}^K} n \lambda_n^{(N)}(x),
\]
(2.14)
and
\[
M^{(N)}(t) = \sum_{n \in \mathbb{Z}^K} n \tilde{H}_n^{(N)}(t).
\]
(2.15)

Under Assumption 2.1, \( M^{(N)}(t) \) is a square-integrable local martingale with tensor quadratic variation\(^4\) [140]
\[
\|M^{(N)}\|(t) = \sum_{n \in \mathbb{Z}^K} nn^\top H_n^{(N)}(t)
\]
(2.16)
and Meyer process
\[
\langle\langle M^{(N)}\rangle\rangle(t) = \int_{0+}^t \sum_{n \in \mathbb{Z}^K} nn^\top \lambda_n^{(N)}(X^{(N)}(s)) \, ds.
\]
(2.17)

### 2.1.2 Law of Large Numbers

Let
\[
F(x) = \sum_{n \in \mathbb{Z}^K} n \lambda_n(x).
\]
(2.18)

---
\(^3\) see A.7 for a discussion of semimartingales and the Doob-Meyer decomposition
\(^4\) see A.7.
As a consequence of Assumptions 2.1 and 2.2, \( F^{(N)} \to F \) uniformly on compact sets. We will assume that \( F \) is \( C^3 \) and thus locally Lipschitz.

We will henceforth let \( \psi_t \) denote the flow of

\[
\dot{Y}(t) = F(Y(t)),
\]

and set

\[
Y^{(N)}(t) := \frac{1}{N} X^{(N)}(t).
\]

**Notation 2.1.** Here, and in subsequent chapters, we will be interested in initial conditions \( X_i^{(N)}(0) \) such that

\[
\lim_{N \to \infty} \frac{1}{N} X_i^{(N)}(0) = x
\]

for some fixed \( x \in \mathbb{R}^K_+ \). We thus adopt the notation

\[
P_x \{ \cdot \} = \mathbb{P} \left\{ \cdot \bigg| \lim_{N \to \infty} \frac{1}{N} X_i^{(N)}(0) = x \right\},
\]

and

\[
\mathbb{E}_x [\cdot] = \mathbb{E} \left[ \cdot \bigg| \lim_{N \to \infty} \frac{1}{N} X_i^{(N)}(0) = x \right].
\]

Let \( x \in \mathbb{R}^K_+ \). By assumption, \( \psi_t x \) is eventually in a compact set, so we may choose a compact set \( K_x \subset \mathbb{R}^K_+ \) such that the forward orbit of \( x \), \( \gamma^+_x := \{ \psi_t x : t \geq 0 \} \) is contained in the interior of \( K_x \), \( \overset{o}{K}_x \). We may thus fix \( \varepsilon > 0 \) such that

\[
K_{x,\varepsilon}(t) := \overline{\{ x' : \| x' - \psi_t x \| < \varepsilon \}}
\]

and

\[
K_{x,\varepsilon} := \bigcup_{t \geq 0} K_{x,\varepsilon}(t)
\]

are contained in \( K_x \). Since \( F \) is locally Lipschitz, there exists a constant \( L_x > 0 \) such
that
\[ \|F(x_1) - F(x_2)\| < L_x \|x_1 - x_2\| \] (2.26)
for all \( x_1, x_2 \in \mathcal{K}_x. \)

In what follows, we will make extensive use of \( \mathcal{K}_x \) and the tubular \( \varepsilon \)-neighbourhood of the deterministic trajectory \( \gamma_x^+, \mathcal{K}_{x,\varepsilon} \). Our arguments in this and subsequent chapters will hinge upon the fact that, provided that \( N \) is sufficiently large, the rescaled process \( N^{-1}X^{(N)}(t) \) will remain inside \( \mathcal{K}_{x,\varepsilon} \) with probability approaching 1 as \( N \to \infty \).

To be precise, we have the following functional Law of Large Numbers for \( Y^{(N)}(t) \), which states that for times of order \( O(\ln N) \), \( N^{-1}X^{(N)}(t) \) may be approximated arbitrarily well by the deterministic flow \( \psi_t x \).

**Proposition 2.1.** Fix \( 0 < r < s < 1 \) and assume that \( E \left[ \|Y^{(N)}(0) - x\| \right] = O(N^{-1}). \)
Then,

(i) for \( N \) sufficiently large,
\[ \mathbb{P}_x \left\{ \sup_{t \leq \frac{(1-s)\ln N}{4L_x}} \|Y^{(N)}(t) - \psi_t x\|^2 > N^{-r} \right\} < N^{-r}, \] (2.27)

(ii) and, for all fixed \( T > 0 \),
\[ \lim_{N \to \infty} \sup_{t \leq T} \|Y^{(N)}(t) - \psi_t x\| = 0 \quad \mathbb{P}_x - \text{a.s.} \] (2.28)

**Remark 2.5.** In [119], (ii) is proved under the assumptions \( Y^{(N)}(0) \to x \), \( \lambda_n^{(N)}(x) \equiv \lambda_n(x) \), and
\[ \sup_{x \in \mathcal{K}} \sum_{n \in \mathbb{Z}^K} \|n\|_2 \lambda_n^{(N)}(x) < \infty. \] (2.29)
Unfortunately, that proof relies on the compactness of \([0, T]\), whereas we shall require estimates when \(t\) is \(O(\ln N)\) throughout the next two chapters.

**Proof.** As above, we may write \(Y^{(N)}(t)\) as

\[
Y^{(N)}(t) = Y^{(N)}(0) + \int_{0+}^{t} F^{(N)}(Y^{(N)}(s)) \, ds + \frac{1}{N} M^{(N)}(t). \tag{2.30}
\]

Define a stopping time

\[
T^{(N)}_{\varepsilon} := \inf \{ t \geq 0 : \| Y^{(N)}(t) - \psi_x x \| > \varepsilon \}, \tag{2.31}
\]

so \(T^{(N)}_{\varepsilon}\) is the first time that the process exits \(K_{x,\varepsilon}\). We will consider the stopped process \(Y^{(N)}(t \wedge T^{(N)}_{\varepsilon})\) (recall, \(x \wedge y := \max\{x, y\}\)):

\[
Y^{(N)}(t \wedge T^{(N)}_{\varepsilon}) - \psi_{t \wedge T^{(N)}_{\varepsilon}} x = Y^{(N)}(0) - x + \int_{0+}^{t \wedge T^{(N)}_{\varepsilon}} F(Y^{(N)}(s)) - F(\psi_x x) \, ds
+ \int_{0+}^{t \wedge T^{(N)}_{\varepsilon}} F^{(N)}(Y^{(N)}(s)) - F(Y^{(N)}(s)) \, ds + \frac{1}{N} M^{(N)}(t \wedge T^{(N)}_{\varepsilon}). \tag{2.32}
\]

Applying the Cauchy–Bunyakovskiy–Schwarz inequality gives

\[
\| Y^{(N)}(t \wedge T^{(N)}_{\varepsilon}) - \psi_{t \wedge T^{(N)}_{\varepsilon}} x \|^2
\leq 4 \left( \| Y^{(N)}(0) - x \|^2 + \int_{0+}^{t \wedge T^{(N)}_{\varepsilon}} F(Y^{(N)}(s)) - F(\psi_x x) \, ds \right)^2
+ \left( \int_{0+}^{t \wedge T^{(N)}_{\varepsilon}} F^{(N)}(Y^{(N)}(s)) - F(Y^{(N)}(s)) \, ds \right)^2 + \frac{1}{N^2} \| M^{(N)}(t \wedge T^{(N)}_{\varepsilon}) \|^2 \right). \tag{2.33}
\]

We consider each of the terms individually:

1. By assumption, we have \(E \left[ \| Y^{(N)}(0) - x \|^2 \right] < \frac{C}{N} \) for some constant \(C\).
2. Applying Jensen’s inequality gives

$$\sup_{t \leq T} \left\| \int_{0^+}^{\tau \wedge T^2(N)} F(Y^{(N)}(s)) - F(\psi_{\tau} x) \, ds \right\|^2 \leq L^2 |x| T \int_{0^+}^{\tau \wedge T^2(N)} \left\| Y^{(N)}(s) - \psi_{\tau} x \right\|^2 \, ds$$

(2.34)

and

$$\sup_{t \leq T} \left\| \int_{0^+}^{\tau \wedge T^2(N)} F^{(N)}(Y^{(N)}(s)) - F(Y^{(N)}(s)) \, ds \right\|^2 \leq T \int_{0^+}^{\tau \wedge T^2(N)} \left\| F^{(N)}(Y^{(N)}(s)) - F(Y^{(N)}(s)) \right\|^2 \, ds,$$

(2.35)

whilst by assumption, we have $$\|F^{(N)}(x) - F(x)\| = O\left(\frac{1}{N}\right)$$ uniformly on $$\mathcal{K}_x$$.

3. Lastly, Doob’s inequality gives

$$\mathbb{E} \left[ \sup_{t \leq T} \left\| M^{(N)}(t \wedge \tau^{(N)}_{\varepsilon}) \right\|^2 \right] \leq 4 \mathbb{E} \left[ \langle M^{(N)} \rangle (T \wedge \tau^{(N)}_{\varepsilon}) \right]$$

$$\leq N \int_{0^+}^{\tau \wedge T^2(N)} \sum_{n \in \mathbb{Z}} \|n\|^2 \mathbb{E} \left[ \lambda^{(N)}_{n} (Y^{(N)}(t)) \right] \, ds,$$

(2.36)

and again, by assumption, $$\sum_{n \in \mathbb{Z}} \|n\|^2 \mathbb{E} \left[ \lambda^{(N)}_{n} (Y^{(N)}(t)) \right]$$ is uniformly bounded on $$\mathcal{K}_x$$.

Combining these, we have

$$\mathbb{E} \left[ \sup_{t \leq T} \left\| Y^{(N)}(t \wedge \tau^{(N)}_{\varepsilon}) - \psi_{t \wedge \tau^{(N)}_{\varepsilon}} x \right\|^2 \right]$$

$$\leq \frac{4C + B|x| T}{N} + 4L^2 |x| T \int_{0}^{\tau \wedge T^2(N)} \mathbb{E} \left[ \left\| Y^{(N)}(s) - \psi_{s} x \right\|^2 \right] \, ds$$

(2.37)
for some constant $B_{x, \varepsilon}$. Applying Gronwall’s inequality, we have

$$
\mathbb{E} \left[ \sup_{t \leq T} \left\| Y^{(N)}(t \wedge T^\varepsilon_{\varepsilon}) - \psi_{t \wedge T^\varepsilon_{\varepsilon}} x \right\|^2 \right] \leq \frac{4C + B_{x, \varepsilon} T}{N} e^{4L^2_{x, \varepsilon} T},
$$

(2.38)

from which, taking $T = \frac{(1-s)}{4L^2_{x, \varepsilon}} \ln N$, we obtain

$$
\sup_{t \leq \frac{(1-s)}{4L^2_{x, \varepsilon}} \ln N} \mathbb{E}_x \left\| Y^{(N)}(t \wedge T^\varepsilon_{\varepsilon}) - \psi_{t \wedge T^\varepsilon_{\varepsilon}} x \right\|^2 \leq \frac{4C + (1-s)B_{x, \varepsilon}}{4L^2_{x, \varepsilon}} (\ln N) N^{-s} < N^{-r}
$$

(2.39)

for $N$ sufficiently large.

To complete the proof of (i), we observe

$$
P_x \{ T^\varepsilon_{\varepsilon} < t \} = P_x \left\{ \left\| Y^{(N)}(t \wedge T^\varepsilon_{\varepsilon}) - \psi_{t \wedge T^\varepsilon_{\varepsilon}} x \right\|^2 \geq \varepsilon^2 \right\}
$$

(2.40)

$$
\leq \mathbb{E}_x \left[ \left\| Y^{(N)}(t \wedge T^\varepsilon_{\varepsilon}) - \psi_{t \wedge T^\varepsilon_{\varepsilon}} x \right\|^2 \right] \leq \frac{4C + (1-s)B_{x, \varepsilon}}{4L^2_{x, \varepsilon}} (\ln N) N^{-s} < N^{-r}
$$

(2.41)

(2.42)

for $N$ sufficiently large.

To prove (ii), write $(\Omega, \mathcal{F}, \mathbb{P})$ for the underlying probability space\textsuperscript{5}, and suppose that

$$
\sup_{t \leq T} \| Y^{(N)}(\omega, t) - \psi_t x \| \not\to 0 \text{ for some } \omega \in \Omega.
$$

Then, there exists $\delta > 0$ and $N_k \to \infty$ such that

$$
\sup_{t \leq T} \| Y^{(N_k)}(\omega, t) - \psi_t x \| > \delta \quad \text{for all } k.
$$

(2.43)

Without loss of generality, we may assume that for all $k$, $N_k^{-r} < \delta$ and $T \leq \frac{(1-s)}{4L^2_{x, \varepsilon}} \ln N_k$. Thus

$$
\omega \in \bigcap_{k=1}^{\infty} \{ \tilde{\omega} : \| Y^{(N_k)}(\tilde{\omega}, t) - \psi_t x \| > N_k^{-r} \}.
$$

(2.44)

By (i), this set has measure 0.

\textsuperscript{5}\text{see Appendix A for a discussion of the probability triple } (\Omega, \mathcal{F}, \mathbb{P}).
2.2 Density-dependent Birth-Death-Mutation Processes

Here we define to the principal object of interest, a subset of the density dependent birth death processes that we will call density dependent birth-death-mutation processes. As in the previous section, \( X_i^{(N)}(t), i = 1, \ldots, K \) is the number of individuals of type \( i \). The number of individuals of each type changes when there is a

- birth/mutation event in which some individual of type \( i \) produces a collection consisting of \(|n| = n_1 + \cdots + n_K\) offspring, of which \( n_j \in \mathbb{N}_0 \) are of type \( j \), which occur at a per capita rate

\[
\beta_{i,n}^{(N)} \left( \frac{X^{(N)}(t)}{N} \right) \tag{2.45}
\]

or

- the death of an individual of type \( i \), which occurs at per capita rate

\[
\delta_{i}^{(N)} \left( \frac{X^{(N)}(t)}{N} \right) \tag{2.46}
\]

As before, the Markov chain \( X^{(N)}(t) \) may be represented as

\[
X^{(N)}(t) = X^{(N)}(0) + \sum_{i=1}^{K} \sum_{n \in \mathbb{N}_0^K} n B_{i,n}^{(N)}(t) - \sum_{i=1}^{K} e_i D_{i}^{(N)}(t) \tag{2.47}
\]

where \( B_{i,n}^{(N)}(t) \) and \( D_{i}^{(N)}(t) \) are counting processes with intensities \( \beta_{i,n}^{(N)} \left( \frac{X^{(N)}(t)}{N} \right) X_i^{(N)}(t) \) and \( \delta_{i}^{(N)} \left( \frac{X^{(N)}(t)}{N} \right) X_i^{(N)}(t) \), respectively. As before, we write \( \tilde{B}_{i,n}^{(N)} \) and \( \tilde{D}_{i}^{(N)} \) for the corresponding compensated processes (see Equation 2.9).

A density dependent birth-death-mutation process corresponds to a density dependent family

\[
\lambda_{n}^{(N)}(x) = \sum_{i=1}^{K} \beta_{i,n}^{(N)}(x) x_i, \quad \lambda_{-e_i}^{(N)} = \delta^{(N)}(x) x_i, \tag{2.48}
\]
for which we continue to assume Assumption 2.1. We replace Assumption 2.2 by the stronger

\textit{Assumption 2.3.} As in classical population genetics, we will assume that the rate of mutation is \( O\left(\frac{1}{N}\right) \). In our context, this is equivalent to the existence a family of functions

\[
\beta_{i,n}(x) = \begin{cases} 
\beta_{i,n}(x) & \text{if } n = ne_i \\
0 & \text{otherwise}
\end{cases}
\]  

such that for all compact sets \( \mathcal{K} \subset \mathbb{R}_+^K \),

\[
\lim_{N \to \infty} \sum_{n \in \mathbb{Z}^K} \|n\|_2 \sup_{x \in \mathcal{K}} \left| \beta_{i,n}^{(N)}(x) - \beta_{i,n}(x) \right| = 0
\]

and

\[
\lim_{N \to \infty} N \sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \sup_{x \in \mathcal{K}} \left| \beta_{i,n}^{(N)}(x) - \beta_{i,n}(x) \right| < \infty.
\]

Thus, the rates at which an individual of type \( i \) produces one or more offspring of some type \( j \neq i \), \( \beta_{i,n}^{(N)} : n \neq ne_i \), are always bounded above by some constant multiple of \( \frac{1}{N} \) on any compact set.

We also assume that there exists \( \delta_i(x) \) such that

\[
\lim_{N \to \infty} \sup_{x \in \mathcal{K}} \left| \delta_i^{(N)}(x) - \delta_i(x) \right| = 0 \quad \text{and} \quad \lim_{N \to \infty} N \sup_{x \in \mathcal{K}} \left| \delta_i^{(N)}(x) - \delta_i(x) \right| < \infty.
\]

\textit{Remark 2.6.} While Assumption 2.3 is made for technical reasons, the conditions imposed are eminently plausible from a biological perspective, as they simply require that the mean and variance in the number of offspring produced in any single reproductive event are both finite. Both are readily satisfied by assuming some fixed maximum on the total number of offspring per reproduction event that is independent of \( N \).
Under Assumptions 2.1 and 2.3, the functional Law of Large Numbers, Proposition 2.1 holds. Setting
\[
\bar{\beta}_i(x) := \sum_{i=1}^{\infty} n_i \beta_{in}(x) \quad (2.53)
\]
and
\[
f_i(x) := \bar{\beta}_i(x) - \delta_i(x), \quad (2.54)
\]
so \( f_i \) is the average per capita net reproductive rate, we see that the limiting process \( Y(t) \) satisfies
\[
\dot{Y}_i = f_i(Y)Y, \quad (2.55)
\]
i.e., the corresponding dynamical system, \( \dot{Y} = F(Y) \) is of Kolmogorov type.

**Definition 2.2.** We will say that the birth-death-mutation process is *density-dependent* if this dynamical system corresponding to \( F \) is dissipative, and *competitive* if the dynamical system is competitive in Kolmogorov’s sense (Definition 1.5).

In the next two chapters, we will repeatedly revisit the following example of a density-dependent birth-death-mutation process, which we call the *Generalized Moran Model* [148, 149, 150, 151]. The Generalized Moran model is a hybrid of the Lotka-Volterra-Gause and Moran models. It was given a heuristic analysis in those papers, and is the inspiration and motivation for the more general and rigorous results derived here. It provides a concrete instance of a density-dependent birth-death-mutation process which is simultaneously rich enough to provide some biological insights, simple enough to be analytically tractable (at least when \( K = 2 \)) and open to intuitive interpretation.

**Example 2.1** (Generalized Moran Model). Consider the density-dependent birth-death-
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mutation process with intensities

$$\beta_{i,n}^{(N)}(x) = \begin{cases} 
(1 - \sum_{j=1}^{K} \frac{\theta_{ij}}{N}) \beta_i & \text{if } n = e_i \\
\frac{\theta_{ij}}{N} \beta_i & \text{if } n = e_j \\
0 & \text{otherwise}
\end{cases}$$

(2.56)
corresponding to reproduction by binary fission, and death rate

$$\delta_i^{(N)}(x) = \delta_i \left(1 + \sum_{j=1}^{K} x_j\right).$$

(2.57)
for $\beta_i, \delta_i > 0$.

The corresponding functional Law of Large Numbers is of Lotka-Volterra-Gause type and competitive:

$$f_i(x) = (\beta_i - \delta_i) - \sum_{j=1}^{K} \delta_i x_j.$$  

(2.58)

Remark 2.7. Although our primary interpretation of the Generalized Moran model will be interspecies competition in an environment with a carrying capacity proportional to $N$, an analogous model has been used to analyze the dynamics of an epidemic passing through a population of fixed size $N$, in which recovery does not entail immunity, the SIS (Susceptible-Infective-Susceptible) model (see *e.g.*, [5, 4] and references therein). We will not discuss it extensively, but our results for the Generalized Moran model have an alternative interpretation regarding evolution in multi-strain epidemics. However, see Chapter 5 for analysis and discussion of the closely related stochastic SIR (Susceptible-Infective-Recovered) model.

### 2.2.1 Individual Fecundity

We conclude this section with a few simple results regarding individual fecundity, which will be useful in subsequent chapters to compare our results to classical population genetic
models. In particular, we will be interested in individual lifetime expected reproduction, or fitness, and the variance in total individual fecundity.

Let \( L_i^{(N)}(0, X^{(N)}(0)) \) be the life span of an individual of type \( i \), born at time \( t = 0 \) into a population in state \( X^{(N)}(0) \), so

\[
P\{L_i^{(N)}(0, X^{(N)}(0)) \geq t\} = E_{X^{(N)}(0)} \left[ e^{-\int_0^t \delta_i^{(N)}(X^{(N)}(s-)) \, ds} \right]
\] (2.59)

and let

\[
O_i^{(N)}(t) = \sum_{n \in \mathbb{N}_0^K} \|n\|_1 P_n \left( \int_0^{t \wedge L_i^{(N)}(0, X^{(N)}(0))} \beta_i^{(N)}(X^{(N)}(s-)) \, ds \right)
\] (2.60)

be the total reproductive output of that individual up to time \( t \).

We begin with a simple lemma:

**Lemma 2.1.** Let \((S, d)\) be a Polish space and let \( C(S) \) be the space of continuous real-valued functions on \( S \), endowed with the compact uniform topology. Suppose that \( F^{(N)} \overset{D}{\to} F \) in \( C(S) \) and that \( X^{(N)} \overset{D}{\to} X \) in \( D_S[0, \infty) \). Then \( F^{(N)} \circ X^{(N)} \overset{D}{\to} F \circ X \) in \( D_\mathbb{R}[0, \infty) \).

**Proof.** Define \( \Psi : C(S) \times D_S[0, \infty) \to D_\mathbb{R}[0, \infty) \) by \( \Psi(f, x) = f \circ x \). By the continuous mapping theorem [17], it suffices to show that \( \Psi \) is continuous at all pairs \((f, x)\). To that end, suppose that \( f_n \to f \) uniformly on compact sets, and that \( x_n \to x \) in the Skorokhod topology. Thus, there exist \( \lambda_n \to id \) such that \( \text{ess sup}_{t \geq 0} |\ln \lambda_n(t)| < \infty \) and

\[
\lim_{n \to \infty} \sup_{t \leq T} d(x_n(t), (x \circ \lambda_n)(t)) = 0
\] (2.61)

for all fixed \( T > 0 \). Moreover, \( \{x_n\} \subseteq D_S[0, \infty) \) is compact, so there exist a compact set
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\[ \Gamma_T \subseteq S \] such that \( x_n(t), (x \circ \lambda_n)(t) \in \Gamma_T \) for all \( t \leq T \wedge \sup_n \lambda_n(T) \). Then

\[
\sup_{t \leq T} |(f_n \circ x_n)(t) - (f \circ x)(\lambda_n(t))| \\
\leq \sup_{t \leq T} |f_n(x_n(t)) - f(x_n(t))| + \sup_{t \leq T} |f(x_n(t)) - f((x \circ \lambda_n)(t))|. \tag{2.62}
\]

Now, \( f_n \to f \) uniformly on \( \Gamma_T \), so the former quantity vanishes as \( n \to \infty \), whilst \( f \), as the limit of a sequence of functions converging uniformly on \( \Gamma_T \), is uniformly continuous on \( \Gamma_T \), and thus the latter term above vanishes as \( n \to \infty \) also. Thus \( f_n \circ x_n \to f \circ x \) in \( \mathbb{D}_\mathbb{R}[0, \infty) \), and the result follows. \( \square \)

In particular, \( \beta_{i,n}^{(N)}(x) \) and \( \delta_i^{(N)}(x) \) converge in the compact uniform topology, so

\[
\beta_{i,n}^{(N)}(Y^{(N)}) \xrightarrow{\mathcal{D}} \begin{cases} 
\beta_{i,n}(Y) & \text{if } n = ne_i, \\
0 & \text{otherwise}
\end{cases}, \tag{2.63}
\]

and \( \delta_i^{(N)}(Y^{(N)}) \xrightarrow{\mathcal{D}} \delta_i(Y) \) as \( N \to \infty \). Moreover, \( F : \mathbb{D}_\mathbb{R}[0, \infty) \to \mathbb{D}_\mathbb{R}[0, \infty) \) given by

\[
F(x)(t) = \int_0^t x_n(s-) \, ds
\]

is continuous, so

\[
\int_0^t \delta_i^{(N)}(Y^{(N)}(s-)) \, ds \xrightarrow{\mathcal{D}} \int_0^t \delta_i(Y(s-)) \, ds \tag{2.65}
\]

etc. We thus have

**Proposition 2.2.** Suppose \( \frac{1}{N} X^{(N)}(0) \to x \). Then

(i) \( L_{i,X^{(N)}(0)}^{(N)} \xrightarrow{\mathcal{D}} L_{i,x} \), where

\[
P \{ L_{i,x} \geq t \} = e^{-\int_0^t \delta_i(\psi_s, x) \, ds}. \tag{2.66}
\]
(ii) $O_{i,X(N)(0)}^{(N)}(t) \overset{P}{\rightarrow} O_{i,x}(t) = \sum_{n=1}^{\infty} n P_n \left( \int_0^{t \wedge L_{i,x}} \beta_{i,n}(\psi_s x) \, ds \right)$, and

(iii) $O_{i,X(N)(0)}^{(N)}(L_{i,X(N)(0)}^{(N)}) \overset{P}{\rightarrow} O_{i,x}(L_{i,x})$.

**Proof.** The first follows immediately from the Portmanteau theorem, since, by the definition of weak convergence,

$$
\mathbb{E}_{X(0)}^{(N)} \left[ e^{-\int_0^t \delta_i^{(N)}(Y(s)) \, ds} \right] \rightarrow \mathbb{E}_x \left[ e^{-\int_0^t \delta_i(Y(s)) \, ds} \right].
$$

(2.67)

The latter two follow from standard results on random time change [50]. □

Computing the expectation and variance of $O_{i,x}(L_{i,x})$ using the Law of Total Expectation and the Law of Total Variance, e.g.,

$$
\mathbb{E} \left[ \sum_{n=0}^{\infty} n P_n \left( \int_0^{L_{i,x}} \beta_{i,n}(\psi_s x) \, ds \right) \right] = \mathbb{E} \left[ \sum_{n=0}^{\infty} n P_n \left( \int_0^{L_{i,x}} \beta_{i,n}(\psi_s x) \, ds \right) \right]
$$

(2.68)

$$
= \mathbb{E} \left[ \mathbb{E} \left[ \sum_{n=0}^{\infty} n P_n \left( \int_0^{L_{i,x}} \beta_{i,n}(\psi_s x) \, ds \right) \bigg| L_{i,x} \right] \right]
$$

(2.69)

$$
= \mathbb{E} \left[ \int_0^{L_{i,x}} \bar{\beta}_i(\psi_s x) \, ds \right]
$$

(2.70)

$$
= \int_0^{\infty} e^{-\int_0^t \delta_i(\psi_s x) \, ds} \bar{\beta}_i(\psi_t x) \, dt,
$$

(2.71)

we thus have the following asymptotic results on expected lifetime reproductive fitness and individual fecundity variance:

**Corollary 2.1.** (i) $\lim_{N \to \infty} \mathbb{E} \left[ O_{i,X(0)}^{(N)}(L_{i,X(N)(0)}^{(N)}) \right] = \int_0^{\infty} e^{-\int_0^t \delta_i(\psi_s x) \, ds} \bar{\beta}_i(\psi_t x) \, dt$, and

$$
\lim_{N \to \infty} \text{Var} \left( O_{i,X(0)}^{(N)}(L_{i,X(N)(0)}^{(N)}) \right) = \int_0^{\infty} e^{-\int_0^t \delta_i(\psi_s x) \, ds} \bar{\beta}_i(\psi_t x) \, dt
$$

$$
+ 2 \int_0^{\infty} e^{-\int_0^t \delta_i(\psi_s x) \, ds} \bar{\beta}_i(\psi_t x) \left( \int_0^t \bar{\beta}_i(\psi_s x) \, ds \right) \, dt - \left( \int_0^{\infty} e^{-\int_0^t \delta_i(\psi_s x) \, ds} \bar{\beta}_i(\psi_t x) \, dt \right)^2.
$$

(2.72)
(ii) In particular, if \( x = x^* \) is a rest point for \( F \), then

\[
\lim_{N \to \infty} \mathbb{E} \left[ O_{i,x}^{(N)}(I_{i,x}^{(N)}(0)) \right] = \frac{\bar{\beta}_i(x^*)}{\delta_i(x^*)} = 1 
\]

and

\[
\lim_{N \to \infty} \text{Var} \left( O_{i,x}^{(N)}(I_{i,x}^{(N)}(0)) \right) = \frac{\hat{\beta}_1(x^*)}{\delta_1(x^*)} + \left( \frac{\hat{\beta}_1(x^*)}{\delta_1(x^*)} \right)^2 = \frac{\hat{\beta}_1(x^*)}{\beta_1(x^*)} + 1 
\]

### 2.3 Strong and Weak Selection

In light of Smale’s construction (Example 1.1), if there are three or more species, essentially any dynamics can arise as the Law of Large Numbers for a density-dependent population process, so attempting to obtain a complete understanding of such processes is a fool’s errand. Nonetheless, it is possible to identify special cases, generalizing the weak and strong selection regimes of classical population genetics, in which something can be said.

**Definition 2.3.** A competitive density-dependent birth-death-mutation process is in the **strong selection** regime if the dynamical system arising as the Law of Large Numbers for the process has a unique globally attracting axial fixed point. It is in the **weak selection** regime if the \( \omega \)-limit set for the Law of Large Numbers is an attracting embedded codimension one submanifold, \( C \) of \( \mathbb{R}^K_+ \).

**Example 2.2.** For the Generalized Moran model, Example 2.1, type 1 is strongly selected if

\[
f \frac{\beta_i}{\delta_i} > \frac{\beta_j}{\delta_j} \text{ for all } j > 1,
\]

in which case \( x^{*1} = \left( \frac{\beta_i}{\delta_i} - 1 \right) e_1 \) is the globally asymptotically stable axial fixed point. Weak selection corresponds to case when \( \frac{\beta_i}{\delta_i} = \frac{\beta_j}{\delta_j} \) for all \( i, j \), in which case every point on

\[
C = \left\{ x \in \mathbb{R}_+^K : \sum_{i=1}^K x_i = 1 \right\}
\]

(2.75)
is a fixed point for the Law of Large Numbers (2.58), corresponding to coexistence of all types. Figure 2.1 shows deterministic flows and sample paths for the weakly selected Generalized Moran model.

Conditions for global stability in the strong and weak selection regimes for the Generalized Moran model follow from Theorem 2.1 and Proposition 2.3 below, respectively.

The strong selection corresponds to the case in which one type (without loss of generality, type 1) will fix under the deterministic dynamics given by the Law of Large numbers, whereas the weak selection case corresponds to deterministic coexistence. In the former case, the problem of determining fixation probabilities and times is thus reduced to determining the probability that, starting from small numbers (i.e., $O(1)$), the number of individuals of type 1 will reach $\varepsilon N$ for some $\varepsilon > 0$ prior to extinction; once the number of type 1 individuals is $O(N)$, the dynamics are essentially deterministic, and fixation is guaranteed. In the weak selection regime, assuming that the population does not vanish at small numbers due to demographic stochasticity, there is an approximately deterministic transient phase, at the end of which all species will be present (deterministic coexistence). After this, there is a much longer period, during which stochasticity in births and deaths causes the densities of each type to vary. On this longer time-scale, the dynamics are asymptotically given by a diffusion on the set of deterministic equilibria.

Given a general process with corresponding Kolmogorov equations $\dot{Y}_i = f_i(Y)Y_i$, there is no general criterion on the $f_i$ that guarantee that one is in the strong or weak selection regimes. Even when the Law of Large Numbers is of Lotka-Volterra-Gause type, finding necessary and sufficient conditions for the existence of a unique globally attracting fixed point remains an open problem [187, 188]. For the strong selection case, however, we have the following sufficient (but not necessary and sufficient, see [187]) conditions:

**Theorem 2.1** (Zeeman [188]). Consider a community of $K$ mutually competing species
Figure 2.1: Sample paths and flows of the Law of Large Numbers for the Generalized Moran model, Example 2.1, under weak selection. Flow lines were generated using (2.58) for parameter values $\beta_1 = 2$, $\delta_1 = 1$, $\beta_2 = 1$, and $\delta_2 = 0.5$. The dashed line gives the $C = \{x_1 + x_2 = 0.5\}$, and the dotted line, $x_1 + x_2 = 1$. Two simulations of the birth-death-mutation process are also shown in red for the same parameter values and $N = 1000$. The simulations had initial conditions $X_1^{(N)}(0) = 10$ and $x_2 = 50$. One simulation shows type 1 fixing, and the other type 2. Both trajectories have the same qualitative behaviour, approximately following the flows of the Law of Large Numbers prior to reaching a small neighbourhood of $C$, and subsequently evolving as a diffusion confined to a neighbourhood about $C$ (reproduced from [149], originally prepared by Christopher Quince)

modelled by the autonomous Lotka-Volterra-Gause system

$$\dot{Y}_i = \left( b_i - \sum_{j=1}^{K} a_{ij}Y_j \right) Y_i,$$

(2.76)

If, up to permutation of the indices, the system satisfies

$$\frac{b_j}{a_{jj}} < \frac{b_i}{a_{ij}} \text{ for all } i < j$$

(2.77)
and
\[ \frac{b_j}{a_{jj}} > \frac{b_i}{a_{ij}} \text{ for all } i > j \] (2.78)

then the axial fixed point \( (b_{11}, 0, \ldots, 0) \) is globally attracting on \( \mathbb{R}_+^K \).

A global stability result is easily obtained in the weak selection regime:

**Proposition 2.3.** If \( \frac{b_j}{a_{jj}} = \frac{b_i}{a_{ij}} \) for all \( i, j \leq K \), then

\[ C = \left\{ x \in \mathbb{R}_+^K : \sum_{j=1}^{K} \frac{a_{jj}}{b_j} x_j = 1 \right\} \] (2.79)

is asymptotically stable in \( \mathbb{R}_+^K - \{0\} \).

**Proof.** Clearly, every point of \( C \) is a fixed point. Let

\[ V(x) = \frac{1}{2} \left( 1 - \sum_{j=1}^{K} \frac{a_{jj}}{b_j} x_j \right)^2. \] (2.80)

Then

\[ \dot{V}(x) = \sum_{i=1}^{K} \frac{\partial V}{\partial x_i} \left( b_i - \sum_{j=1}^{K} a_{ij} x_j \right) x_i = - \left( 1 - \sum_{j=1}^{K} \frac{a_{jj}}{b_j} x_j \right)^2 \left( \sum_{i=1}^{K} a_{ii} x_i \right) < 0 \] (2.81)

on \( \mathbb{R}_+^K - (\{0\} \cup C) \). The result follows by Lyapunov’s stability theorem.

\[ \square \]

### 2.4 Summary

The intent of this chapter is to define the birth-death-processes that are our object of study and to identify the strategy we will use in analyzing them. We begin (Section 2.1) with a notion of density dependent population processes that we adapt from Kurtz [116, 117, 118, 119], for which we can prove a functional Law of Large Numbers, Proposition 2.1.
While the result is only a slight generalization of the Kurtz’s result [116], it is crucial to our efforts in three regards:

(i) By associating a dynamical system to our stochastic processes, we are able to translate crucial notions from the deterministic theory to the stochastic context, in particular, dissipativity, which for us is an appropriately general formalization of the physical constraints that prevent populations from growing indefinitely, and the very general definition of competition given by Kolmogorov.

(ii) The domain of applicability of our deterministic approximation (initial numbers of order $O(N)$ and times of order $O(\ln N)$) indicate which limiting regimes must be analyzed to understand the dynamics of the underlying birth-death-mutation process. This indicates our overall strategy: we know that once the population reaches $\varepsilon N$ for any $\varepsilon > 0$ independent of $N$, it can effectively be approximated by a deterministic process, for a time span long enough that the approximation only fails once the process is in a $o(1)$ neighbourhood of the attractor of the deterministic dynamics. We thus need to determine the probability the population reaches $\varepsilon N$ prior to “fizzling out”, and to analyze the stochastic dynamics in the vicinity of the attractor if the deterministic dynamics.

(iii) The bifurcation structure of the deterministic limit indicates the different qualitative dynamics possible in the stochastic system. In particular, we identify two regimes of asymptotic behaviour that generalize the notions of weak and strong selection in classical population genetics (Section 2.3). For our purposes, the former corresponds to deterministic fixation of one type, whereas the latter corresponds to deterministic coexistence.

The next two chapters will implement this strategy. Chapter 2 uses branching process approximations to the address the problem of escaping extinction at small numbers and
applies these results in the strong selection regime. Chapter 3 considers the weak selection regime using diffusion approximations, analogously to classical population genetics.
Chapter 3

Invasion Dynamics and Strong Selection

In this chapter, we consider the case when a small initial number of individuals of (without loss of generality) type 1 attempt to invade a resident population of types 2, \ldots, K. For present purposes, type 1 is said to successfully invade, if starting from $O(1)$ individuals (usually taken to be a single individual, as our primary interest is the fixation of a novel allele), the number of individuals of type $i$ is eventually greater than $\varepsilon N$ for some $\varepsilon > 0$, at which point the dynamics of that type are effectively given by the Law of Large Numbers of the previous chapter. \textit{i.e.}, throughout this chapter,

$$
\lim_{N \to \infty} \frac{1}{N} X_i^{(N)}(0) = \begin{cases} 
0 & \text{if } i = 1 \\
X_i & \text{if } i = 2, \ldots, K.
\end{cases} \quad (3.1)
$$

As we saw previously in Proposition 2.1, under these assumptions, the rescaled process

$$
Y^{(N)}(t) = \frac{1}{N} X^{(N)}(t) \quad (3.2)
$$

converges almost surely to the deterministic flow $\psi_t x$, $x = (0, x_2, \ldots, x_K)$, for the vector
Chapter 3. Invasion Dynamics and Strong Selection

field \( F \),

\[
F_i(x) = f_i(x)x_i = (\beta_i(x) - \delta_i(x))x_i.
\]

In particular, writing \( \psi_t x = (\psi^1_t x, \ldots, \psi^K_t x) \), we have \( \psi^1_t x \equiv 0 \) for all \( t > 0 \).

In this chapter, we will limit our focus to examples without mutation, so

\[
\beta_{i,n}^{(N)}(x) \equiv 0
\]  

(3.3)

for all \( n \neq ne_i \). Under this assumption, when \( X_1^{(N)}(0) \ll N \), we can approximate \( X_i^{(N)}(t) \) by a time-inhomogeneous Markov branching process \( Z_1(t) \) (i.e., a Markov branching process in a *varying environment*) with transition rates

\[
\beta_{1,n}(t) = \beta_{i,n}(0, \psi^2_t x, \ldots, \psi^K_t x)
\]  

(3.4)

and

\[
\delta_1(t) = \delta_i(0, \psi^2_t x, \ldots, \psi^K_t x),
\]  

(3.5)

in a sense that we will make precise via a coupling argument in Section 3.2.1. When mutation is allowed, coupling with a branching process with immigration is still possible (see [34, 33]), but will not be discussed here.

Armed with these results, we will obtain explicit expressions for the probability that a single individual with an advantageous mutation can *invade* – that is, exceed \( \varepsilon N \) individuals prior to extinction – a resident population that is already abundant (i.e., the number of individuals of all types \( j > 1 \) is \( \mathcal{O}(N) \)). The resident species enter into our expressions only through the deterministic approximation obtained as the functional Law of Large Numbers, Proposition 2.1, which allows us to use insights previously obtained from deterministic studies in theoretical population ecology.

As we saw in the previous chapter, once the number of individuals of type 1 exceed \( \varepsilon N \), their subsequent dynamics are essentially deterministic. In particular, if type 1 is
strongly selected, then a successful invasion implies fixation with probability approaching 1 as \( N \to \infty \). We will use this to obtain expressions for the the fixation probability and the expected fixation time in the strong selection regime. We find that when the resident population is at a stable fixed point, we recover results analogous to Haldane’s 2s approximation \([71]\). Unlike classical results, however, we do not require the resident “wild-type” population to be at equilibrium. In particular, our expressions provide an excellent tool for investigating the ultimate fate of mutants arising in a population that has undergone a recent bottleneck, in which case we find that the life-history strategy of an invading mutant influences its probability of fixation.

First, however, we develop some results regarding branching processes in a varying environment that will be useful in the sequel. These are simple adaptations of results for the Bienaymé–Galton–Watson in varying environments in \([87, 29, 36]\). We then prove the coupling lemma, which allows us to apply the results obtained for branching processes to find the probability that a novel mutant is able to invade an established “wild-type” population in a birth-death-mutation process, and thus the fixation probability of a strongly selected mutant. We then specialize our results to the case when the established population is approaching a globally stable fixed point in the hyperplane \( x_1 = 0 \), in which case we obtain an asymptotic for the time to fixation of a strongly selected mutant.

### 3.1 Continuous Time Markov Branching Process in a Varying Environment

In this section, we will assume \( Z(t) \) is a non-autonomous birth-and-death process, with time varying transition intensities

\[
q_{Z,Z+n}(t) = \beta_n(t) \quad \text{and} \quad q_{Z,Z-1}(t) = \delta(t). \tag{3.6}
\]
so the generator of the process \( Z(t) \) is
\[
(\mathcal{G}_t f)(z) = \sum_{n=1}^{\infty} \beta_n(t) z (f(z + n) - f(z)) + \delta(t) z (f(z - 1) - f(z)) \tag{3.7}
\]
for functions \( f : \mathbb{N}_0 \to \mathbb{R} \).

We begin by recalling the following sufficient condition for non-explosion, which will be assumed throughout:

**Condition 3.1** (Non-explosion Condition, [74]). Assume that
\[
\bar{\beta}(t) = \sum_{n=1}^{\infty} n \beta_n(t), \tag{3.8}
\]
converges uniformly in \( t \) on compact intervals. Then
\[
P \{ Z(t) < \infty \} = 1 \tag{3.9}
\]
for all \( t \), and there is a unique process \( Z(t) \) with generator \( \mathcal{G}_t \).

### 3.1.1 Moments of \( Z(t) \)

Taking \( f(z) = z^k \), we have
\[
(\mathcal{G}_t f)(z, x) = \sum_{n=1}^{\infty} \beta_n(t) z ((z + n)^k - z^k) + \delta(t) z ((z - 1)^k - z^k) \tag{3.10}
\]
\[
= \sum_{j=1}^{k} \binom{k}{j-1} \left( \sum_{n=1}^{\infty} n^{k-j+1} \beta_n(t) + (-1)^{k-j+1} \delta(t) \right) z^j. \tag{3.11}
\]

Thus, provided that the series
\[
\bar{\beta}^{(m)}(t) = \sum_{n=1}^{\infty} n^m \beta_n(t), \tag{3.12}
\]
converges uniformly for \( m = 1, \ldots, k \), we have

\[
\frac{d}{dt} \mathbb{E} \left[ Z(t)^k | Z(s) = z \right] = \sum_{j=1}^{k} \binom{k}{j-1} \left( \beta^{(j+1)}(t) + (-1)^{k-j+1} \delta(t) \right) \mathbb{E} \left[ Z(t)^j | Z(\tau) = z \right]
\]

\[
= k \left( \beta(t) - \delta(t) \right) \mathbb{E}_z [Z(t)^k] + \sum_{j=1}^{k-1} \binom{k}{j-1} \left( \beta^{(j+1)}(t) + (-1)^{k-j+1} \delta(t) \right) \mathbb{E} \left[ Z(t)^j | Z(\tau) = z \right]
\]

whence

\[
\mathbb{E} \left[ Z(t)^k | Z(s) = z \right] = e^{k \int_s^t \beta(u) - \delta(u) \, du} z^k + \int_s^t e^{-k \int_u^t \beta(u) - \delta(u) \, du} \sum_{j=1}^{k-1} \binom{k}{j-1} \left( \beta^{(j+1)}(\tau) + (-1)^{k-j+1} \delta(\tau) \right) \mathbb{E}_z [Z(\tau)^j | Z(\tau) = z] \, d\tau.
\]

(3.13)

In particular,

\[
\mathbb{E} \left[ Z(t) | Z(s) = z \right] = e^{\int_s^t \beta(u) - \delta(u) \, du} z,
\]

\[
\mathbb{E} \left[ Z(t)^2 | Z(s) = z \right] = e^{\int_s^t \beta(u) - \delta(u) \, du} \left( z^2 + \int_s^t e^{-2 \int_u^t \beta(u) - \delta(u) \, du} \left( \beta(\tau) + \delta(\tau) \right) \, d\tau \right),
\]

and

\[
\text{Var} \left( Z(t) | Z(s) = z \right) = \int_s^t e^{2 \int_u^t \beta(u) - \delta(u) \, du} \left( \dot{\beta}(\tau) + \delta(\tau) \right) \, d\tau
\]

where

\[
\dot{\beta}(t) = \sum_{n=0}^{\infty} n^2 \beta_n(t).
\]

(3.15)

In what follows, we adopt the notation

\[
m(s, t) := \mathbb{E} [Z(t) | Z(s) = 1] = e^{\int_s^t \beta(u) - \delta(u) \, du}
\]

(3.16)
and \( m(t) := m(0, t) \).

### 3.1.2 The Probability Generating Function and Extinction Probabilities

Let

\[
F_z(\xi, s, t) := \mathbb{E} \left[ \xi^{Z(t)} | Z(s) = z \right].
\]

(3.17)

Then, \( F_z = F_1^z \), and assuming Condition 3.1, \( F_1(\xi, s, t) \) is the unique solution to the backward equation

\[
\frac{\partial F_1}{\partial t} = -\mathcal{G}_t F_1
\]

with initial condition \( F_1(t, t-, t) = \xi^1 [74] \).

We begin with the appropriate generalization of the key lemma for the Bienaymé–Galton–Watson process from [77]:

\[
\int_s^t \tilde{\beta} (\tau) m(\tau, t) \, d\tau \leq \frac{m(s, t)}{1 - F_1(\xi, s, t)} - \frac{1}{1 - \xi} \leq \int_s^t m(\tau, t) \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) \, d\tau,
\]

(3.19)

with equality if and only if \( \tilde{\beta}(t) = \hat{\beta}(t) \), which occurs if and only if \( \beta_n(t) \equiv 0 \) for \( n > 1 \).

\[\text{footnote}{1}\text{We will use the notational shorthand}\]

\[f(t-) = \lim_{s \to t-} f(s)\]

throughout.
Proof. From 3.18, we have

\[
\frac{\partial F_1}{\partial \tau} = - \left[ \sum_{n=1}^{\infty} \beta_n(\tau) \left( F_1(\xi, \tau, t)^{n+1} - F_1(\xi, \tau, t) \right) + \delta(\tau) (1 - F_1(\xi, \tau, t)) \right]
\]

\[
= - (1 - F_1(\xi, \tau, t)) \left( \delta(\tau) - \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{m=1}^{n} F_1(\xi, \tau, t)^m \right)
\]

\[
= - (1 - F_1(\xi, \tau, t)) \left( \delta(\tau) - \bar{\beta}(\tau) - \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{m=1}^{n} (F_1(\xi, \tau, t)^m - 1) \right)
\]

\[
= - (1 - F_1(\xi, \tau, t)) \times \left( \delta(\tau) - \bar{\beta}(\tau) + (1 - F_1(\xi, \tau, t)) \left( \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) F_1(\xi, \tau, t)^k \right) \right).
\]  

Thus,

\[
\frac{\partial}{\partial \tau} \frac{m(\tau, t)}{1 - F_1(\xi, \tau, t)} = \frac{(\delta(\tau) - \bar{\beta}(\tau) m(\tau, t))}{1 - F_1(\xi, \tau, t)} + \frac{m(\tau, t) \frac{\partial F_1}{\partial \tau}}{1 - F_1(\xi, \tau, t)}
\]

\[
= - m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) F_1(\xi, \tau, t)^k;
\]  

and integrating, recalling \(m(t, t) = 1\) and \(F_1(\xi, t, t) = \xi\), we have

\[
\frac{1}{1 - \xi} - \frac{m(s, t)}{1 - F_1(\xi, s, t)} = - \int_s^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) F_1(\xi, \tau, t)^k \, d\tau.
\]  

(3.22)

Since \(0 \leq F_1(\xi, \tau, t) \leq 1\), we have

\[
n \leq \sum_{k=0}^{n-1} (n - k) F_1(\xi, \tau, t)^k \leq \sum_{k=0}^{n-1} (n - k) = \frac{n(n + 1)}{2}.
\]  

(3.23)

and thus

\[
\int_0^t m(\tau, t) \sum_{n=1}^{\infty} n \beta_n(\tau) \, d\tau \leq \frac{m(0, t)}{1 - F_1(\xi, 0, t)} - \frac{1}{1 - \xi}
\]

\[
\leq \int_0^t m(\tau, t) \sum_{n=1}^{\infty} \frac{n(n + 1)}{2} \beta_n(\tau) \, d\tau.
\]  

(3.24)
The result follows. \hfill \square

We then have

**Proposition 3.1 (Extinction Probabilities).** Let

\[ q(s, t) := \mathbb{P} \{ Z(t) = 0 | Z(s) = 1 \}. \] (3.25)

Then,

\[
\frac{\int_s^t e^{-\int_s^\tau \beta(u) - \delta(u) du} \delta(\tau) d\tau}{1 + \int_s^t e^{-\int_s^\tau \beta(u) - \delta(u) du} \delta(\tau) d\tau} \leq q(s, t) \\
\leq \frac{\int_s^t e^{-\int_s^\tau \beta(u) - \delta(u) du} \left( \delta(\tau) + \frac{\hat{\beta}(\tau) - \bar{\beta}(\tau)}{2} \right) d\tau}{1 + \int_s^t e^{-\int_s^\tau \beta(u) - \delta(u) du} \left( \delta(\tau) + \frac{\hat{\beta}(\tau) - \bar{\beta}(\tau)}{2} \right) d\tau}. \] (3.26)

**Proof.** This follows immediately from the lemma, as \( q(s, t) = F(0, s, t) \). \hfill \square

As remarked previously, when \( \beta_1(t) = \beta(t) \) and \( \beta_n(t) \equiv 0 \) for \( n > 1 \), we have \( \bar{\beta}(t) = \beta(t) \) and

\[
\frac{m(t)}{1 - F(\xi, t)} - \frac{1}{1 - \xi} = \int_0^t e^{\int_0^s \beta(u) - \delta(u) du} \beta(s) ds,
\] (3.27)

from which the exact form of the probability generating function may be obtained:

**Proposition 3.2.** Suppose \( \beta_1(t) = \beta(t) \) and \( \beta_n(t) \equiv 0 \) for \( n > 1 \). Then, \( Z(t) \) has probability generating function

\[ F(\xi, t) = 1 - \frac{m(t)}{1 - \xi + \int_0^t e^{\int_0^s \beta(u) - \delta(u) du} \bar{\beta}(s) ds}. \] (3.28)

In particular,

\[ q(t) = \frac{\int_0^t e^{-\int_0^s \beta(u) - \delta(u) du} \delta(s) ds}{1 + \int_0^t e^{-\int_0^s \beta(u) - \delta(u) du} \delta(s) ds}, \] (3.29)

and, setting

\[ \chi_t := \frac{e^{\int_0^t \delta(u) - \beta(u) du} \delta(s) ds}{1 + \int_0^t e^{\int_0^s \delta(u) - \beta(u) du} \delta(s) ds}, \] (3.30)
and \( P_n(t) := \mathbb{P}\{Z(t) = n\} \), we have

\[ P_0(t) = q(t) \text{ and } P_n(t) = (1 - P_0(t))(1 - \chi_t)\chi_t^{n-1}. \]  

Moreover, taking \( t \to \infty \), we have

**Corollary 3.1.** The probability of ultimate extinction, \( q(\infty) \) is

\[
\frac{\int_0^\infty e^{\int_0^s \delta(u) - \beta(u) \, du} \delta(s) \, ds}{1 + \int_0^\infty e^{\int_0^s \delta(u) - \beta(u) \, du} \delta(s) \, ds},
\]

which is equal to 1 if and only if the integral \( I := \int_0^\infty e^{\int_0^s \delta(u) - \beta(u) \, du} \delta(s) \, ds \) diverges.

**Remark 3.1.** Proposition 3.2 and Corollary 3.1 originally appeared in [97], with a different proof based upon the forward equation.

### 3.1.3 Criticality for the Markov Branching Process in Varying Environments

Unlike the time-inhomogeneous case, there doesn’t appear to be an equally tidy number like the Malthusian parameter to characterize of the asymptotic behaviour of processes in varying environments. Proposition 3.1 gives us a necessary condition for the process started from 1 individual at time \( s \) to persist indefinitely, namely that

\[
\int_s^\infty e^{-\int_s^\tau \beta(u) - \delta(u) \, du} \bar{\beta}(\tau) \, d\tau < \infty
\]

and a sufficient condition, as well, that

\[
\int_s^\infty e^{-\int_s^\tau \beta(u) - \delta(u) \, du} \left( \frac{\hat{\beta}(\tau) + \bar{\beta}(\tau)}{2} \right) \, d\tau < \infty,
\]

but unfortunately not a necessary and sufficient condition (though, see Corollary 3.1). (3.33) holds whenever \( \delta \) is integrable, a case we will exclude, as otherwise, we could have
individuals that never perish. We will henceforth assume that

\[ \int_s^\infty \delta(\tau) \, d\tau \]  

(3.35)
diverges for all \( s \), and say that a process is supercritical if (3.33) holds, in which case \( m(s, t) \to \infty \) as \( t \to \infty \) for all fixed \( s \). The latter is unfortunately not a sufficient condition for supercriticality, as the following simple example indicates:

**Example 3.1.** Let \( \beta_1(t) = 1 + \frac{1}{(t+2)\ln(t+2)} \), \( \beta_n(t) \equiv 0 \) for \( n > 1 \), and \( \delta(t) = 1 \). Then, the corresponding birth and death process in a varying environment satisfies

(i) \( m(s, t) = \ln(t+2) - \ln(s+2) \to \infty \) as \( t \to \infty \) for all fixed \( s \), whereas

(ii) \( \int_s^t \frac{\delta(\tau)}{m(s, \tau)} \, d\tau = \int_s^t \frac{d\tau}{\ln(t+2) - \ln(s+2)} \), which diverges,

so the process goes extinct with probability one.

We subdivide those processes for which

\[ \int_s^\infty e^{-\int_0^t \bar{\beta}(u) - \delta(u) \, du} \bar{\beta}(\tau) \, d\tau \]  

diverges into critical and subcritical as

\[ 0 < \inf_{t \geq 0} m(t) \leq \sup_{t \geq 0} m(t) < \infty \]  

(3.36)

and \( m(s, t) \to 0 \) as \( t - s \to \infty \) respectively. In the next three section, we will develop analogues, where available to the limit theorems of Harris, Sevastyanov, Yaglom and Kolmogorov under appropriate second moment conditions.

### 3.1.4 Supercritical Processes

We next recall the standard result for the long-term behaviour of a branching process. Let

\[ W(t) := \frac{Z(t)}{m(t)}. \]  

(3.37)
$W(t)$ is a martingale with $\mathbb{E}[W(t)] = 1$. By Doob’s martingale convergence theorem,

$$W := \lim_{t \to \infty} W(t)$$  \hspace{1cm} (3.38)

events pointwise almost surely, and, provided

$$\mathbb{E} [W(t)^2 | Z(s) = 1] = 1 + \int_s^t e^{-\int_s^u \beta(u) - \delta(u) \, du} \left( \hat{\beta}(\tau) + \delta(\tau) \right) d\tau,$$  \hspace{1cm} (3.39)

is bounded for all $s, t$, $W(t) \to W$ in $L^2(\mathbb{P})$ as well. In particular, if $\sup_t \mathbb{E}[W(t)^2] < \infty$, we have $\mathbb{E}[W] = 1$. Presumably, the latter holds under weaker moment conditions than those imposed above, but we will not consider that question here, as a second moment condition is eminently plausible in the biological problems of interest here.

Proposition 3.3. Assume that

$$\inf_{s \geq 0} \int_s^\infty e^{-\int_s^u \sum_{n=1}^\infty \beta_n(u) + \delta(u) \, du} \delta(\tau) \, d\tau > p > 0$$  \hspace{1cm} (3.40)

i.e., the probability of an individual dying without offspring is bounded below. Then,

$$q(\infty) := \lim_{t \to \infty} q(t) = \mathbb{P} \{ W = 0 \}.$$  \hspace{1cm} (3.41)

We begin with a pair of simple lemmas

Lemma 3.2. Assume (3.40). Then,

$$\mathbb{P} \left\{ \lim_{t \to \infty} Z(t) = 0 \right\} + \mathbb{P} \left\{ \lim_{t \to \infty} Z(t) = +\infty \right\} = 1$$  \hspace{1cm} (3.42)

Proof. This is a simple consequence of Theorem 2 in [89], we need only show that for
any $M > 0$, there exists $\delta > 0$ such that
\[
\mathbb{P} \left\{ \lim_{t \to \infty} Z(t) = 0 \mid Z(s) < M \right\} > \delta
\]  
(3.43)

for all $s < t$. This follows immediately from our assumption, as
\[
\mathbb{P} \left\{ \lim_{t \to \infty} Z(t) = 0 \mid Z(s) < M \right\} > p^{Z(s)} > p^{[M]} > 0.
\]  
(3.44)

\[\square\]

Lemma 3.3. Assume (3.39). Then
\[
\mathbb{P} \{ W = 0 \mid Z(s) = 1 \} \leq \frac{\int_{s}^{\infty} e^{-2 \int_{s}^{\tau} \hat{\beta}(u) - \delta(u) \, du} \left( \hat{\beta}(\tau) + \delta(\tau) \right) d\tau}{1 + \int_{s}^{\infty} e^{-2 \int_{s}^{\tau} \hat{\beta}(u) - \delta(u) \, du} \left( \hat{\beta}(\tau) + \delta(\tau) \right) d\tau}
\]  
(3.45)

**Proof.** This is a simple consequence of the Cauchy–Bunyakovsky–Schwarz inequality:
\[
1 = \mathbb{E} \left[ W \mid Z(s) = 1 \right]^2 = \mathbb{E} \left[ 1_{W > 0} W \mid Z(s) = 1 \right]^2
\leq \mathbb{E} \left[ 1_{W > 0} \mid Z(s) = 1 \right] \mathbb{E} \left[ W^2 \mid Z(s) = 1 \right] = \mathbb{P} \{ W > 0 \mid Z(s) = 1 \} \mathbb{E} \left[ W^2 \mid Z(s) = 1 \right].
\]  
(3.46)

The result follows upon rearranging. \[\square\]

Proof of Proposition 3.3. We begin by observing that
\[
\{ Z(s) = 0 \} \subseteq \{ Z(t) = 0 \} \subseteq \{ W = 0 \}
\]  
(3.47)

for all $s \leq t$, so $q(t) = \mathbb{P} \{ Z(t) = 0 \}$ is increasing and bounded above i.e., $q(\infty)$ exists and $q(\infty) \leq \mathbb{P} \{ W = 0 \}$. 
For the other inequality, let \( w_t = \mathbb{P}\{W = 0|Z(t) = 1\} \) and let

\[
\bar{w} := \sup_{s \geq 0} \frac{\int_{s}^{\infty} e^{-2 \int_{s}^{\tau} \beta(u) - \delta(u) \, du} \left( \hat{\beta}(\tau) + \delta(\tau) \right) \, d\tau}{1 + \int_{s}^{\infty} e^{-2 \int_{s}^{\tau} \beta(u) - \delta(u) \, du} \left( \hat{\beta}(\tau) + \delta(\tau) \right) \, d\tau} < 1. \tag{3.48}
\]

Using Lemma 3.3, we have

\[
\mathbb{P}\{W = 0\} = \mathbb{E}[\mathbb{P}\{W = 0|Z(t)\}] = \mathbb{E}\left[w_t^{Z(t)}\right] \leq \mathbb{E}\left[\bar{w}^{Z(t)}\right]. \tag{3.49}
\]

Applying Lebesgue’s dominated convergence theorem, in light of Lemma 3.2, gives

\[
\lim_{t \to \infty} \mathbb{E}\left[\bar{w}^{Z(t)}\right] = \mathbb{E}\left[\mathbb{I}_{\{\lim_{t \to \infty} Z(t) = 0\}}\right] = q(\infty). \tag{3.50}
\]

We end this section by observing that when \( \beta_1(t) = \beta(t) \) and \( \beta_n(t) \equiv 0 \) for \( n > 1 \), we can explicitly characterize the process \( W \) in the supercritical case:

**Proposition 3.4.** Suppose \( I < \infty \). Then \( W \) has characteristic function

\[
\mathbb{E}\left[e^{-\theta W}\right] = \frac{I}{1 + I} + \frac{I}{(1 + I)^2} \theta + \frac{1}{1 + I} \tag{3.51}
\]

i.e., \( \mathbb{P}\{W \leq x\} = \frac{I}{1 + I} + \frac{1}{1 + I} \left( 1 - e^{-\frac{\theta x}{1 + I}} \right) \) and \( \mathbb{P}\{W \leq x|W > 0\} = 1 - e^{-\frac{\theta x}{1 + I}} \).

**Proof.** Substitute \( \xi = e^{-\frac{\theta m(t)}{l(t)}} \) into (3.27) and take the limit as \( t \to \infty \). \( \square \)

### 3.1.5 Subcritical Processes

In the subcritical case, we have the following weaker analogue of the Yaglom-Kolmogorov theorem, which is an immediate consequence of Lemma 3.1:
Proposition 3.5. Assume that

$$\limsup_{t \to \infty} \int_0^t \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) m(\tau, t) d\tau < \infty. \quad (3.52)$$

Then

$$0 < \liminf_{t \to \infty} \frac{1 - q(t)}{m(t)} \leq \limsup_{t \to \infty} \frac{1 - q(t)}{m(t)} < 1. \quad (3.53)$$

In [87, 88], a stronger result is claimed for a Galton Watson process in varying environments, $Z_n$, under similar second moment conditions on the offspring distribution, namely that if $m_n = \mathbb{E}[Z_n]$, then

$$\lim_{n \to \infty} \frac{P\{Z_n > 0\}}{m_n}$$

exists and is constant. The equivalent assertion does not hold in our case, as the following example shows.

Example 3.2. Let $\beta_1(t) = 1 + \frac{1}{2} \sin t + \frac{1}{2} \cos t$, $\beta_n(t) \equiv 0$ for $n > 1$, and $\delta(t) = 1 + \beta(t)$.

Then, the corresponding birth and death process in a varying environment satisfies

(i) $\bar{\beta}(t) = \hat{\beta}(t) = \beta_1(t),$

(ii) $m(\tau, t) = e^{-(t-\tau)} \to 0$ as $t - \tau \to \infty,$

(iii) $\int_0^t e^{-\int_0^\tau \delta(u) - \beta(u) du} \delta(\tau) d\tau = \left(2(1 - e^{-t}) + \frac{1}{2} \sin t\right) e^t \to \infty$, so $q(t) \to 1,$

(iv) $\int_0^t \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) m(\tau, t) d\tau = \int_0^t \beta_1(\tau)m(\tau, t) d\tau = 1 - e^{-t} + \frac{1}{2} \sin t$, so

$$\limsup_{t \to \infty} \int_0^t \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) m(\tau, t) d\tau = \frac{3}{2}, \quad (3.55)$$

and

(v) $\frac{m(t)}{1 - q(t)} = 1 + \int_0^t \beta_1(\tau)m(\tau, t) d\tau.$
However, we then have

$$\frac{3}{2} = \liminf_{t \to \infty} \frac{m(t)}{1 - q(t)} < \limsup_{t \to \infty} \frac{m(t)}{1 - q(t)} = \frac{5}{2},$$

(3.56)

in contradiction to the continuous time analogue of the claim in [87, 88].

### 3.1.6 Critical Processes

For the sake of completeness, we conclude this discussion with an analogue of Yaglom’s theorem in the critical case. Unlike the previous results, we shall not have need of this in the sequel.

**Proposition 3.6.** Assume that

$$0 < \inf_{t \geq 0} m(t) \leq \sup_{t \geq 0} m(t) < \infty$$

(3.57)

$$\inf_{t \geq 0} \bar{\beta}(t) > 0,$$

(3.58)

and

$$\sum_{n=1}^{\infty} n^2 \beta_n(t) \text{ converges uniformly in } t.$$  

(3.59)

(3.60)

Then

(i) \( \mathbb{P} \{ Z(t) > 0 \} \sim \frac{1}{\int_0^t \left( \frac{2(\bar{\beta}(\tau))^{1/2}}{m(\tau, t)} \right) d\tau} \) as \( t \to \infty \).

(ii) \( \mathbb{P} \left\{ \frac{Z(t)}{m(t)I(t)} > u \left| Z(t) > 0 \right\} \to e^{-u} \text{ as } t \to \infty. \)

\(^2\) we use the notation \( f(t) \asymp g(t) \) if

$$\lim_{t \to \infty} \frac{f(t)}{g(t)} = 1.$$
Proof. For simplicity of notation, let
\[ I(t) = \int_0^t \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) m(\tau,t) d\tau. \] (3.61)

We begin by observing that assumptions (3.57) and (3.58) imply that
\[ \int_s^t \bar{\beta}(\tau)m(\tau,t) d\tau \] (3.62)
and thus
\[ \int_s^t \left( \frac{\bar{\beta}(\tau) + \hat{\beta}(\tau)}{2} \right) m(\tau,t) d\tau \] (3.63)
diverge as \(|t - s| \to \infty\). Recalling, Lemma 3.1,
\[ 0 \leq 1 - F_1(\xi,s,t) \leq \frac{1}{\int_s^t \bar{\beta}(\tau)m(\tau,t) d\tau} \] (3.64)
so that \(F_1(\xi,s,t) \to 1\) uniformly in \(\xi\) as \(|t - s| \to \infty\).

Similarly to the proof of Lemma 3.1, we have
\[ \frac{m(t)}{1 - F(\xi,t)} - \frac{1}{1 - \xi} = I(t) + \int_0^t m(\tau,t) \sum_{n=1}^\infty \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) (1 - F_1(\xi,\tau,t)^k) d\tau. \] (3.65)

Now,
\[ \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) (1 - F_1(\xi,\tau,t)^k) \leq \beta_n(\tau) \frac{n(n + 1)}{2}, \] (3.66)
so, by assumption (3.59), the former sum converges uniformly in \((\xi,\tau,t)\). In particular,
\[ \lim_{\xi \uparrow 1} \sum_{n=1}^\infty \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) (1 - F_1(\xi,\tau,t)^k) = 0, \] (3.67)
uniformly in \( \xi \) and \( \tau \) as \(|t - \tau| \to \infty\). Fix \( \varepsilon > 0 \) and choose \( T \) such that

\[
0 \leq \frac{1}{m(\tau)} \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) < \varepsilon
\]

for all \( t - \tau > T \). Then,

\[
\int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau
\]

\[
= \frac{\int_0^{t-T} m(\tau) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau}{I(t)}
\]

\[
= \frac{\int_t^{t-T} m(\tau) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau}{I(t)}
+ \frac{\int_{t-T}^{t} \frac{1}{m(\tau)} \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau}{I(t)}
\]

\[
\leq \frac{t - T}{t} \inf_{\tau \geq 0} \frac{m(\tau)}{\beta(\tau) + \bar{\beta}(\tau)} \frac{2 \sup_{\tau \geq 0} m(\tau)}{\varepsilon} + T \frac{\sup_{\tau \geq 0} (\beta(\tau) + \bar{\beta}(\tau))}{\inf_{\tau \geq 0} m(\tau)}
\]

i.e., \( \int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau \)

\[
\Rightarrow \text{can be made arbitrarily small as } t \to \infty,
\]

uniformly in \( \xi \).

In particular, we have

\[
\frac{1}{I(t)} \frac{1}{1 - F(0, t)} = 1 + \frac{\int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(0, \tau, t)^k \right) d\tau}{I(t)} \to 1
\]

as \( t \to \infty \), proving (i)

Next, rearrange (3.65) as

\[
\frac{m(t)}{1 - F(\xi, t)} = 1 + \frac{1}{m(t) I(t) (1 - \xi)} + \int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n - k) \left( 1 - F_1(\xi, \tau, t)^k \right) d\tau
\]

(3.71)
Now, recall from the previous theorem that

\[ E \left[ \xi Z(t) \big| Z(t) > 0 \right] = 1 - \frac{1 - F(\xi, t)}{1 - F(0, t)}, \quad (3.72) \]

so that

\[
E \left[ \frac{\theta Z(t)}{e^{m(t)I(t)}} \big| Z(t) > 0 \right] = 1 - \frac{1 - F \left( \frac{e^{\theta m(t)I(t)}}{1 - e^{\theta m(t)I(t)}}, t \right)}{1 - F(0, t)}
\]

\[
= 1 - \frac{1 + \frac{1}{m(t)I(t)} + \frac{1}{m(t)} \int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n-k) \left( 1 - F_1(e^{\theta m(t)I(t)}, \tau, t)^k \right) d\tau}{1 + \frac{1}{m(t)I(t)(1 - e^{\theta m(t)I(t)})} + \frac{1}{m(t)} \int_0^t m(\tau, t) \sum_{n=1}^{\infty} \beta_n(\tau) \sum_{k=0}^{n-1} (n-k) \left( 1 - F_1(e^{\theta m(t)I(t)}, \tau, t)^k \right) d\tau},
\]

\[
(3.73)
\]

which converges to \( 1 - \frac{1}{1+\theta} = \frac{1}{1+\theta} \) as \( t \to \infty \). (ii) follows.

\[ \square \]

**Remark 3.2.** We briefly note that the integral appearing in the asymptotic for the extinction probability in the critical case, i, is the same as that which appears in our expression for the extinction probability in general (Proposition 3.1). This suggests (but does not prove) that the upper bound in Proposition 3.1 is tight.

### 3.1.7 Time Asymptotics for Processes with a Malthusian Parameter

Throughout this section, we assume that \( \bar{\beta}(t) \) and \( \delta(t) \) converge to finite, non-zero limits \( \bar{\beta}(\infty) \) and \( \delta(\infty) \) as \( t \to \infty \), and moreover that \( \bar{\beta}(t) - \beta(\infty) \) and \( \delta(t) - \delta(\infty) \) are integrable. Set

\[ \alpha := \bar{\beta}(\infty) - \delta(\infty). \quad (3.74) \]
In a slight abuse of terminology, we refer to $\alpha$ as the *Malthusian parameter* for the process $Z(t)$. We then have

$$\phi = \lim_{t \to \infty} e^{-\alpha t} m(t) = e^{\int_0^t (\beta(u) - \beta(\infty)) - (\delta(u) - \delta(\infty)) \, du}$$

(3.75)

exists and is bounded. In particular, we have

$$\lim_{t \to \infty} \mathbb{E} [e^{-\alpha t} Z(t)] = \phi$$

(3.76)

and, if $M > 0$,

$$\lim_{t \to \infty} e^{-\alpha t} Z(t) = \phi W$$

(3.77)

in $L^2$.

This latter limit gives us the following asymptotic first hitting time result in the super-critical case, a simple adaptation of the result in [88] for the general (time-homogeneous) branching process:

**Proposition 3.7.** Suppose $\alpha > 0$ and let

$$\tau_M = \inf \{ t : Z(t) \geq M \}.$$  

(3.78)

Then, as $M \to \infty$,

$$\tau_M \sim \frac{1}{\alpha} (\ln M - \ln W - \ln \phi),$$

(3.79)

where we understand the right hand side to be $+\infty$ if $W = 0$.

**Proof.** By definition

$$Z(\tau_M - \delta) < M < Z(\tau_M)$$

(3.80)

for all $\delta > 0$. Thus

$$e^{-\alpha \delta} e^{-\alpha (\tau_M - \delta)} Z(\tau_M - \delta) < e^{-\alpha \tau_M} M \leq e^{-\alpha \tau_M} Z(\tau_M).$$

(3.81)
Now, $Z(t)$ is non-explosive, so $\tau_M \to \infty$ as $M \to \infty$. Thus, taking $M \to \infty$ and $\delta \to 0$, both the left and right sides converge to $\phi W$, and

$$\lim_{M \to \infty} e^{-\alpha \tau_M} M = \phi W.$$  \hfill (3.82)

The result follows by taking logarithms. \hfill \qed

With some additional conditions on the process $W$, which are adequate for the following examples, but somewhat unsatisfying (we would prefer to assert, rather than assume them, but at present, we are unable to prove that these conditions hold in general), we can give the following asymptotic for the expected first hitting time of $M > 0$:

**Corollary 3.2.** Suppose that $W$ has a density $w(x)$ that is continuous on $(0, \infty)$ and that there exists $\gamma < 1$ such that

$$\liminf_{x \to 0} x^\gamma w(x)$$  \hfill (3.83)

exists. Then, as $M \to \infty$,

$$\mathbb{E}[\tau_M | W > 0] \sim \frac{1}{\alpha} \ln M.$$  \hfill (3.84)

**Remark 3.3.** Proposition 3.4 shows that assumption (3.83) holds in the case when $\beta_n(x) \equiv 0$ for all $n > 1$, which is adequate for the examples we will consider in this chapter and in Chapter 5. The result for the time homogeneous case suggests that (3.83) holds in general. In that case, $W$ has a density, $w(x)$, which is continuous on $(0, \infty)$. Moreover, the Laplace-Stieltjes transform of $W$ can be completely characterized [73, 168]: if $\Phi(\theta) = \mathbb{E}[e^{-\theta W}]$,\n
$$a = \sum_{n=1}^{\infty} \beta_n + \delta$$ \hfill (3.85)

is the cumulative rate of all births and deaths, and $f$ is the generating function for the
individual offspring distribution, i.e.,

\[ f(\xi) = \sum_{n=1}^{\infty} \frac{\beta_n}{a} \xi^n + \frac{\delta}{a}, \]  

then

\[ \Phi^{-1}(x) = (1 - x) e^{-f_1^1 \left( \frac{f'(q)-1}{f'(1)-1} + \frac{1}{x-1} \right) d\xi}. \]  

(3.87)

In particular, if \( \gamma = \frac{f'(q)-1}{f'(1)-1} \), then \( \gamma < 1 \), and a simple calculation using l'Hôpital's rule shows

\[ \lim_{x \to q} (x - q)^{\frac{1}{\gamma}} \Phi^{-1}(x) \]  

exists and is finite. Now, \( \lim_{\theta \to \infty} \Phi(\theta) = q \), so there exists a constant \( A \) such that \( \Phi(\theta) \approx q + A\theta^\gamma \) as \( \theta \to \infty \). Applying the Hardy-Littlewood Tauberian theorem (see e.g., [57]), we then have

\[ \lim_{x \to 0} x^\gamma w(x) \]  

exists, as in assumption (3.83). We have yet to verify or refute the analogous result for the time-inhomogeneous case.

\textbf{Proof.} It only remains to show that \( \mathbb{E} [\ln W | W > 0] \) is bounded.

The upper bound is trivial: we begin by observing that for all \( x > 0 \), \( \ln x \leq x - 1 \), so that

\[ \mathbb{E} [\ln W | W > 0] \leq \mathbb{E} [W | W > 0] - 1 = \frac{q}{1 - q}, \]  

(3.90)

since \( \mathbb{E} [W | W > 0] \mathbb{P} \{ W > 0 \} = \mathbb{E} [W] = 1 \), and \( \mathbb{E} [W | W > 0] = \frac{1}{1 - q} \).

For the lower bound, let \( \lim \inf_{x \to 0} x^\gamma w(x) = C \) and fix \( \varepsilon > 0 \). Choose \( \delta > 0 \) so that
\[ x^{\gamma}w(x) \geq C - \varepsilon \text{ for all } x \in [0, \delta). \] Then,

\[
\mathbb{E} [\ln W | W > 0] = \frac{1}{1-q} \int_0^\infty w(x) \ln x \, dx \geq \frac{1}{1-q} \int_0^\delta w(x) \ln x \, dx \\
= \frac{1}{1-q} \int_0^\delta w(x) \ln x \, dx + \frac{1}{1-q} \int_\delta^1 w(x) \ln x \, dx \\
\geq (C - \varepsilon) \frac{1}{1-q} \int_0^\delta x^{-\gamma} \ln x + \tilde{C} \frac{1}{1-q} \int_\delta^1 \ln x \, dx, \quad \text{(3.91)}
\]

for some constant \( \tilde{C} \), as \( w(x) \) is continuous, and thus bounded below on \([\delta, 1]\). Now,

\[
\int_0^1 x^{-\gamma} \ln x \, dx = -\frac{1}{(\gamma - 1)^2}. \quad \text{(3.92)}
\]

for all \( \tilde{\gamma} < 1 \), so \( \mathbb{E} [\ln W | W > 0] \) is bounded below as well. The result follows. \( \square \)

An asymptotic for the time to extinction, starting from large numbers, can also be obtained in the subcritical case, similarly to the result for the Harris-Bellman process in [91]:

**Proposition 3.8.** Suppose \( \alpha < 0 \) and let

\[
\tau_0 = \inf \{ t : Z(t) = 0 \}. \quad \text{(3.93)}
\]

Then, as \( M \to \infty \),

\[
\mathbb{E}_M [\tau_0] \sim \frac{1}{|\alpha|} \ln M. \quad \text{(3.94)}
\]

**Proof.** From Proposition 3.5, there are constants \( C_- \) and \( C_+ \) such that

\[
0 < C_- = \liminf_{t \to \infty} e^{-\alpha t} (1 - q(t)) \leq \limsup_{t \to \infty} e^{-\alpha t} (1 - q(t)) = C_+ \quad \text{(3.95)}
\]

Fix \( \varepsilon > 0 \), and choose \( T > 0 \) such that

\[
C_+ + \varepsilon > e^{-\alpha t} (1 - q(t)) > C_- - \varepsilon > 0 \quad \text{(3.96)}
\]
for all $t > T$ and

$$(C_+ + \varepsilon)e^{\alpha T} < 2. \quad (3.97)$$

Then,

$$E_M[\tau_0] = \int_0^\infty P_M\{\tau_0 > t\} \, dt \quad (3.98)$$

$$= \int_0^\infty P_M\{Z(t) > 0\} \, dt \quad (3.99)$$

$$= \int_0^T P_M\{Z(t) > 0\} \, dt + \int_T^\infty P_M\{Z(t) > 0\} \, dt. \quad (3.100)$$

Now, for any fixed $T$, we may apply the dominated convergence theorem to conclude that

$$\lim_{M \to \infty} \int_0^T P_M\{Z(t) > 0\} \, dt = T, \quad (3.101)$$

leaving us with the task of computing the tail,

$$\int_T^\infty P_M\{Z(t) > 0\} \, dt = \int_T^\infty 1 - q(t)^M \, dt \quad (3.102)$$

By assumption,

$$\int_T^\infty 1 - (1 - (C_+ + \varepsilon)e^{\alpha t})^M \, dt \leq \int_T^\infty 1 - q(t)^M \, dt \leq \int_T^\infty 1 - (1 - (C_- - \varepsilon)e^{\alpha t})^M \, dt. \quad (3.103)$$

We are thus left with the task of computing

$$\int_T^\infty 1 - (1 - \tilde{C}e^{\alpha t})^M \, dt = \int_T^\infty \sum_{i=0}^{M-1} \tilde{C}e^{\alpha t}(1 - \tilde{C}e^{\alpha t})^i \quad (3.104)$$
for $\tilde{C} = C \pm \varepsilon$. After a change of variable, $x = Ce^{\alpha t}$, this equals

$$- \frac{1}{\alpha} \int_0^{\tilde{C}e^{\alpha T}} \sum_{i=0}^{M-1} (1 - x)^i dx = \frac{1}{|\alpha|} \left( \sum_{i=0}^{M-1} \frac{1}{i+1} - \sum_{i=0}^{M-1} \frac{(1 - \tilde{C}e^{\alpha T})^{i+1}}{i+1} \right)$$

$$= \frac{1}{|\alpha|} \left( \ln M + \gamma + \ln \tilde{C}e^{\alpha T} + O\left(\frac{1}{M}\right) \right)$$

$$= \frac{1}{|\alpha|} \left( \ln M + \gamma + \ln \tilde{C} + O\left(\frac{1}{M}\right) \right) - T,$$  \hspace{1cm} (3.107)

where $\gamma$ is Euler’s constant [8]. By assumption $|1 - \tilde{C}e^{\alpha T}|$ is within the radius of convergence of the logarithm. The result follows. $\square$

In Section ??, we will use these estimates to obtain an asymptotic value (in $N$) for the fixation time of an advantageous allele for a strongly selected density dependent birth-death-mutation process $X^{(N)}(t)$.

### 3.2 Application to Density-Dependent Birth-Death-Mutation Processes

We now return to the primary task of studying the process density dependent birth-death-mutation process $X_1^{(N)}(t)$. We take our inspiration from [174], and use a coupling argument, constructing a probability space upon which $X_1^{(N)}(t)$ is defined, along with branching processes $Z_{1:x,+}^{(e)}$ and $Z_{1:x,-}^{(e)}$ that bound $X_1^{(N)}(t)$ above and below, respectively. Equipped with these bounds, we can then use the results of the preceding section to obtain estimates of the invasion probability of a novel mutant and the probability of fixation and expected time to fixation of a strongly advantageous mutant.

**Remark 3.4.** For clarity of exposition, we have chosen to present the case when only $X_1^{(N)}(0)$ is of order $O(1)$. All the results of this and subsequent sections continue to hold...
when $X_1^{(N)}(0), \ldots, X_d^{(N)}(0)$ are all $O(1)$. In that case, we would have

$$\lim_{N \to \infty} \frac{1}{N} X^{(N)}(0) = x \quad (3.108)$$

for $x = (0, \ldots, 0, x_{d+1}, \ldots, x_K$, and $\psi_i^t x \equiv 0$ for $i = 1, \ldots, d$. We could then construct independent time-inhomogeneous branching processes $Z_{i, x, -}^{(e)}(t), i = 1, \ldots, d$, such that

$$Z_{i, x, -}^{(e)}(t) \leq X_i^{(N)}(t) \leq Z_{i, x, -}^{(e)}(t) \quad (3.109)$$

for $i = 1, \ldots, d$.

### 3.2.1 A Coupling Result

Recall that in Section 2.1.2 we introduced a compact set $\mathcal{K}_x \subset \mathbb{R}^K_+$ such that the forward orbit of $x$, $\gamma^+_x := \{ \psi_t x : t \geq 0 \}$, is contained in $\mathcal{K}_x$.

Let

$$\epsilon_n^{(N)}(\mathcal{K}_x) = \sup_{1, x' \in \mathcal{K}_x} \left| \beta_1^{(N)}(x') - \beta_{1,n}(x') \right| \quad (3.110)$$

and

$$\epsilon^{(N)}(\mathcal{K}_x) = \sup_{1, x' \in \mathcal{K}_x} \left| \delta_1^{(N)}(x') - \delta_1(x') \right| \quad . \quad (3.111)$$

Then, by Assumption 2.3,

$$\lim_{N \to \infty} \sum_{n \in \mathbb{Z}^K_+} \|n\|_2 \epsilon_n^{(N)}(\mathcal{K}_x) = 0 \quad (3.112)$$

and

$$\lim_{N \to \infty} N \sum_{n \in \mathbb{Z}^K_+} \|n\|_2 \epsilon_n^{(N)}(\mathcal{K}_x) < \infty. \quad (3.113)$$

eq etc.
Fix $\varepsilon > 0$ sufficiently small so that

$$
\mathcal{K}_{x,\varepsilon}(t) = \left\{ x' \in \mathbb{R}_+^K : \| x' - \psi_t x \| < \varepsilon \right\} \subseteq \mathcal{K}_x
$$

(3.114)

for all $t$, and choose $N_\varepsilon$ such that

$$
\sum_{n \in \mathbb{Z}_+^K} \| n \|_2 \epsilon_n^{(N)}(\mathcal{K}_x) < \varepsilon
$$

(3.115)

for all $N \geq N_\varepsilon$.

Let

$$
\beta_{1,n,x,+}^{(\varepsilon)}(t) := \sup_{1, x' \in \mathcal{K}_{x,\varepsilon}(t)} \beta_{1,n}(x') + \epsilon_n^{(N_\varepsilon)}(\mathcal{K}_x),
$$

(3.116)

$$
\beta_{1,n,x,-}^{(\varepsilon)}(t) := \inf_{1, x' \in \mathcal{K}_{x,\varepsilon}(t)} \beta_{1,n}(x') - \epsilon_n^{(N_\varepsilon)}(\mathcal{K}_x),
$$

(3.117)

$$
\delta_{1,x,+}^{(\varepsilon)}(t) := \sup_{1, x' \in \mathcal{K}_{x,\varepsilon}(t)} \delta_1(x') + \epsilon^{(N_\varepsilon)}(\mathcal{K}_x),
$$

(3.118)

and

$$
\delta_{1,x,-}^{(\varepsilon)}(t) := \inf_{1, x' \in \mathcal{K}_{x,\varepsilon}(t)} \delta_1(x') - \epsilon^{(N_\varepsilon)}(\mathcal{K}_x).
$$

(3.119)

(3.120)

We will also write

$$
\beta_{1,n,x}(t) := \beta_{1,n,x,+}^{(0)}(t) = \beta_{1,n}(\psi_t x)
$$

(3.121)

and

$$
\delta_{1,x}(t) := \delta_{1,x,+}^{(0)}(t) = \delta_1(\psi_t x).
$$

(3.122)

Finally, let

$$
T_{\varepsilon}^{(N)} = \inf\{ t \geq 0 : \| Y^{(N)}(t) - \psi_t x \| > \varepsilon \}.
$$

(3.123)
By definition, provided $N \geq N_\varepsilon$ and $t < T^{(N)}_\varepsilon$, we have

\[
\beta^{(\varepsilon)}_{1,n,x,-}(t) < \beta^{(N)}_{1,ne_1}(Y^{(N)}(t)) < \beta^{(\varepsilon)}_{1,n,x,+}(t)
\]
\[
\delta^{(\varepsilon)}_{1,x,-}(t) < \delta^{(N)}_{1}(Y^{(N)}(t)) < \delta^{(\varepsilon)}_{1,x,+}(t).
\]

**Remark 3.5.** Given (3.113), all of the inequalities above continue to hold if $\varepsilon$ is replaced by $\varepsilon_N$, where \( \{\varepsilon_N\}_{N=1}^\infty \) is a monotonically decreasing sequence, provided \( \{N\varepsilon_N\}_{N=1}^\infty \) is increasing, and $N\varepsilon_N \to \infty$ as $N \to \infty$. We shall use this extensively in the next section.

We then have

**Proposition 3.9.** There exist nonautonomous Markov processes $Z^{(\varepsilon)}_{1,x,+}$ and $Z^{(\varepsilon)}_{1,x,-}$, and counting processes $B^{(\varepsilon)}_{1,n,x,-}(t)$, $B^{(\varepsilon)}_{1,n,x,+}(t)$, $D^{(\varepsilon)}_{1,x,-}(t)$, and $D^{(\varepsilon)}_{1,x,+}(t)$ with intensities $\beta^{(\varepsilon)}_{1,n,x,-}(t)Z^{(\varepsilon)}_{1,x,+}(t)$, $\beta^{(\varepsilon)}_{1,n,x,+}(t)Z^{(\varepsilon)}_{1,x,-}(t)$, $\delta^{(\varepsilon)}_{1,x,-}(t)Z^{(\varepsilon)}_{1,x,+}(t)$, and $\delta^{(\varepsilon)}_{1,x,+}(t)Z^{(\varepsilon)}_{1,x,-}(t)$, respectively such that

\[
Z^{(\varepsilon)}_{1,x,-}(t) = X_1(0) + \sum_{n=0}^\infty nB^{(\varepsilon)}_{1,n,x,-}(t) - D_{1,x,+}(t),
\]
\[
Z^{(\varepsilon)}_{1,x,+}(t) = X_1(0) + \sum_{n=0}^\infty nB^{(\varepsilon)}_{1,n,x,+}(t) - D_{1,x,-}(t),
\]

and, if

\[
T_{\varepsilon,N} = \sup\{t : X^{(N)}(t) < \varepsilon N\}, \quad (3.124)
\]

then

\[
B^{(\varepsilon)}_{1,n,x,-}(t) \leq B^{(N)}_{1,ne_1}(t) \leq D^{(\varepsilon)}_{n,x,+}(t),
\]
\[
D^{(\varepsilon)}_{1,x,-}(t) \leq D^{(N)}_{1}(t) \leq D^{(\varepsilon)}_{1,x,+}(t),
\]

and

\[
Z^{(\varepsilon)}_{1,x,-}(t) \leq X^{(N)}_1(t) \leq Z^{(\varepsilon)}_{1,x,+}(t),
\]
in distribution for all
\[ t < T_{\varepsilon,N} \wedge T^{(N)}_{\varepsilon} \] (3.125)
and \( N \) sufficiently large.

**Proof.** We construct the coupled processes inductively up to an arbitrary time \( T \); the existence of the process for all time then follows from Kolmogorov’s extension theorem (see e.g., [37]). To begin, let
\[
B^{(e)}_{1,n,x,-}(0) = B^{(N)}_{1,n,\varepsilon,1}(0) = B^{(e)}_{1,n,x,+}(0) = 0,
\]
\[
D^{(e)}_{1,x,-}(0) = D^{(N)}_{1}(0) = D^{(e)}_{1,x,+}(0) = 0,
\]
and
\[
Z^{(e)}_{1,x,-}(0) = Z^{(e)}_{1,x,+}(0) = X^{(N)}_{1}(0).
\]
and let \( U_j \) and \( V_j \), \( j = 1, 2, \ldots \) be i.i.d. random variables, uniformly distributed on \([0, 1]\). Now, suppose the processes have been constructed up to a jump time \( \tau_j \). Let \( \tau_{j+1} \) be a random variable with distribution
\[
\mathbb{P}\{\tau_{j+1} > t\} = e^{-\int_0^t \left( \sum_{n=1}^{\infty} \beta^{(e)}_{1,n,x,+}(s) + \delta^{(e)}_{1,x,+}(s) \right) Z^{(e)}_{1,x,+}(s \wedge \tau_j) \, ds}
\] (3.126)
For \( \tau_j \leq t < \tau_{j+1} \), let
\[
B^{(e)}_{1,n,x,-}(t) = B^{(e)}_{1,n,x,-}(\tau_j),
\]
\[
B^{(N)}_{1,n,\varepsilon,1}(t) = B^{(N)}_{1,n,\varepsilon,1}(\tau_j),
\]
\[
B^{(e)}_{1,n,x,+}(t) = B^{(e)}_{1,n,x,+}(\tau_j),
\]
then let

\[
D_{1,x,+}^{(e)}(\tau_{j+1}) = D_{1,x,+}^{(e)}(t)(\tau_{j}) + 1 \quad \text{and} \quad Z_{1,x,+}^{(e)}(\tau_{j+1}) = Z_{1,x,+}^{(e)}(\tau_{j}) - 1 \quad \text{if} \quad V_{j+1} \leq \frac{\delta_{1,x,+}^{(e)}(\tau_{j+1})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}{\delta_{1,x,+}^{(e)}(\tau_{j})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}
\]

\[
D_{1}^{(N)}(\tau_{j+1}) = D_{1}^{(N)}(\tau_{j}) + 1 \quad \text{and} \quad X_{1}^{(N)}(\tau_{j+1}) = X_{1}^{(N)}(\tau_{j}) - 1 \quad \text{if} \quad V_{j+1} \leq \frac{\delta_{1,x,+}^{(e)}(\tau_{j+1})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}{\delta_{1,x,+}^{(e)}(\tau_{j})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}
\]

and

\[
D_{1,x,-}^{(e)}(t)(\tau_{j+1}) = D_{1,x,-}^{(e)}(t)(\tau_{j}) + 1 \quad \text{and} \quad Z_{1,x,+}^{(e)}(\tau_{j+1}) = Z_{1,x,+}^{(e)}(\tau_{j}) - 1 \quad \text{if} \quad V_{j+1} \leq \frac{\delta_{1,x,+}^{(e)}(\tau_{j+1})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}{\delta_{1,x,+}^{(e)}(\tau_{j})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}
\]

Similarly, if

\[
\frac{\sum_{n=1}^{m-1} \beta_{1,n,x,+}^{(e)}(\tau_{j+1}) + \delta_{1,x,+}^{(e)}(\tau_{j+1})}{\sum_{n=1}^{\infty} \beta_{1,n,x,+}^{(e)}(\tau_{j+1}) + \delta_{1,x,+}^{(e)}(\tau_{j+1})} \leq U_{j+1} \leq \frac{\sum_{n=1}^{m} \beta_{1,n,x,+}^{(e)}(\tau_{j+1}) + \delta_{1,x,+}^{(e)}(\tau_{j+1})}{\sum_{n=1}^{\infty} \beta_{1,n,x,+}^{(e)}(\tau_{j+1}) + \delta_{1,x,+}^{(e)}(\tau_{j+1})}
\]

then, let \( B_{m,+}^{(e)}(\tau_{j+1}) = B_{m,+}^{(e)}(\tau_{j}) + 1 \), \( Z_{1,x,+}^{(e)}(\tau_{j+1}) = Z_{1,x,+}^{(e)}(\tau_{j}) + m \) and

\[
B_{1,m,x,+}^{(N)}(\tau_{j+1}) = B_{1,m,x,+}^{(N)}(\tau_{j}) + 1 \quad \text{if} \quad V_{j+1} \leq \frac{\beta_{1,m,x,+}^{(N)}(\tau_{j+1})X_{1}^{(N)}(\tau_{j+1}-)}{\beta_{1,m,x,+}^{(e)}(\tau_{j})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}
\]

and

\[
B_{m,-}^{(e)}(\tau_{j+1}) = B_{m,-}^{(e)}(\tau_{j}) + 1 \quad \text{and} \quad Z_{1,x,+}^{(e)}(\tau_{j+1}) = Z_{1,x,+}^{(e)}(\tau_{j}) + m \quad \text{if} \quad V_{j+1} \leq \frac{\beta_{1,m,x,-}^{(e)}(\tau_{j+1})Z_{1,x,-}^{(e)}(\tau_{j+1}-)}{\beta_{1,m,x,+}^{(e)}(\tau_{j})Z_{1,x,+}^{(e)}(\tau_{j+1}-)}
\]
Proceeding in this manner, we obtain the desired Markov chains.

Remark 3.6. Given an arbitrary sequence (finite or countably infinite) of values $0 \leq \varepsilon_0 < \varepsilon_1 < \varepsilon_2 \cdots$, we may proceed as in the proof of Lemma 3.9 to construct a family of coupled processes $B^{(\varepsilon_j)}_{1,n,x,\pm}(t)$, $D^{(\varepsilon_j)}_{1,x,\pm}(t)$ and $Z^{(\varepsilon_j)}_{1,x,\pm}(t)$ such that

$$\cdots \leq Z^{(\varepsilon_1)}_{1,x,-}(t) \leq Z^{(\varepsilon_0)}_{1,x,-}(t) \leq Z^{(\varepsilon_0)}_{1,x,+}(t) \leq Z^{(\varepsilon_1)}_{1,x,+}(t) \leq \cdots$$

(3.129)

etc. In particular, in what follows, we shall routinely assume that we have coupled processes

$$Z^{(\varepsilon)}_{1,x,-}(t) \leq Z^{(\varepsilon)}_{1,x}(t) := Z^{(0)}_{1,x,-}(t) = Z^{(0)}_{1,x,+}(t) \leq Z^{(\varepsilon)}_{1,x,-}(t).$$

(3.130)

We shall need the mean and extinction probabilities of the processes $Z^{(\varepsilon)}_{1,x,-}(t)$, $Z^{(\varepsilon)}_{1,x}(t)$, and $Z^{(\varepsilon)}_{1,x,-}(t)$, which we denote as follows:

Definition 3.1. For fixed $\varepsilon > 0$, we will write

$$m^{(\varepsilon)}_{1,x,\pm}(t) := \mathbb{E} \left[ Z^{(\varepsilon)}_{1,x,\pm}(t) \mid Z^{(\varepsilon)}_{1,x,\pm}(0) = 1 \right]$$

$$m_{1,x}(t) := \mathbb{E} \left[ Z^{(\varepsilon)}_{1,x}(t) \mid Z^{(\varepsilon)}_{1,x}(0) = 1 \right]$$

$$q^{(\varepsilon)}_{1,x,\pm}(t) := \mathbb{P} \left\{ Z^{(\varepsilon)}_{1,x,\pm}(t) = 0 \mid Z^{(\varepsilon)}_{1,x,\pm}(0) = 1 \right\}$$

and

$$q_{1,x}(t) := \mathbb{P} \left\{ Z^{(\varepsilon)}_{1,x}(t) = 0 \mid Z^{(\varepsilon)}_{1,x}(0) = 1 \right\}$$

We write $q^{(\varepsilon)}_{1,x,\pm}(\infty) = \lim_{t \to \infty} q^{(\varepsilon)}_{1,x,\pm}(t)$ and $q_{1,x}(\infty) = \lim_{t \to \infty} q_{1,x}(t)$ for the probability of eventual extinction of the processes $Z^{(\varepsilon)}_{1,x,\pm}$ and $Z_{1,x}$ respectively.
3.2.2 Invasion and Fixation in the Supercritical Case

Recall that the process $Z_{1,x}(t)$ has mean $e^{\int_0^\infty \bar{\beta}_{1,x}(s) - \delta_{1,x}(s) \, ds}$, where

$$\bar{\beta}_{1,x}(t) = \sum_{n=1}^{\infty} n\beta_{1,n,x}(t). \tag{3.131}$$

We now assume that

$$\int_0^\infty \bar{\beta}_{1,x}(s) - \delta_{1,x}(s) \, ds = +\infty, \tag{3.132}$$

so that $m_{1,x}(t) \to \infty$ as $t \to \infty$. Let

$$\rho_{1,x} := \left| \sup_{t \in \mathbb{R}_+} \bar{\beta}_i(t) - \delta_i(t) \right|. \tag{3.133}$$

$\rho_{1,x}$ is the maximum of $\bar{\beta}(\phi_t x) - \delta(\phi_t x)$ over the compact trajectory $\{\phi_t x : t \in \mathbb{R}_+\}$, and is thus finite, and positive by our assumption of supercriticality.

Recall that $L_{1,x} > 0$ is a constant such that

$$\|F(y_1) - F(y_2)\| < L_{1,x} \|y_1 - y_2\| \tag{3.134}$$

for all $y_1, y_2 \in K_x$. Fix $0 < r < s < 1$ as in Proposition 2.1 and choose $\delta, \chi > 0$ such that $0 < \chi < \frac{r}{2}$ and $0 \wedge \frac{\rho_{1,x}(1-s)}{4L_{1,x}} < \eta < 1 - \chi$. Let

$$t_N = \frac{1 - \chi - \eta}{\rho_{1,x}} \ln N \tag{3.135}$$

and

$$\varepsilon_N = N^{-\chi}. \tag{3.136}$$

We then have

(i) $t_N \to \infty$,
(ii) \( m_{1,x}(t_N) \to \infty \),

(iii) \( t_N \leq \frac{(1-s)}{4L_{1,x}^2} \ln N \),

(iv) \( \varepsilon_N \to 0 \),

(v) \( N^2\varepsilon \to \infty \), and thus, \( N\varepsilon \to \infty \), and

(vi) \( \varepsilon_N t_N \to 0 \),

as \( N \to \infty \).

Let
\[
W_{1,x} = \lim_{t \to \infty} \frac{Z_{1,x}(t)}{m_{1,x}(t)}.
\]  

(3.137)

As we observed in Section 3.1.4, this limit holds almost surely and in \( L^1(\mathbb{P}) \), and \( \mathbb{E}[W_{1,x}] = 1 \). We then have

**Lemma 3.4.** As \( N \to \infty \),
\[
W_{1,x}^{(N)} := \frac{Z_{1,x}^{(N)}(t_N)}{m_{1,x}^{(N)}(t_N)} \to W_{1,x,\pm}
\]  

(3.138)

in \( L^1(\mathbb{P}) \) as \( N \to \infty \), and \( \mathbb{E}[W_{1,x,\pm}] = 1 \), where
\[
W_{1,x,-} \overset{\mathbb{P}}{=} W_{1,x,+} \overset{\mathbb{P}}{=} W_{1,x}.
\]  

(3.139)

**Proof.** The existence of the limits and the topology of convergence follow from Doob’s martingale convergence theorem, as in 3.1.4. To characterize the limit, let
\[
F_{1,x,\pm}^{(e)}(\xi, t) := \mathbb{E} \left[ \xi Z_{1,x,\pm}(t) \right]
\]  

(3.140)

and
\[
F_{1,x}(\xi, t) := \mathbb{E} \left[ \xi Z_{1,x}(t) \right]
\]  

(3.141)
be the probability generating functions of $Z_{1,x,±}^{(ε)}$ and $Z_{1,x}$ respectively. Then,

$$\lim_{ε \to 0} F_{1,x,±}^{(ε)}(ξ, t) = F_{1,x}(ξ, t)$$

(3.142)

uniformly in $t$. In particular, the $W_{1,x,±}^{(N)}$ have characteristic functions

$$\varphi^{(N)}(θ) = F_{1,x,±}^{(ε)(N)}\left( e^{iθ}_{m_{1,x,±}^{(ε)(N)}, t_N} \right),$$

(3.143)

and

$$\lim_{N \to \infty} \varphi^{(N)}(θ) = \varphi(θ),$$

(3.144)

where $\varphi(θ) = \lim_{t \to ∞} F_{1,x}\left( e^{iθ}_{m_{1,x}^{(ε)}, t} \right)$ is the characteristic function for $W_{1,x}$. The result follows by Lévy’s convergence theorem [37].

**Lemma 3.5.** As $N \to \infty$, $\mathbb{P}\left\{ \frac{X_{1,N}^{(ε)}(t_N)}{ε_N N} > 1 \right\} \to 0$.

**Proof.** We begin by observing that, provided $t_N < T_{ε_N}^{(N)}$,

$$\frac{X_{1,N}^{(ε)}(t_N)}{ε_N N} \leq \frac{Z_{1,x,+}^{(ε)}(t_N)}{ε_N N} = \frac{m_{1,x,+}^{(ε)}(t_N)}{ε_N N} \frac{Z_{1,x,+}^{(ε)}(t_N)}{m_{1,x,+}^{(ε)}(t_N)} = \frac{m_{1,x,+}^{(ε)}(t_N)}{ε_N N} W_{1,x,+}^{(N)}.$$  

(3.145)

We consider the two terms in the product independently. First,

$$\frac{m_{1,x,+}^{(ε)}(t_N)}{ε_N N} = e^{\int_0^{t_N} \bar{β}_{1,x,+}^{(ε)}(u) - \delta_{1,x,-}^{(ε)}(u) du} - \ln N - \ln ε_N$$

(3.146)

Now, $β_{1,nec}(x)$ and $δ_1(x)$ are $C^1$ and thus Lipschitz on the compact set $K_{x,ε_N}(t)$, and, by definition, $\|\psi_t x - x'\| < ε_N$ for all $x' \in K_{x,ε_N}(t)$, so there exists a constant $C$ such that

$$\bar{β}_{1,x,+}^{(ε)}(t) - \delta_{1,x,-}^{(ε)}(t) \leq \bar{β}_{1,x}(t) - δ_{1,x}(t) + Cε_N$$

(3.147)
whence

\[
\frac{m_{1,x_+}^{(\epsilon_N)}(t_N)}{\epsilon N} \leq e^{t_N \sup_{\epsilon \geq 0} |\tilde{\beta}_{1,x}(t) - \delta_{1,x}(t)| + C\epsilon_N t_n - N - \ln \epsilon_N}
\]

(3.148)

\[
= e^{\rho_{1,x} t_N + C\epsilon_N t_N - N + \chi \ln N}
\]

(3.149)

\[
= e^{-\eta \ln N + C\epsilon_N t_N} \asymp N^{-\eta}
\]

(3.150)

as \( N \to \infty \).

On the other hand, by the previous lemma, \( W_1^{(N)} \to W_{1,x} \). Thus, for any \( 0 < \eta' < \eta \),

\[
\mathbb{P} \left\{ \frac{Z_{1,x_+}^{(\epsilon_N)}(t_N)}{m_{1,x_+}^{(\epsilon_N)}(t_N)} > N^{\eta'} \right\} \leq \frac{\mathbb{E}\left[ W_1^{(N)} \right]}{N^{\eta'}} \to 0
\]

(3.151)

as \( N \to \infty \), so the product \( \frac{m_{1,x_+}^{(\epsilon_N)}(t_N)}{\epsilon N} W_1^{(N)} \) is \( o(1) \) provided \( t_N < T_{\epsilon_N}^{(N)} \).

Lastly, recalling the proof of Proposition 2.1, we have

\[
\mathbb{P}_{1,x} \left\{ T_{\epsilon_N}^{(N)} < t_N \right\} < \frac{N^{-p}}{\epsilon_N^2}
\]

(3.152)

which tends to 0 as \( N \to \infty \). The result follows.

We then have

**Proposition 3.10.** As \( N \to \infty \)

\[
\frac{X_1^{(N)}(t_N)}{m_{1,x}(t_N)} \to W_{1,x}
\]

(3.153)

almost surely and in \( L^2(\mathbb{P}) \).

**Proof.** This follows immediately from the coupling, the preceding lemma and its proof; we have \( \mathbb{P} \left\{ \frac{X_1^{(N)}(t_N)}{\epsilon N} > 1 \right\} \to 0 \), so for \( N \) sufficiently large, we have

\[
Z_{1,x_-}^{(\epsilon_N)}(t_N) \leq X^{(N)}(t_N) \leq Z_{1,x_+}^{(\epsilon_N)}(t_N)
\]

(3.154)
with probability tending to 1 as \( N \to \infty \). Thus,

\[
\frac{m^{(\varepsilon N)}_{1,x,-}(t_N)}{m^{(\varepsilon N)}_{1,x}(t_N)} Z^{(\varepsilon N)}_{1,x,-}(t_N) \leq \frac{X^{(N)}(t_N)}{m^{(\varepsilon N)}_{1,x}(t_N)} \leq \frac{m^{(\varepsilon N)}_{1,x,+}(t_N)}{m^{(\varepsilon N)}_{1,x}(t_N)} Z^{(\varepsilon N)}_{1,x,+}(t_N). 
\] (3.155)

with probability tending to 1 as \( N \to \infty \) as well.

From above, we have

\[
\frac{Z^{(\varepsilon N)}_{1,x,+}(t_N)}{m^{(\varepsilon N)}_{1,x,+}(t_N)} \rightarrow W_{1,x,+} = W_{1,x}, 
\] (3.156)

and in a similar manner,

\[
\frac{Z^{(\varepsilon N)}_{1,x,-}(t_N)}{m^{(\varepsilon N)}_{1,x,-}(t_N)} \rightarrow W_{1,x,-} = W_{1,x}. 
\] (3.157)

Proceeding as in the previous lemma, it is readily shown that

\[
\frac{m^{(\varepsilon N)}_{1,x}(t_N)}{m^{(\varepsilon N)}_{1,x,-}(t_N)} \rightarrow 1 \quad \text{and} \quad \frac{m^{(\varepsilon N)}_{1,x}(t_N)}{m^{(\varepsilon N)}_{1,x,+}(t_N)} \rightarrow 1. 
\] (3.158)

The result follows.

Now, fix \( \varepsilon > 0 \) independent of \( N \). Let

\[
\tau^{(\varepsilon,N)}_1 = \inf\{t \geq 0 : X^{(N)}_1(t) \geq \varepsilon N\}. 
\] (3.159)

Then we have

**Corollary 3.3.** As \( N \to \infty \),

\[
\mathbb{P}_{1,x}\{\tau^{(\varepsilon,N)}_1 = +\infty\} = \mathbb{P}_{1,x}\{W_{1,x} = 0\} = q_{1,x}(\infty). 
\] (3.160)

**Proof.** Proceeding as in Lemma 3.9, choosing \( \varepsilon > 0 \) sufficiently small, we may construct i.i.d. supercritical branching processes \( Z^{(\varepsilon,j)}_{1,x,-}(t) \) and \( Z^{(\varepsilon,j)}_{1,x,+}(t) \), \( j = 1, \ldots, X^{(N)}(t_N) \), such that

\[
\sum_{j=1}^{X^{(N)}(t_N)} Z^{(\varepsilon,j)}_{1,x,-}(t) \leq X^{(N)}(t_N + t) \leq \sum_{j=1}^{X^{(N)}(t_N)} Z^{(\varepsilon,j)}_{1,x,+}(t) 
\] (3.161)
for all $t$ such that $t_N + t < \tau_1^{(e,N)}$. Then, if

$$q^{(e)}_{\psi \tau_N x, \pm}(t) := \mathbb{P}\left\{ Z^{(e,1)}_{1,x,\pm}(t) = 0 \ \bigg| \ Z^{(e,1)}_{1,x,\pm}(0) = 1 \right\}, \quad (3.162)$$

we have that

$$q^{(e)}_{\psi \tau_N x, -}(t)^{X(N)(t_N)} = \mathbb{P}\left\{ \sum_{j=1}^{X^{(N)}(t_N)} Z^{(e,j)}_{1,x, -}(t) = 0 \right\} \leq \mathbb{P}\left\{ X^{(N)}(t_N + t) = 0 \right\} \leq \mathbb{P}\left\{ \sum_{j=1}^{X^{(N)}(t_N)} Z^{(e,j)}_{1,x, -}(t) = 0 \right\} = q^{(e)}_{\psi \tau_N x, -}(t)^{X(N)(t_N)}. \quad (3.163)$$

From Proposition 3.10, we have

$$\frac{X^{(N)}(t_N)}{m_{1,x}(t_N)} \to W_{1,x}. \quad (3.164)$$

Thus, for any $\omega \notin \{W_{1,x} = 0\}$, we can pick $\delta > 0$ such that $\delta < W_{1,x}(\omega)$, and there exists $N_\delta$ such that

$$(W_{1,x}(\omega) - \delta)m_{1,x}(t_N) < X^{(N)}(t_N) < (W_{1,x}(\omega) + \delta)m_{1,x}(t_N), \quad (3.165)$$

for all $N > N_\delta$. Since $m_{1,x}(t_N) \to \infty$, $X^{(N)}(t_N) \to \infty$ as well. In particular,

$$q^{(e)}_{\psi t_N x, -}(t)^{X(N)(t_N)} \to 0 \quad (3.166)$$

and

$$q^{(e)}_{\psi t_N x, -}(t)^{X(N)(t_N)} \to 0, \quad (3.167)$$

so, for $t < \tau_1^{(e,N)}$, we have $\mathbb{P}\left\{ X^{(N)}(t_N + t) = 0 \right\} \to 0$.

Moreover, from Lemma 3.2, we know that either there exists $T$ such that $Z^{(e)}_{1,x, -}(t) = 0$ for all $t \geq T$, or $Z^{(e)}_{1,x, -}(t) \to \infty$. If the latter holds, we must have $\tau_1^{(e,N)} < \infty$, as
Lastly, once $X^{(N)}(t) \geq \epsilon N$, Proposition 2.1 tells us that the dynamics are effectively deterministic, giving us

**Corollary 3.4.** If $\mathbf{x}^{*} = r_{i} \mathbf{e}_{i}$ is the unique stable attractor of $\dot{Y}(t) = \mathbf{F}(Y(t))$, i.e., type $i$ can exclude other types, then type $i$ fixes with probability approaching $1 - q_{1,\mathbf{x}}$ as $N \to \infty$.

**Remark 3.7 (Fecundity Variance Polymorphism).** From Lemma 3.1 and Corollary 3.4 we have that

$$
\frac{1}{1 + \int_{0}^{\infty} e^{-\int_{0}^{s} \tilde{\beta}_{1}(\psi_{u}\mathbf{x}) - \delta_{1}(\psi_{u}\mathbf{x}) \, du} \delta_{1}(\psi_{s}\mathbf{x}) \, ds} \geq 1 - q_{1,\mathbf{x}}
$$

In particular, the upper bound is equal to the fixation probability for type 1 in a density-dependent birth-death-mutation process with reproduction rates

$$
\lim_{N \to \infty} \beta_{1,N}^{(N)}(\mathbf{x}) = \begin{cases} 
\tilde{\beta}_{1}(\mathbf{x}) & \text{if } \mathbf{n} = \mathbf{e}_{1}, \\
0 & \text{otherwise}
\end{cases}
$$

i.e., with probability approaching 1 as $N \to \infty$, all reproductions produce exactly one offspring of the same type as the parent. Moreover, unless this condition holds, the lower bound (and $q_{1,\mathbf{x}}$) is strictly smaller than the upper bound. In particular, among all types with the same mean growth rate, those that achieve that growth rate by minimizing the variance in the number and frequency of offspring per reproductive event have the highest probability of invasion. Thus, when the invading types are able to exclude their competitors, then the trend in evolution is towards minimizing fecundity variance. This phenomenon has been observed previously via heuristic analyses of the diffusion limit of the Wright-Fisher process in the weak selection regime [66, 171, 67, 68, 61]. Corollary
3.4 generalizes these results to the a wide class of processes in the strong selection case.

Recall that if $\gamma$ is a curve in $\mathbb{R}^K$ and $x : [0, t] \to \mathbb{R}^K$ is any parameterization of that curve, then
\[
\int f(x) \, dx = \int_0^t f(x(s)) \| \dot{x}(s) \| \, ds.
\] (3.170)

Since $\frac{d}{dt} \psi_t x = F(\psi_t x)$, we then have the following

**Corollary 3.5.** Let $\gamma_x^+ = \{ \psi_x : t \geq 0 \}$ be the forward orbit of $x$. Then,
\[
\int_{\gamma_x^+} e^{-\int f_{1,x} \left( \frac{\delta(\xi) - \delta(\epsilon)}{\| F(\epsilon) \|} \right) d\xi} d\epsilon \leq q_{1,x} \leq \int_{\gamma_x^+} e^{-\int f_{1,x} \left( \frac{\beta(\xi) - \beta(\epsilon)}{\| F(\epsilon) \|} \right) d\xi} d\epsilon,
\] (3.171)

In particular, in the case of binary reproduction, $\beta_{1,n}(x) \equiv 0$ for all $n \neq e_1$, so $\tilde{\beta}_1(x) = \tilde{\beta}_1(x) = \beta_{1,e_1}(x)$, we have
\[
q_{1,x} = \int_{\gamma_x^+} e^{-\int f_{1,x} \left( \frac{\beta(\xi) - \beta(\epsilon)}{\| F(\epsilon) \|} \right) d\xi} d\epsilon.
\] (3.172)

**Example 3.3.** In general, the curve $\gamma_x^+$ above will be quite complicated, but consider for a moment the Generalized Moran model, Example 2.1, without mutation, for $K = 2$. In that case,
\[
\tilde{\beta}_n^{(N)}(x) = \begin{cases} 
\beta_i, & \text{if } n = e_i, \\
0, & \text{otherwise}
\end{cases}
\] (3.173)

and
\[
\tilde{\delta}_i^{(N)}(x) = \delta_i(1 + x_1 + x_2),
\] (3.174)

so that $F_i(x) = x_i (\beta_i - \delta_i(1 + x_1 + x_2))$.

Assuming $X_1(0)$ individuals invade a resident population of type 2 with initial density
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$x_2$, then $x = (0, x_2)$, and, as $t \to \infty$,

$$\psi_t x \to x^{*, 2}$$

(3.175)

where $x_1^{*, 2} = 0$ and $x_2^{*, 2} = \frac{\delta_1}{\delta_2} - 1$. Here, $\gamma^+_x = \{ \xi : \xi_1 = 0, x_2 \leq \xi_2 \leq x^{*}_2 \}$, so $F_1 \equiv 0$ on $\gamma^+_x$. The extinction probability is then

$$\left( \int_{x_2^*}^{x_2} e^\int_{x_2}^{x_2} \frac{\beta_1 - \delta_1(1 + \xi)}{\xi(\beta_2 - \delta_2(1 + \xi))} \, d\xi \right) \frac{\delta_1(1 + \xi)}{\xi(\beta_2 - \delta_2(1 + \xi))} \frac{d\xi}{d\xi} X_{1}(0)$$

(3.176)

Let

$$\Phi(x_2) := \int_{x_2}^{x_2^*} e^\int_{x_2}^{\xi} \frac{\beta_1 - \delta_1(1 + \xi)}{\xi(\beta_2 - \delta_2(1 + \xi))} \, d\xi \frac{\delta_1(1 + \xi)}{\xi(\beta_2 - \delta_2(1 + \xi))} \, d\xi$$

(3.177)

$$= \int_{x_2}^{x_2^*} \frac{\beta_2 - \delta_2(1 + \xi)}{\beta_2 - \delta_2(1 + \xi)} \left| \frac{\beta_1 \beta_2 - \delta_1 \delta_2}{\beta_2 \beta_2 - \delta_2 \delta_2} \right| \frac{\beta_1 \beta_1 - \delta_1 \delta_1}{\beta_1 \beta_1 - \delta_1 \delta_1} \frac{\delta_1(1 + \xi)}{\xi(\beta_2 - \delta_2(1 + \xi))} \, d\xi.$$  

(3.178)

After some rearranging, the extinction probability is

$$\left( 1 + \frac{1}{\Phi(x_2)} \right)^{-X_{1}(0)}$$

(3.179)

which, as Figure 3.1 shows, provides an excellent match to numerically determined fixation probabilities, across a range of initial densities, for $N$ as small as 1000.

In contrast, the heuristic argument of [148] gave a fixation probability of $e^{-X_{1}(0) \Phi(x_2)}$, which arises from Feller’s diffusion approximation to the branching process [55, 56]. The two are approximately equal for $\Phi(x_2)$ large, but the heuristic result consistently underestimates the fixation probability.

We obtain a particularly intuitive expression for the fixation probability when a single individual of type 1 invades a resident population at equilibrium, i.e., $\lim_{N \to \infty} \frac{1}{N} x_2^{(N)}(0) = x^{*}_2$. 

In this case,

\[
\lim_{x_2 \to x_2^*} \Phi(x_2) = \frac{1}{1 - \frac{\beta_1}{\delta_2}},
\]

so, if we set

\[
1 + s = \frac{\beta_1}{\delta_2}
\]

the fixation probability is

\[
\frac{1}{1 - s} = s + \mathcal{O}(s^2),
\]

echoing Haldane’s result [71]: \( \frac{\beta_i}{\delta_i} \) is the expected lifetime reproductive success of type \( i \) absent competition, so \( \alpha \) is the relative fitness of type 1 to type 2, less one, which corresponds to the classical selection coefficient. Numerical integration of \( \Phi(x_2) \) shows that in contrast to the classical result from population genetics, the intrinsic birth and death rates contribute independently to the fixation probability, so that two types may have the same carrying capacity, but differing fixation probabilities, contrary to the arguments made in [165]. In particular, comparing fixation probabilities for two invaders
which have the same fitness relative to the resident population (i.e., same ratio $1 + s$),
but different birth and death rates, one finds that the invader with the higher birth rate
(and correspondingly elevated death rate) is more likely to fix in a growing population
($x_2 < x_2^*$) and less likely to fix in shrinking populations ($x_2 > x_2^*$) than the mutant
with lower birth and death rates, as was conjectured by Fisher [59]. We thus see $r$ vs. $K$
selection in this example of a fecundity-mortality tradeoff. We refer the interested reader
to [148] for further discussion of the biological implications of this result.

### 3.2.3 Fixation Time Asymptotics When the Resident Dynamics

have an Attracting Fixed Point

For a subset $I \subseteq \{1, \ldots, K\}$, we will write $\mathbb{R}^I$ for the space $\mathbb{R}^{|I|}$, which we identify
with the coordinate hyperplane $\{x \in \mathbb{R}^K : x_i = 0 \text{ for all } i \notin I\}$, and $F^I$ for the vector
field $(F_i)_{i \in I}$ on $\mathbb{R}^I$, which can be identified with the vector field generated by $F$ on the
hyperplane $x_i = 0, i \notin I$. For each $I \subseteq \{1, \ldots, K\}$, $\mathbb{R}_+^I$ is an invariant subspace for $F$, and thus for $x \in \mathbb{R}_+^I$, $\psi_t$ is also a flow map for $F^I$.

In this section, we will be interested in the case when $I = I_1 := \{2, \ldots, K\}$ and the
dynamical system corresponding to $F^I$ has a fixed point $x^*$ that is globally attracting on
$\mathbb{R}_+^I$. Under this assumption, functions of the form $f(\psi_t x)$ converge exponentially fast,
and are integrable:

**Lemma 3.6.** Assume that $x^*$ is a locally stable fixed point for some vector field $G$ and $x$ is in the basin of attraction of $x^*$, and that $f : \mathbb{R}^d \to \mathbb{R}$ is Lipschitz. Then,

$$
\lim_{t \to \infty} \int_0^t f(\psi_u x) - f(x^*) \, du
$$

exists and is finite. Moreover, regarded as a function of $x$, it is continuous at $x^*$. 
Proof. By assumption, $x$ is hyperbolic, so applying the Hartman-Grobman theorem, there exists a positively invariant neighbourhood $U$ of $x^*$ and a diffeomorphism $h: U \to \mathbb{R}^d$ such that $h(x^*) = 0$ and

$$h(x) = e^{tDG(x^*)}h(x)$$

for all $t$ such that $t \in U$. Moreover, $\psi_t x \to x^*$, so there exists $T > 0$ such that $t \in U$ for all $t > T$. It suffices to show that the tail

$$\int_T^t f(\psi_u x) - f(x^*) \, du$$

is finite for all $t$. Now, $f$ is Lipschitz and $h$ is a diffeomorphism, so $f \circ h^{-1}$ is also Lipschitz, and

$$\left| \int_T^t f(\psi_u x) - f(x^*) \, du \right| = \left| \int_T^t (f \circ h^{-1})(h(\psi_u x)) - (f \circ h^{-1})(h(x^*)) \, du \right|$$

$$= \left| \int_T^t (f \circ h^{-1})(e^{tDG(x^*)}h(x)) - (f \circ h^{-1})(0) \, du \right|$$

$$\leq \int_T^t L \left\| e^{tDG(x^*)}h(x) \right\| \, du$$

$$\leq L \int_T^t Me^{\omega_0} \left\| h(x) \right\| \, du$$

$$\leq \frac{LM}{\omega_0} \left\| h(x) \right\| \left( e^{\omega_0} - e^{T \omega_0} \right),$$

where the growth bound for $DG$,

$$\omega_0 := \lim_{t \to 0} \frac{1}{t} \ln \left\| e^{tDG(x^*)} \right\| = \inf \{ \Re(\lambda) : \lambda \in \sigma(DG(x^*)) \},$$

is negative, since $DG$ is stable (see e.g., [44], Theorem 3.6). Hence

$$\lim_{t \to \infty} \int_T^t f(\psi_u x) - f(x^*) \, du$$
is bounded.

Lastly, if \( x \in U \), then we may take \( T = 0 \), and, from the previous calculation, we have

\[
\left| \int_0^\infty f(\psi_u x) - f(x^*) \, du \right| \leq \frac{LM}{|\omega_0|} \|h(x)\|,
\]

which, by the continuity of \( h \), tends to 0 as \( x \to x^* \), proving continuity at \( x^* \).

In particular, we have \( \tilde{\beta}_i(\psi_t x) - \tilde{\beta}_i(x^*) \) and \( \delta_i(\psi_t x) - \delta_i(x^*) \) are integrable for all \( i \), and, if we constrict branching processes \( Z_{i,x} \) as in Section 3.2.1, then \( Z_{i,x} \) is Malthusian with parameter

\[
f_i(x^*) = \tilde{\beta}_i(x^*) - \delta_i(x^*). \tag{3.194}
\]

Now, by assumption, the limiting dynamical system is dissipative, so the forward orbit \( \gamma_x^+ = \{ \psi_t x : t \geq 0 \} \) is compact. Thus, \( \tilde{\beta}_i, \tilde{\beta}, \) and \( \delta_i \) are bounded, and provided \( \delta_i > 0 \) on \( \gamma_x^+ \), there exists \( \delta_\infty \) such that \( \delta_i(x') > \delta_\infty \) for all \( x' \in \gamma_x^+ \). Under these assumptions, Proposition 3.1 implies \( q_{i,x}(\infty) < 1 \) if and only if \( f_i(x^*) > 0 \).

Notice that the sign of the values \( f_i(x^*) \) also determine the local stability of \( x^* \). For \( x \in \mathbb{R}^I_d \) and \( i \in \{1, \ldots, d\} \),

\[
(\partial_j F_i)(x) = x_j (\partial_j f_i(x)) + \delta_{ij} f_i(x) = \delta_{ij} f_i(x), \tag{3.195}
\]

so that

\[
(DF)(x^*) = \begin{pmatrix}
  f_1(x^*) & \cdots & 0 \\
  \vdots & \ddots & \vdots \\
  f_d(x^*) & \cdots & \delta_d (DF^I_d)(x^*)
\end{pmatrix}. \tag{3.196}
\]

By assumption, \( (DF^I_d)(x^*) \) is a stable matrix, so \( (DF)(x^*) \) is stable if and only if
\( f_i(x^*) < 0 \) for all \( i \in \{1, \ldots, d\} \), i.e., if and only if the corresponding branching processes \( Z_{i,x} \) are subcritical.

In particular, if \( K = 2 \), and type 1 is strongly selected, then \( x^*:1 \) is globally attracting on \( \mathbb{R}^1 \cup \mathbb{R}^2_+ \), whereas \( x^*:2 \) is a saddle point, and we can use Corollary 3.2 and Proposition 3.8 to obtain an asymptotic for the expected time to fixation (i.e., the expected time to absorption, conditioned on type 1 fixing):

**Proposition 3.11.** Let \( \tau^{(N)} := \inf\{t > 0 : X^{(N)}_1(t) = 0 \land X^{(N)}_2(t) = 0\} \). Then, as \( N \to \infty \),

\[
\mathbb{E} \left[ \tau^{(N)} \middle| X^{(N)}_2(\tau^{(N)}) = 0, X^{(N)}_1(0) = 1, \lim_{N \to \infty} \frac{1}{N} X^{(N)}_2(0) = x_2 \right] \sim \left( \frac{1}{f_1(x^*_2)} + \frac{1}{f_2(x^*_1)} \right) \ln N.
\]

**Proof.** We consider three phases:

(i) \( X^{(N)}_1(t) < \varepsilon N \),

(ii) \( X^{(N)}_1(t) \geq \varepsilon N \) and \( X^{(N)}_2(t) \geq \varepsilon N \), and

(iii) \( X^{(N)}_2(t) < \varepsilon N \).

In phases (i) and (iii), we will approximate \( X^{(N)}_1 \) and \( X^{(N)}_2 \) by super- and subcritical branching processes respectively. By assumption, we have \( f_1(x^*_2) > 0 \), so for \( \varepsilon > 0 \) sufficiently small and \( N \) sufficiently large,

\[
f^{(e)}_1 := \frac{\beta^{(e)}_{1,x,+}(\infty)}{\sigma^{(e)}_{1,x,-}(\infty)} - \frac{\delta^{(e)}_{1,x,-}(\infty)}{\delta^{(e)}_{1,x,+}(\infty)} > 0
\]

and

\[
f^{(e)}_1 := \frac{\beta^{(e)}_{1,x,-}(\infty)}{\sigma^{(e)}_{1,x,+}(\infty)} - \frac{\delta^{(e)}_{1,x,+}(\infty)}{\delta^{(e)}_{1,x,-}(\infty)} > 0,
\]

where the rates \( \beta^{(e)}_{1,x,\pm} \) and \( \sigma^{(e)}_{1,x,\pm} \) are defined as in Equation 3.116. Thus, the branching processes \( Z^{(e)}_{1,x,\pm} \) are both supercritical. Similarly, \( f_2(x^*_1) < 0 \), so, for sufficiently small
\( \varepsilon > 0 \) and large \( N \), we have

\[
f_{2,+}^{(e)} := \bar{\beta}_{2,x,+}^{(e)}(\infty) - \delta_{2,x,-}^{(e)}(\infty) > 0 \quad \text{and} \quad f_{2,-}^{(e)} := \bar{\beta}_{2,x,-}^{(e)}(\infty) - \delta_{2,x,+}^{(e)}(\infty) > 0
\]

(3.200)

where the rates \( \bar{\beta}_{2,x,\pm}^{(e)} \) and \( \delta_{2,x,\pm}^{(e)} \) are defined analogously. Hence, the corresponding branching processes \( Z_{2,x,\pm}^{(e)} \) are subcritical. In what follows, we assume that a fixed \( \varepsilon > 0 \) has been chosen so that all these inequalities hold, and as usual that a neighbourhood of radius \( \varepsilon \) of the forward orbit \( \gamma^+_{x} \) is contained in \( K_x \).

We now consider phase (i). Recall that

\[
\tau_{1}^{(e,N)} := \inf \{ t : X_1^{(N)}(t) \geq \varepsilon N \}
\]

(3.201)

and define

\[
\tau_{1,\pm}^{(e,N)} := \inf \{ t : Z_{1,x,\pm}^{(e)}(t) \geq \varepsilon N \}
\]

(3.202)

Now, for \( t < \tau_{1}^{(e,N)} \),

\[
Z_{1,x,-}^{(e)}(t) \leq X_1^{(N)}(t) \leq Z_{1,x,+}^{(e)}(t),
\]

(3.203)

so we must have \( \tau_{1,+}^{(e,N)} \leq \tau_{1}^{(e,N)} \leq \tau_{1,-}^{(e,N)} \) and

\[
\mathbb{E}\left[ \tau_{1,+}^{(e,N)} \right] Z_{1,x,+}^{(e)}(\tau_{1,+}^{(e,N)}) \geq \varepsilon N \right] < \mathbb{E}\left[ \tau_{1}^{(e,N)} \right] X_1^{(N)}(\tau_{1}^{(e,N)}) \geq \varepsilon N \right] < \mathbb{E}\left[ \tau_{1,-}^{(e,N)} \right] Z_{1,x,-}^{(e)}(\tau_{1,-}^{(e,N)}) \geq \varepsilon N \right]
\]

(3.204)

Then, by Corollary 3.2,

\[
\mathbb{E}\left[ \tau_{1,\pm}^{(e,N)} \right] Z_{1,x,\pm}^{(e)}(\tau_{1,\pm}^{(e,N)}) > \varepsilon N \right] \sim \frac{1}{f_{1,\pm}^{(e)}} \ln \varepsilon N.
\]

(3.205)
We next consider region (ii). Let
\[
x^{(e)} := \lim_{N \to \infty} \frac{1}{N} X^{(N)}(\tau^{(e,N)}),
\] (3.206)
so \(x_1^{(e)} \geq \varepsilon\). We begin by considering the time required for the deterministic limiting process to reach a neighbourhood of the stable attractor \(x_1^*\). Let
\[
\tau^{(e)}_{1 \to 2} := \inf\{t \geq 0 : \psi_2^2 x^{(e)} = \varepsilon\},
\] (3.207)
where \(\psi_1 x = (\psi_1^1 x, \psi_1^2 x)\), and fix some arbitrary point \(x'\) in the trajectory \(\{\psi t x^{(e)} : 0 < t < \tau^{(e)}_{1 \to 2}\}\). Then, \(\tau^{(e)}_{1 \to 2} = \tau^{(e)}_{1,x' \to 1} + \tau^{(e)}_{1,x' \to 2}\), where
\[
\tau^{(e)}_{1,x' \to 2} := \inf\{t \geq 0 : \psi_2^2 x' < \varepsilon\} \quad \text{and} \quad \tau^{(e)}_{1,x' \to 1} := \inf\{t \geq 0 : \psi_1^1 x' < \varepsilon\}. \quad (3.208)
\]

We start by estimating \(\tau^{(e)}_{1,x' \to 2}\). Now,
\[
\frac{d}{dt} \psi_1^2 x' = \psi_1^2 x' f_2(\psi_1 x'),
\] (3.209)
so
\[
\ln \psi_1^2_{\tau^{(e)}_{1,x' \to 2}} x' - \ln x'_2 = \int_0^{\tau^{(e)}_{1,x' \to 2}} f_2(\psi_1 x') \, dt.
\] (3.210)
Further, as \(t \to \infty\), \(\psi_1 x' \to x^{*1}\), so applying Lemma 3.6, we see that \(f_2(\psi_1 x') - f_2(x^{*1})\) is integrable. In particular,
\[
\int_0^{\tau^{(e)}_{1,x' \to 2}} f_2(\psi_1 x') \, dt = \int_0^{\tau^{(e)}_{1,x' \to 2}} f_2(\psi_1 x') - f_2(x^{*1}) \, dt + f_2(x^{*1}) \tau^{(e)}_{1,x' \to 2},
\] (3.211)
and
\[
\int_0^{\tau^{(e)}_{1,x' \to 2}} f_2(\psi_1 x') - f_2(x^{*1}) \, dt < \int_0^\infty f_2(\psi_1 x') - f_2(x^{*1}) \, dt < \infty. \quad (3.212)
\]
Moreover, we have $\psi_{t_{1',x' \to 2}}^2(\epsilon) = \epsilon$, so that

$$
\tau_{1',x' \to 2}^{(\epsilon)} = \frac{1}{f_2(x^* \cdot 2)} \ln \epsilon
$$

(3.213)

is bounded.

To determine $\tau_{1' \to 1}^{(\epsilon)}$, we first observe $\psi^1_{-t}$ is the flow of the vector field $-F$, which has a stable attractor at $x^* \cdot 2$. Proceeding as above, we can conclude that

$$
\tau_{1' \to 1}^{(\epsilon)} + \frac{1}{f_1(x^* \cdot 2)} \ln \epsilon
$$

(3.214)

is bounded. Thus,

$$
\tau_{1 \to 2}^{(\epsilon)} = -\left(\frac{1}{|f_2(x^* \cdot 1)|} + \frac{1}{f_1(x^* \cdot 2)}\right) \ln \epsilon + O(1).
$$

(3.215)

We complete the analysis of phase (ii) by observing that for fixed $\epsilon$, we may apply Proposition 2.1, (ii),

$$
\lim_{N \to \infty} \sup_{t \leq \tau_{1' \to 2}^{(\epsilon)}} \left\| \frac{1}{N} X^{(N)}_t - \psi_{t} x \right\| = 0 \quad \mathbb{P}_{1,x} - a.s.
$$

(3.216)

to conclude that

$$
\lim_{N \to \infty} \frac{1}{N} X^{(N)}_{\tau_{1' \to 2}^{(\epsilon)}} \leq \epsilon.
$$

(3.217)

We are thus in phase (iii), and it only remains to determine the time to extinction of type 2. As with phase (i) we may bound $X^{(N)}_{2, x, \pm}$ above and below by subcritical branching processes $Z^{(\epsilon)}_{2, x, \pm}$, and proceed similarly, observing that

$$
\mathbb{E} \left[ \tau_{1, +}^{(\epsilon,N)} \mid Z^{(\epsilon)}_{2, x, +}(\tau_{1, +}^{(\epsilon,N)}) \geq \epsilon N \right] < \mathbb{E} \left[ \tau_{1}^{(\epsilon,N)} \mid X^{(N)}_{2}(\tau_{1}^{(\epsilon,N)}) \geq \epsilon N \right]
\leq \mathbb{E} \left[ \tau_{1, -}^{(\epsilon,N)} \mid Z^{(\epsilon)}_{2, x, -}(\tau_{1, -}^{(\epsilon,N)}) \geq \epsilon N \right],
$$

(3.218)
and, recalling Proposition 3.8, that

\[
E\left[\tau_1^{(\epsilon,N)} | Z_{2,x,\pm}(\tau_1^{(\epsilon,N)}) > \epsilon N \right] \sim \frac{1}{f_2^{(\epsilon)}(\tau_1^{(\epsilon,N)})} \ln \epsilon N. \tag{3.219}
\]

Combining all the above, we see that for \( N \) sufficiently large,

\[
\tau_{1 \rightarrow 2}^{(\epsilon)} + \frac{1}{f_{1,1}^{(\epsilon)}} \ln \epsilon N + \frac{1}{f_{2,1}^{(\epsilon)}} \ln \epsilon N \leq E(1,Nx^2) \left[ \tau_1^{(N)} \right] X_2^{(N)}(\tau^{(N)}) = 0
\]

\[
\leq \tau_{1 \rightarrow 2}^{(\epsilon)} + \frac{1}{f_{1,1}^{(\epsilon)}} \ln \epsilon N + \frac{1}{f_{2,1}^{(\epsilon)}} \ln \epsilon N \tag{3.220}
\]

By definition of \( f_{i,\pm}^{(\epsilon)} \), we have that \( f_1(x^*,2) - f_{1,1}^{(\epsilon)} = O(\epsilon) \), and \( f_2(x^*,1) - f_{2,1}^{(\epsilon)} = O(\epsilon) \) so that

\[
\left( \frac{1}{f_{1,1}^{(\epsilon)}} - \frac{1}{f_1(x^*,2)} \right) \ln \epsilon \rightarrow 0, \quad \text{and} \quad \left( \frac{1}{f_{2,1}^{(\epsilon)}} - \frac{1}{f_2(x^*,1)} \right) \ln \epsilon \rightarrow 0 \tag{3.221}
\]

as \( \epsilon \rightarrow 0 \). The result follows.

\[\square\]

**Example 3.4.** Applying this result to the Generalized Moran model, Example 2.1, for which \( x^{*,i} = \left( \frac{\delta_i}{\delta} - 1 \right) e_i \), we get the following simple and appealing form for the fixation time,

\[
\left( \frac{1}{\delta_1} + \frac{1}{\delta_2} \right) \frac{\delta_1}{\delta} - \frac{\delta_2}{\delta} \ln N.
\]

Note that \( \frac{1}{\delta_i} \) is the expected lifetime of an individual of type \( i \) in the absence of competition, whereas

\[
\frac{1}{\delta_1} + \frac{1}{\delta_2}
\]

is the harmonic mean of the individual intrinsic death rates (absent competition). In particular, we can interpret the leading term in the fixation time, \( \frac{1}{\delta_1} + \frac{1}{\delta_2} \), as an effective expected individual life span in a mixed population. Thus, measured in units of "effec
tive life spans”, the fixation time depends only on the difference in per-capita expected lifetime reproductive success \( \frac{\beta_1}{\delta_1} - \frac{\beta_2}{\delta_2} \), and not on individual life histories. This is an interesting contrast to the fixation probabilities (Corollary 3.5), which may be understood via Equation 3.180. There, we saw that if the mutant invades when the wild-type is already at equilibrium, then the fixation probability was determined by difference in per-capita expected lifetime reproductive success. Now, fixation probabilities are determined in the very short term, where numbers are small and the resident may still be far from equilibrium. Here, we have conditioned on non-extinction of the invading type, so we know it will survive. It will also, crucially, spend considerable time growing from small to intermediate numbers, and during this period the resident will have long since arrived at equilibrium. Similarly, the balance of the fixation time will be spent with the final few wild-type individuals fizzling out while type 1 is at it’s equilibrium density – the proof of Proposition 3.11 shows that the time of traverse of phase space from \( \varepsilon N \) individuals of type 1 to \( \varepsilon N \) individuals of type 2 is negligible in comparison to the required to get from 1 to \( \varepsilon N \) individuals of type 1 or \( \varepsilon N \) to no individuals of type 2. Thus, the fixation time is determined by the dynamics near the unstable attractor \( x^{*-2} \) and the stable attractor \( x^{*-1} \).

### 3.3 Summary

In this chapter, we sought to understand the dynamics of a birth-death-mutation process when a single mutant of type 1 invades an established wild-type population. The crucial tool was Proposition 3.9, which showed that when the number of individuals of type 1 is less than \( \varepsilon N \), their numbers can be stochastically bounded above and below by time-inhomogeneous Markov branching processes. We could thus adapt previously obtained results on the survival probability of a branching process (Corollary 3.1) to obtain the probability that type 1 successfully invades, that is, the probability that the
number of individuals of type 1 hits $\varepsilon N$ prior to extinction. In the last chapter, we saw that should this happen, the subsequent dynamics are essentially deterministic. We thus have a relatively complete picture of the dynamics in the strong selection case, where invasion implies fixation. In particular, we can obtain explicit expressions for the fixation probabilities (Corollary 3.5) and fixation times (Proposition 3.11) for quite general models. When the mutant invades a wild-type population at its demographic equilibrium, we recover Haldane’s classical result, that the fixation probability is approximately the relative fitness of the invading type. In departure from the classical case, we see that life history strategy matters in determining fixation probabilities when the wild-type is away from equilibrium. We find that $r$ vs. $K$ selection occurs, and that among types with the same expected lifetime reproductive success, those that achieve it through higher birth rates (and correspondingly elevated death rates) do better when the resident population has dropped below equilibrium, whereas longer-living types that forego allocation to reproduction in favour of self-preservation are more likely to successfully invade a resident population near carrying capacity. This has interesting implications for the study of bottlenecks and the way they shape evolution.
Chapter 4

Weak Selection

In this chapter, we consider the case of weak selection, when the dynamical system arising as the functional Law of Large Numbers (Proposition 2.1) for a density dependent birth-death-mutation process $X^{(N)}(t)$ has an attracting embedded submanifold of fixed points, $C$. As we observed previously, each point of $C$ is an equilibrium point for the deterministic dynamics at which two or more types stably coexist. In this chapter, we will see that, unlike the approximating deterministic process, the stochastic birth-death-mutation process does not remain at rest, but continues to traverse $C$ until all but one of the types disappear.

To be precise, we assume that the initial number of individuals of all types is proportional to $N$, and show that the time-rescaled process

$$Z^{(N)}(t) := \frac{1}{N}X^{(N)}(Nt)$$

converges in distribution to a diffusion process $Z(t)$ on $C$. In fact, we will show that this is true for a broader class of density dependent processes, of which birth-death-mutation processes are only a subset.

We then show how the infinitesimal generator of the limiting diffusion may be computed from the transition rates of the original discrete process, and give an explicit
expression for the generic generator when \( C \) has co-dimension one.

Both the proof of existence and characterization of the limiting process critically involve a projection map, \( \pi(x) \). As before, we take \( \psi_t \) to be the flow map for the deterministic dynamical system that arises in the functional Law of Large Numbers. Given a point \( x \in \mathbb{R}_+^K \),

\[
\pi(x) = \lim_{t \to \infty} \psi_t x,
\]

so \( \pi(x) \) is the stationary point on \( C \) at which the deterministic process comes to rest when started from an initial point \( x \). We will show that, given a family of density dependent processes \( X^{(N)}(t) \) such that

\[
\lim_{N \to \infty} \frac{1}{N} X^{(N)}(t) = x,
\]

the limiting process \( Z(t) \) jumps instantaneously from its initial condition \( Z(0) = x \) to \( \pi(x) \), after which it diffuses across \( C \). Knowing the first and second partial derivatives of \( \pi \) will be crucial in characterizing \( Z \), so we dedicate some effort to devising several means of computing them from the vector field \( F \) that defines \( \psi_t \).

We then specialize these results to the case of a weakly selected density dependent birth-death-mutation processes in co-dimension one. We show that when the process \( X^{(N)}(t) \) is exchangeable, we recover Kimura’s diffusion after an appropriate time-change. We then consider the consequences of relaxing the various assumptions that constitute exchangeability, seeing how different individual traits give rise to novel drift terms in the limiting diffusion, and how they can be interpreted as selection coefficients. Finally, we end the chapter by giving explicit expressions for the fixation probabilities, absorption times, and fixation times for the two-type Generalized Moran model without mutation, compute the quasi-stationary distribution when mutation between types is possible, and discuss the potential implications of more biologically realistic life-history strategies for current approaches to inferring natural selection.
4.1 Convergence to a Diffusion on $\mathcal{C}$

Throughout this section, we assume that $X^{(N)}$ is the family of density dependent population processes corresponding to the family of rate functions $\{\lambda_n^{(N)}(x)\}$, subject to Assumptions 2.1 and 2.2. Thus,

$$\mathbf{F}^{(N)}(x) = \sum_{n \in \mathbb{Z}^K} n\lambda_n^{(N)}(x) \rightarrow \mathbf{F}(x) = \sum_{n \in \mathbb{Z}^K} n\lambda_n(x) \quad (4.2)$$

and

$$\nu^{(N)}(x) := N \sum_{n \in \mathbb{Z}^K} n \left( \lambda_n^{(N)}(x) - \lambda_n(x) \right) \rightarrow \nu(x) \quad (4.3)$$

uniformly on compact sets.

Throughout this section, we assume that $\mathbf{F} \in C^2(\mathbb{R}_+^K, \mathbb{R}^K)$ and that the $\omega$-limit set, $\mathcal{C}$, of the corresponding dynamical system is a embedded submanifold (possibly with corners) of $\mathbb{R}_+^K$ consisting of fixed points of $\mathbf{F}$. By assumption, the dynamical system corresponding to the vector field $\mathbf{F}$ is dissipative, so $\mathcal{C}$ is compact.

We also set

$$M^{(N)}(t) := \frac{1}{N} \sum_{n \in \mathbb{Z}^K} n\tilde{H}_n^{(N)}(Nt), \quad (4.4)$$

where $H_n^{(N)}(t)$ is a counting process with intensity $\lambda_n^{(N)}(X^{(N)}(t))$ and $\tilde{H}_n^{(N)}$ is the corresponding centered process. Thus,

$$Z^{(N)}(t) = Z^{(N)}(0) + \int_{0^+}^t N\mathbf{F}^{(N)}(Z^{(N)}(s-)) \, ds + M^{(N)}(t), \quad (4.5)$$

while $M^{(N)}(t)$ is a square integrable local martingale with tensor quadratic variation\(^1\)

$$[M^{(N)}](t) = \frac{1}{N^2} \sum_{n \in \mathbb{Z}^K} nn^\top H_n^{(N)}(Nt). \quad (4.6)$$

\(^1\)see A.7 for a definition of the tensor quadratic variation and Meyer process
and corresponding Meyer process

\[ \langle M^{(N)} \rangle (t) = \frac{1}{N^2} \int_{0^+}^{t} \sum_{n \in \mathbb{Z}^K} \mathbf{n}^\top \lambda_n^{(N)} (Z_n^{(N)}(s-)) \, ds. \] (4.7)

As always, we write \( \psi_t \) for the flow map of the dynamical system

\[ \dot{\psi}_t \mathbf{x} = F(\psi_t \mathbf{x}). \] (4.8)

Set

\[ \pi(\mathbf{x}) := \lim_{t \to \infty} \psi_t \mathbf{x}, \] (4.9)

so \( \pi \) is a projection onto the \( \omega \)-limit set for \( F \), taking the initial state \( \mathbf{x} \) to the corresponding equilibrium. Note that \( \psi_t \) — and thus \( \pi \) — is also \( C^2 \) [81].

We now turn to the main result of this chapter, which is to characterize the limit of \( \pi(Z^{(N)}(t)) \) as \( N \to \infty \). The proof proceeds in several steps:

(i) We begin with a local convergence result, showing that if the time-rescaled process starts on \( \mathcal{C} \) (to be precise, \( Z^{(N)}(0) \overset{\mathcal{D}}{\to} Z(0) \in \mathcal{C} \)), then the process will remain on \( \mathcal{C} \). We proceed by constructing a Lyapunov function, \( V \), for \( \psi_t \) in a neighbourhood of \( \mathcal{C} \), and then show that \( V(Z^{(N)}(t)) \overset{\mathcal{D}}{\to} 0 \).

(ii) From the previous step, we conclude that \( \pi(Z^{(N)}(t)) \overset{\mathcal{D}}{\to} \pi(Z(t)) \), and show that the latter is a diffusion process on \( \mathcal{C} \).

(iii) Finally, we observe that when \( Z(0) \notin \mathcal{C} \), the process \( Z(t) \) fails to be Feller, but that the process

\[ \tilde{Z}^{(N)}(t) := Z^{(N)}(t) - \psi_N t Z^{(N)}(0) + \pi(Z^{(N)}(0)), \] (4.10)

which gives the fluctuations about the deterministic trajectory, converges weakly to a diffusion process on \( \mathcal{C} \).

Throughout, we assume that the first and second derivatives of \( \pi(\mathbf{x}) \) are known. In the
next section, we will turn to the task of computing these derivatives, given the vector field \( F(x) \).

**Definition 4.1.** Let \( U \subset \mathbb{R}_+^K \) be a neighbourhood of \( C \). A function \( V: U \to \mathbb{R}_+ \) is a strong Lyapunov function for \( F \) if

(i) \( V(x) \geq 0 \) and \( V(x) = 0 \) if and only if \( x \in C \), and

(ii) There exists a constant \( \lambda < 0 \) such that

\[
\dot{V}(x) := D V(x) \cdot F(x) \leq \lambda V(x) \tag{4.11}
\]

for all \( x \in U \).

If we assume that \( C \) is an embedded submanifold, then constructing a strong Lyapunov function near \( C \) is a straightforward generalization of the construction of a Lyapunov function near a hyperbolic fixed point (see e.g., [70]).

**Proposition 4.1.** Assume that \( C \) is an embedded submanifold of \( \mathbb{R}^K \). Then, there is a strong Lyapunov function for \( F \).

**Proof.** The proof proceeds in two steps. First, we consider a fixed \( x^* \in C \) and construct a strong Lyapunov function \( V_{x^*} \) in a neighbourhood \( U_{x^*} \) of \( x^* \). We then show that if \( C \) is compact, then finitely many such functions may be pieced together to form a global Lyapunov function.

Let \( \Phi_{x^*} \) be a slice chart defined in a neighbourhood \( \tilde{U}_{x^*} \) of \( x^* \), so \( \Phi_{x^*}(x^*) = 0 \) and

\[
\Phi_{x^*}^{d+1}(x) = \cdots = \Phi_{x^*}^{d+n}(x) = 0 \quad \text{for all } x \in C \cap \tilde{U}_{x^*}. \tag{4.12}
\]

Let

\[
G(x) := (D \Phi_{x^*})(\Phi_{x^*}^{-1}(x))F(\Phi_{x^*}^{-1}(x)). \tag{4.13}
\]

Then,
Chapter 4. Weak Selection

(i) \( G(0) = 0 \),

(ii) \((DG)(0)\) is similar to \((DF)(x^*)\), with change of basis matrix \((D\Phi_{x^*})(x^*)\), and

(iii) \( \text{Ker}(DG)(0) = \{ x \in \mathbb{R}^K : x_{d+1} = \cdots x_n = 0 \} \).

Moreover, without loss of generality, \( \Phi_{x^*} \) may be chosen so that \((DG)(0)\) is in real Jordan canonical form, i.e.,

\[
(DG)(0) = \begin{bmatrix}
J_0 \\
J_1 \\
\vdots \\
J_p
\end{bmatrix},
\]

where \( J_0 \) is a \( d \times d \) matrix of zeroes and \( J_1, \ldots, J_p \) are non-zero \( d_i \times d_i \) Jordan blocks.

We introduce a further change of coordinates. Suppose \( J_i \) corresponds to a real eigenvalue \( \lambda_i \),

\[
J_i = \begin{bmatrix}
\lambda_i & 1 \\
& \lambda_i & \ddots \\
& & \ddots & 1 \\
& & & \lambda_i
\end{bmatrix}.
\]

Then set

\[
Q_i := \begin{bmatrix}
\varepsilon^{-1} \\
& \varepsilon^{-2} \\
& & \ddots \\
& & & \varepsilon^{-d_i}
\end{bmatrix}.
\]

If \( J_i \) corresponds to a complex conjugate pair of eigenvalues, \( \lambda_i \pm i\omega_i \), i.e.,

\[
J_i = \begin{bmatrix}
\Lambda_i & \mathbf{I}_{2 \times 2} \\
& \Lambda_i & \ddots \\
& & \ddots & \mathbf{I}_{2 \times 2} \\
& & & \Lambda_i
\end{bmatrix}.
\]
for $\Lambda_i = \begin{bmatrix} \lambda_i & -\omega_i \\ \omega_i & \lambda_i \end{bmatrix}$, then let

$$Q_i := \begin{bmatrix} \varepsilon^{-1} I_{2 \times 2} & & & \\ & \varepsilon^{-2} I_{2 \times 2} & & \\ & & \ddots & \\ & & & \varepsilon^{-d_i} I_{2 \times 2} \end{bmatrix}. \quad (4.18)$$

Finally, let

$$Q := \begin{bmatrix} I_{d \times d} & & & \\ & Q_1 & & \\ & & \ddots & \\ & & & Q_p \end{bmatrix}. \quad (4.19)$$

and let $\tilde{G}(x) := QG(Q^{-1}x)$. Then $(DG)(0)$ is a block-diagonal matrix with blocks

$$Q_i J_i Q_i^{-1} = \begin{bmatrix} \lambda_i & \varepsilon \\ \varepsilon & \ddots \\ & \ddots & \ddots \\ & & \ddots & \lambda_i \end{bmatrix}, \quad (4.20)$$

or

$$Q_i J_i Q_i^{-1} = \begin{bmatrix} \Lambda_i & \varepsilon I_{2 \times 2} \\ \varepsilon I_{2 \times 2} & \ddots \\ & \ddots & \ddots \\ & & \ddots & \Lambda_i \end{bmatrix}. \quad (4.21)$$

if the corresponding eigenvalues are real or complex, respectively. Let $m_i = d + \sum_{j=1}^{d_i} d_j$. 

If \( J_i \) corresponds to a real eigenvalue, then

\[
(D\tilde{G})(0)_{mj} = \begin{cases} 
\lambda_i x_{m_i+j} + \varepsilon x_{m_i+j+1} & \text{if } j < d_i \\
\lambda_i x_{m_i+d_i} & \text{otherwise},
\end{cases}
\]  

(4.22)

whereas if \( J_i \) corresponds to a complex eigenvalue,

\[
(D\tilde{G})(0)_{mj} = \begin{cases} 
\lambda_i x_{m_i+j} - \omega_i x_{m_i+j+1} + \varepsilon x_{m_i+j+2} & \text{if } j = 2k - 1 < d_i - 1 \\
\omega_i x_{m_i+j-1} + \lambda_i x_{m_i+j} + \varepsilon x_{m_i+j+2} & \text{if } j = 2k < d_i \\
\lambda_i x_{m_i+d_i-1} - \omega_i x_{m_i+d_i} & \text{if } j = d_i - 1 \\
\omega_i x_{m_i+d_i-1} + \lambda_i x_{m_i+d_i} & \text{if } j = d_i.
\end{cases}
\]  

(4.23)

Now, let

\[
\tilde{V}_x^*(x) = \sum_{i=d+1}^{n} x_i^2.
\]  

(4.24)

We claim that \( \tilde{V}_x^*(x) \) is a Lyapunov function for \( \tilde{G}(x) \). Firstly,

\[
D\tilde{V}_x^*(x) \cdot \tilde{G}(x) = \sum_{j=d+1}^{n} x_j \tilde{G}_j
\]  

(4.25)

can be considered as the sum of terms corresponding to the blocks \( Q_i J_i Q_i^{-1} \). If if \( J_i \)
corresponds to a real eigenvalue,

$$\sum_{j=1}^{d_i} x_{m_i+j} \tilde{G}_{m_i+j}(x) = \lambda_i \sum_{j=1}^{d_i} x_{m_i+j}^2 + \varepsilon \sum_{j=1}^{d_i-1} x_{m_i+j} x_{m_i+j+1} + O(|x|^3)$$

$$= \left(\lambda_i - \frac{\varepsilon}{2}\right) \left(\sum_{j=1}^{d_i} x_{m_i+j}^2 + x_{m_i+d_i}^2\right) + \left(\lambda_i - \varepsilon\right) \sum_{j=1}^{d_i} x_{m_i+j}^2 + \frac{\varepsilon}{2} \sum_{j=2}^{d_i-1} (x_{m_i+j} + x_{m_i+j+1})^2 + O(|x|^3)$$

$$\leq \left(\lambda_i - \frac{\varepsilon}{2}\right) \left(\sum_{j=1}^{d_i} x_{m_i+j}^2 + x_{m_i+d_i}^2\right) + \left(\lambda_i - \varepsilon\right) \sum_{j=1}^{d_i} x_{m_i+j}^2 + \varepsilon \sum_{j=2}^{d_i-1} (x_{m_i+j} + x_{m_i+j+1})^2 + O(|x|^3)$$

$$= \left(\lambda_i + \frac{\varepsilon}{2}\right) \left(\sum_{j=1}^{d_i} x_{m_i+j}^2 + x_{m_i+d_i}^2\right) + \lambda_i \sum_{j=1}^{d_i} x_{m_i+j}^2 + O(|x|^3) \quad (4.26)$$

Proceeding similarly, the same inequality holds for terms arising from a block corresponding to a complex eigenvalue. In particular, if we take $\max\{\lambda_1, \ldots, \lambda_r\} < \lambda_{x^*} < 0$ and choose $\varepsilon > 0$ such that $(\lambda_i + \varepsilon) < \lambda_{x^*}$, then

$$\sum_{j=d+1}^{n} x_j \tilde{G}_j(x) \leq \lambda_{x^*} \sum_{j=1}^{d_i} x_{m_i+j}^2 + O(|x|^3). \quad (4.27)$$

Lastly, since $\lambda_{x^*}, \tilde{V}_{x^*}(x) < 0$ for all $x \not\in C$, we see that for $x$ in a sufficiently small neighbourhood $\tilde{V}$ of $0$, $D \tilde{V}_{x^*}(x) \cdot \tilde{G}(x) \leq \lambda_{x^*} \tilde{V}_{x^*}(x)$.

Now, let $U_{x^*} = \tilde{U}_{x^*} \cap \Phi_{x^*}^{-1}(Q^{-1} W)$ and $V_{x^*}(x) = \tilde{V}_{x^*}(Q \Phi_{x^*}(x))$. Clearly, $V_{x^*}(x) = 0$ if and only if $x \not\in U_{x^*} \cap C$. Direct calculation shows that

$$DV_{x^*}(x) \cdot F(x) \leq \lambda_{x^*} V_{x^*}(x) \quad \text{for all } x \in U_{x^*}. \quad (4.28)$$

To complete the proof, take a family $\{(U_{x^*}, V_{x^*})\}_{x^* \in C}$ of strong Lyapunov functions along $C$, and for each $x^* \in C$ let $\psi_{x^*}(x)$ be bump function vanishing off $U_{x^*}$ and equal to 1 on a neighbourhood $W_{x^*} \subset U_{x^*}$ of $x^*$. Since $C$ is compact, $\{W_{x^*}\}_{x^* \in C}$ admits a finite
subcover \( \{ \mathcal{W}_{x_1}, \ldots, \mathcal{W}_{x_s} \} \). Then

\[
V(x) = \lim_{y \to x} \frac{1}{\sum_{j=1}^{s} \psi_{x_j}(y)} \psi_{x_j}(y) V_{x_j}(y)
\]

is a strong Lyapunov function on the neighbourhood \( \mathcal{U} = \bigcup_{j=1}^{s} \mathcal{W}_{x_j} \) of \( C \) for \( \lambda = \max\{\lambda_{x_1}, \ldots, \lambda_{x_s}\} \). \( \square \)

**Remark 4.1.** A sufficient condition for \( C \) to be an embedded manifold of co-dimension \( d \), which will be adequate for the examples contained herein, is the existence of a submersion \( f : \mathbb{R}^K \to \mathbb{R}^{N-d} \) such that \( C = f^{-1}(0) \). To see this, consider \( x^* \in C \). Reordering the coordinates, if necessary, we can assume that \( \frac{\partial (f_1, \ldots, f_{N-d})}{\partial (x_{d+1}, \ldots, x_N)}(x^*) \) is invertible, so

\[
\Phi_{x^*}(x) = (x_1 - x_1^*, \ldots, x_d - x_d^*, f(x))
\]

has rank \( N \) at \( x^* \), and thus has a differentiable inverse in a neighbourhood \( \mathcal{U}_{x^*} \), yielding the desired slice chart.

**Remark 4.2.** If \( f : \mathbb{R}^K \to \mathbb{R}^K \) is not a submersion, its zero set need not be an embedded submanifold, e.g., let \( f : \mathbb{R}^2 \to \mathbb{R}^2 \) be given by

\[
f_i(x) = c_i(x_1^2 - x_2^3),
\]

for fixed constants \( c_1, c_2 \). Then \( f^{-1}(0) \) has a cusp at \( 0 \), and is thus not an embedded submanifold.

Now, recall from Section 2.1.2 that, for \( x \in \mathbb{R}^K_+ \), \( \mathcal{K}_x \) is assumed to be a compact set containing a neighbourhood of the forward orbit \( \gamma_x^+ \), and \( L_x > 0 \) is a constant such that

\[
\|F(x_1) - F(x_2)\| < L_x \|x_1 - x_2\|
\]

for all \( x_1, x_2 \in \mathcal{K}_x \).
Corollary 4.1. Let $V : \mathcal{U} \to \mathbb{R}^+$ be a strong Lyapunov function for $F$ with corresponding constant $\lambda$, and fix $r$, $r'$ and $s$ such that $0 < r' < \frac{\lambda/(1-s)}{4L_{x,c}}$ and $r' < r < s < 1$. Then

$$\mathbb{P} \left\{ \left| V \left( Y^{(N)} \left( \frac{(1-s)}{4L_{x,c}} \ln N \right) \right) \right| > N^{-r'} \right\} < N^{-r} \quad (4.33)$$

for $N$ sufficiently large.

Proof. From the previous proposition, we have

$$\frac{d}{dt} V(\psi_t x) \leq \lambda V(\psi_t x) \quad (4.34)$$

for all $x \in \mathcal{U}$.

Choose $\delta > 0$ sufficiently small that $C_\delta := V^{-1}([0, \delta]) \subseteq \mathcal{U}$. By definition, $\psi_t x$ is eventually in $C_\delta$ for all $x \in \mathbb{R}^K_x$. Thus, there exists $T_{\delta,x}$ such that $\psi_t x \in \mathcal{U}$ for all $t \geq T_{\delta,x}$. Then, using Gronwall’s inequality, we have

$$V(\psi_t x) \leq V(\psi_{T_{\delta,x}} x) e^{\lambda(t-T_{\delta,x})} \quad \text{for} \quad t > T_{\delta,x} \quad (4.35)$$

In particular, for $N$ sufficiently large, $(1-s)/(4L_{x,c}) \ln N > T_{\delta,x}$, and

$$V \left( \psi_{(1-s)/(4L_{x,c}) \ln N} x \right) \leq V(\psi_{T_{\delta,x}} x) e^{-\lambda T_{\delta,x} N \frac{(1-s)}{4L_{x,c}}} . \quad (4.36)$$

Now, $V$ is locally Lipschitz on $C_\delta$, so there exists $L_\delta$ such that $|V(x) - V(y)| \leq L_\delta \|x - y\|$ for all $x, y \in C_\delta$. Thus,

$$\left| V \left( Y^{(N)} \left( \frac{(1-s)}{4L_{x,c}} \ln N \right) \right) \right| \leq \left| V \left( Y^{(N)} \left( \frac{(1-s)}{4L_{x,c}} \ln N \right) \right) - V \left( \psi_{(1-s)/(4L_{x,c}) \ln N} x \right) \right| + \left| V \left( \psi_{(1-s)/(4L_{x,c}) \ln N} x \right) \right|$$

$$\leq L_\delta \left\| Y^{(N)} \left( \frac{(1-s)}{4L_{x,c}} \ln N \right) - \psi_{(1-s)/(4L_{x,c}) \ln N} x \right\| + V \left( \psi_{T_{\delta,x}} x \right) e^{-\lambda T_{\delta,x} N \frac{(1-s)}{4L_{x,c}}} . \quad (4.37)$$
The result then follows from Proposition 2.1, as

\[
P \left\{ \left\| Y^{(N)} \left( \frac{(1 - s)}{4L_{\xi,\varepsilon}^2} \ln N \right) - \psi \left( \frac{(1 - s)}{4L_{\xi,\varepsilon}^2} \ln N \right) \right\| > N^{-r} \right\} < N^{-r}. \tag{4.38}
\]

From the Corollary, we see that as as \( N \to \infty \) the process will come arbitrarily close to the manifold of fixed points. We next show that in the limit, the process is then effectively confined to the \( \omega \)-limit set; in the next section, we will characterize the process there.

**Theorem 4.1.** Let \( V : \mathcal{U} \to \mathbb{R}_+ \) be a strong Lyapunov function for \( F \) with constant \( \lambda \), and assume \( Z^{(N)}(0) \xrightarrow{\mathcal{D}} Z(0) \in \mathcal{C} \). Then,

\[
V(Z^{(N)}(t)) \xrightarrow{\mathcal{D}} 0 \tag{4.39}
\]

in \( \mathbb{D}_R[0, \infty) \).

**Remark 4.3.** It follows immediately [17] that \( V(Z^{(N)}) \xrightarrow{P} 0 \) as \( N \to \infty \).

**Proof.** Choose \( \delta > 0 \) sufficiently small that \( \mathcal{C}_\delta := V^{-1}([0, \delta]) \subseteq \mathcal{U} \), and define a family of stopping times

\[
T^{(N)}_\delta = \inf\{ t > 0 : V(Z^{(N)}(t)) > \delta \}. \tag{4.40}
\]

We will show that the stopped processes \( V(Z^{(N)}(t \wedge T^{(N)}_\delta)) \) converge in \( L^2 \) for \( t \in [0, T] \) for any \( T > 0 \). Weak convergence to 0 in \( \mathbb{D}_R[0, T] \) is immediate, whilst weak convergence in \( \mathbb{D}_R[0, \infty) \) follows from Theorem 3' in [128]. Thus (see e.g., [17])

\[
V(Z^{(N)}(t \wedge T^{(N)}_\delta)) \xrightarrow{P} 0 \tag{4.41}
\]
as $N \to \infty$ also. Given this, the theorem follows immediately, as

$$
\mathbb{P}\{t > T^{(N)}_\delta\} = \mathbb{P}\{V(Z^{(N)}(t \wedge T^{(N)}_\delta)) > \delta\} \to 0 \quad \text{as} \; N \to \infty. \quad (4.42)
$$

Applying Itô’s formula [161] to the pure jump process $e^{-NM}V(Z^{(N)}(t \wedge T^{(N)}_\delta))$ and rearranging yields

$$
V(Z^{(N)}(t \wedge T^{(N)}_\delta)) = e^{NM}V(Z^{(N)}(0))
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} Ne^{N\lambda(t-s)} (DV(Z^{(N)}(s-)) \cdot F^{(N)}(Z^{(N)}(s-)) - \lambda V(Z^{(N)}(s-))) \, ds
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} e^{N\lambda(t-s)} DV(Z^{(N)}(s-)) \cdot dM^{(N)}(s) + \varepsilon^{(N)}(t)
$$

$$
= e^{NM}V(Z^{(N)}(0)) + \int_{0^+}^{t \wedge T^{(N)}_\delta} Ne^{N\lambda(t-s)} (DV(Z^{(N)}(s-)) \cdot F^{(N)}(Z^{(N)}(s-)) - \lambda V(Z^{(N)}(s-))) \, ds
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} Ne^{N\lambda(t-s)} DV(Z^{(N)}(s-)) \cdot (F^{(N)}(Z^{(N)}(s-)) - F(Z^{(N)}(s-))) \, ds
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} e^{N\lambda(t-s)} DV(Z^{(N)}(s-)) \cdot dM^{(N)}(s) + \varepsilon^{(N)}(t \wedge T^{(N)}_\delta) \quad (4.43)
$$

where

$$
\varepsilon^{(N)}(t) = \sum_{0 < s \leq t} \left\{ V(Z^{(N)}(s)) - V(Z^{(N)}(s-)) - DV(Z^{(N)}(s-)) \cdot \Delta Z^{(N)}(s) \right\}. \quad (4.44)
$$

Now, $V$ is a strong Lyapunov function and $Z^{(N)}(t) \in \mathcal{U}$ for $t \leq T^{(N)}_\delta$, so $DV(Z^{(N)}(s-)) \cdot F(Z^{(N)}(s-)) - \lambda V(Z^{(N)}(s-)) \leq 0$ and

$$
0 \leq V(Z^{(N)}(t \wedge T^{(N)}_\delta)) \leq V(Z^{(N)}(0))
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} Ne^{N\lambda(t-s)} DV(Z^{(N)}(s-)) \cdot (F^{(N)}(Z^{(N)}(s-)) - F(Z^{(N)}(s-))) \, ds
$$

$$
+ \int_{0^+}^{t \wedge T^{(N)}_\delta} e^{N\lambda(t-s)} DV(Z^{(N)}(s-)) \cdot dM^{(N)}(s) + \varepsilon^{(N)}(t \wedge T^{(N)}_\delta). \quad (4.45)
$$
In particular, applying the Cauchy–Bunyakovsky–Schwarz inequality, we have

\[
0 \leq V(Z^{(N)}(t \wedge T_{\delta}^{(N)}))^2 \leq 4 \left[ V(Z^{(N)}(0))^2 + \left( \int_{0+}^{t \wedge T_{\delta}^{(N)}} N e^{N \lambda (t \wedge T^{(N)}) - s} \Delta V(Z^{(N)}(s-)) \cdot (F^{(N)}(Z^{(N)}(s-)) - F(Z^{(N)}(s-))) \, ds \right)^2 \right. \\
+ \left. \left( \int_{0+}^{t \wedge T_{\delta}^{(N)}} e^{N \lambda (t \wedge T^{(N)}) - s} \Delta V(Z^{(N)}(s-)) \cdot dM^{(N)}(s) \right)^2 + \left( \epsilon^{(N)}(t \wedge T_{\delta}^{(N)}) \right)^2 \right].
\]  \tag{4.46}

Applying Jensen’s inequality, we have

\[
\frac{\epsilon^{(N)}(t \wedge T_{\delta}^{(N)})}{e^{N \lambda (t - s)}} \leq e^{2N \lambda (s - (t \wedge T^{(N)})}) ds = \frac{1}{2N \lambda} (e^{N \lambda (t \wedge T_{\delta}^{(N)})} - 1),
\]  \tag{4.47}

i.e., \( \sup_{t \leq T} \frac{\epsilon^{(N)}(t \wedge T_{\delta}^{(N)})}{e^{N \lambda (t - s)}} \leq \frac{C_{1, \delta}}{2N |\lambda|} \) for some constant \( C_{1, \delta} \).

Using Doob’s Inequality, we have

\[
\mathbb{E} \left[ \sup_{t \leq T} \frac{\epsilon^{(N)}(t \wedge T_{\delta}^{(N)})}{e^{N \lambda (t \wedge T_{\delta}^{(N)}) - s}} \Delta V(Z^{(N)}(s-)) \cdot dM^{(N)}(s) \right] \leq \mathbb{E} \left[ \left( \int_{0+}^{t \wedge T_{\delta}^{(N)}} e^{N \lambda (t \wedge T_{\delta}^{(N)}) - s} \Delta V(Z^{(N)}(s-)) \cdot dM^{(N)}(s) \right)^2 \right]
\]

\[
= \mathbb{E} \left[ \int_{0+}^{t \wedge T_{\delta}^{(N)}} e^{2N \lambda (t \wedge T_{\delta}^{(N)}) - s} \sum_{i=1}^{K} \sum_{j=1}^{K} D_iV(Z^{(N)}(s-))D_jV(Z^{(N)}(s-))d(M^{(N)}_i, M^{(N)}_j)(s) \right].
\]  \tag{4.49}
Moreover,
\[
\langle M_i^{(N)}, M_j^{(N)} \rangle(t) = \int_{0^+}^t \sum_n n_i n_j \lambda_n^{(N)}(Z^{(N)}(s-)) \, ds
\]  
(4.50)

and by Assumption 2.1,
\[
\sup_{x \in K} \sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \lambda_n^{(N)}(x)
\]  
(4.51)
is uniformly bounded on \(C_{\delta}\), so for \(t \leq T_{\delta}^{(N)}\), there exists a constant \(C_{\delta}\) such that \(\langle M_i^{(N)}, M_j^{(N)} \rangle(t) < C_{\delta} t\). and a constant \(C_{2,\delta}\) such that
\[
\mathbb{E} \left[ \sup_{t \leq T} \| \mathcal{O} \| \right] \leq \frac{C_{2,\delta}}{2N |\lambda|}
\]  
(4.52)

Lastly, Taylor’s theorem gives
\[
V(Z^{(N)}(s)) - V(Z^{(N)}(s-)) - DV(Z^{(N)}(s-)) \cdot \Delta Z^{(N)}(s)
\]
\[
= \sum_{i=1}^K \sum_{j=1}^K \partial_i \partial_j V(\zeta) \Delta Z_i^{(N)}(s) \Delta Z_j^{(N)}(s)
\]  
(4.53)
for some \(\zeta\) such that \(\|Z^{(N)}(s-) - \zeta\| \leq \|\Delta Z^{(N)}(s)\| \leq \frac{1}{N}\), so, as before, there is a constant \(C\) such that \(V(Z^{(N)}(s)) - V(Z^{(N)}(s-)) - DV(Z^{(N)}(s-)) \cdot \Delta Z^{(N)}(s)\) is bounded above by
\[
C \sum_{i=1}^K \sum_{j=1}^K \left| \Delta Z_i^{(N)}(s) \right| \left| \Delta Z_j^{(N)}(s) \right| \leq CK \sum_{i=1}^K \left| \Delta Z_i^{(N)}(s) \right|.
\]  
(4.54)

Thus,
\[
|\varepsilon^{(N)}(t)|^2 \leq C^2 K^2 \left( \sum_{0<s \leq t} \sum_{i=1}^K e^{N\lambda(s-t)} \left| \Delta Z_i^{(N)}(s) \right|^2 \right)^2
\]
\[
= C^2 K^2 \left( \sum_{i=1}^K \int_{0^+}^t e^{N\lambda(s-t)} \, d[M_i^{(N)}](s) \right)^2
\]  
(4.55)
Recalling (4.4), (4.6) and (4.7), we have
\[
[M_i^{(N)}](t) = \langle M_i^{(N)} \rangle(t) + M_i^{(N)}(t)
\] (4.56)
so that
\[
|\varepsilon^{(N)}(t)|^2 \leq 2C^2K^3 \sum_{i=1}^{K} \left( \left( \int_{0}^{t} e^{N\lambda(s-t)} dM_i^{(N)}(s) \right)^2 + \left( \int_{0}^{t} e^{N\lambda(s-t)} d\langle M_i^{(N)} \rangle(s) \right)^2 \right)
\] (4.57)
and, proceeding as above, there exists a constant $C_{T,\delta}$ such that
\[
\mathbb{E} \left[ \sup_{t \leq T \wedge \delta} |\varepsilon^{(N)}(t)|^2 \right] \leq \frac{C_{T,\delta}}{2N|\lambda|}.
\] (4.58)
Combining all the above, we see that for any $T > 0$,
\[
\mathbb{E} \left[ \sup_{t \leq T \wedge \delta} |V(Z^{(N)}(t))|^2 \right] = O\left(\frac{1}{N}\right).
\] (4.59)
The result follows.

**Corollary 4.2.** If $Z^{(N)}(0) \overset{D}{\rightarrow} Z(0) \in \mathcal{C}$, then $Z^{(N)} - \pi(Z^{(N)}) \overset{D}{\rightarrow} 0$ for all $t$.

**4.1.1 Diffusion Process**

In this section, we characterize the limiting process on $\mathcal{C}$. We begin by introducing some notation that will simplify subsequent expressions. For $f : \mathbb{R}^K \to \mathbb{R}$, let
\[
(D^2f)(x)\langle X, Y \rangle = Y^\top (D^2f)(x)X \quad \text{for } X, Y \in \mathbb{R}^K,
\] (4.60)
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and, if \( f : \mathbb{R}^K \to \mathbb{R}^K \), let

\[
(D^2 f)(x) \langle X, Y \rangle = \begin{bmatrix}
(D^2 f_1)(x) \langle X, Y \rangle \\
\vdots \\
(D^2 f_K)(x) \langle X, Y \rangle
\end{bmatrix},
\]

so that \( f \) has Taylor expansion

\[
f(y) = f(x) + (Df)(x) (y - x) + (D^2 f)(x) \langle y - x, y - x \rangle + O(\|y - x\|^3).
\]

Further, following [43], given semimartingales \( X(t) \) and \( Y(t) \), taking values in a subset of \( \mathbb{R}^d \), we adopt the notation

\[
\int_{0+}^t (D^2 f)(X(s-)) \langle dY(s), dY(s) \rangle := \int_{0+}^t \sum_{i=1}^d \sum_{j=1}^d (\partial_i \partial_j f)(X(s)) \, d[Y_i, Y_j](s)
\]

and write

\[
\int_{0+}^t (D^2 f)(X(s-)) \langle dY(s), dY(s) \rangle
\]

for the vector-valued process with components

\[
\int_{0+}^t \sum_{i=1}^d \sum_{j=1}^d \partial_i \partial_j f_k(X(s-)) \, d[Y_i, Y_j](s).
\]

With this notation, Itô’s formula becomes

\[
f(Y(t)) = f(Y(0)) + \int_0^t (Df)(Y(s-)) \, dY(s) + \frac{1}{2} \int_0^t (D^2 f)(X(s-)) \langle dY(s), dY(s) \rangle + \sum_{s \leq t} f(Y(s)) - f(Y(s-)) - (Df)(Y(s-)) \Delta Y(s) - \frac{1}{2} (D^2 f)(Y(s-)) \langle \Delta Y(s), \Delta Y(s) \rangle.
\]

**Theorem 4.2.** Let \( \{W_n : n \in \mathbb{Z}^K\} \) be independent Brownian motions. Assume that
\( Z^{(N)}(0) \xrightarrow{\mathcal{D}} Z(0) \in \mathcal{C} \) and that the solution to

\[
Z(t) = Z(0) + \int_{0^+}^{t} (D\pi)(Z(s-))\nu(Z(s-)) + \sum_{n \in \mathbb{Z}^K} \frac{1}{2}(D^2\pi)(Z(s))\langle n,n \rangle \lambda_n(Z(s-)) \, ds
\]


\[\quad + (D\pi)(Z(s-)) \left( \sum_{n \in \mathbb{Z}^K} n \int_{0^+}^{t} \sqrt{\lambda_n(Z(s-))} \, dW_n(s) \right) \tag{4.67}\]

exists and is unique. Then \( Z^{(N)}(t) \xrightarrow{\mathcal{D}} Z(t) \).

**Proof.** We begin by recalling that

\[
Z^{(N)}(t) = Z^{(N)}(0) + \int_{0}^{t} NF^{(N)}(Z^{(N)}(s-)) \, ds + \frac{1}{N} \sum_{n \in \mathbb{Z}^K} n\tilde{H}_n(Nt). \tag{4.68}\]

We start with the martingale terms. For each \( n \in \mathbb{Z}^K \), let

\[
W^{(N)}_n = \frac{1}{N} \int_{0^+}^{t} \frac{d\tilde{H}^{(N)}_n(Ns)}{\sqrt{\lambda^{(N)}(Z^{(N)})(s-)}} \tag{4.69}\]

so that

\[
\frac{1}{N} \tilde{H}_n(Nt) = \int_{0^+}^{t} \sqrt{\lambda^{(N)}(Z^{(N)})(s-)} \, dW^{(N)}_n(s), \tag{4.70}\]

whilst

\[
[W^{(N)}_n]_t = \frac{1}{N^2} \int_{0^+}^{t} \frac{d[H^{(N)}_n]_Ns}{\lambda^{(N)}(Z^{(N)})(s-))} \tag{4.71}\]

\[
= \frac{1}{N^2} \int_{0^+}^{t} \frac{dH^{(N)}_n(Ns)}{\lambda^{(N)}(Z^{(N)})(s-))}, \tag{4.72}\]

which, decomposing \( H^{(N)}_n \) into a local martingale and a finite variation components (Equation 2.9), can be written

\[
= \int_{0^+}^{t} ds + \frac{1}{N} \int_{0^+}^{t} \frac{d\tilde{H}^{(N)}_n(Ns)}{\lambda^{(N)}(Z^{(N)})(s-))}, \tag{4.73}\]
Now,
\[
\mathbb{E} \left[ \left( \frac{1}{N} \int_{0+}^{t} \frac{d\tilde{H}_n^{(N)}(Ns)}{\lambda^{(N)}(Z^{(N)}(s-))} \right)^2 \right] = \frac{1}{N^2} \mathbb{E} \left[ \int_{0+}^{t} \frac{d[\tilde{H}_n^{(N)}]_{Ns}}{\lambda^{(N)}(Z^{(N)}(s-))} \right] ^2
\]
\[
= \frac{1}{N} \mathbb{E} \left[ \int_{0+}^{t} \frac{ds}{\lambda^{(N)}(Z^{(N)}(s-))} \right],
\]
(4.74)

so \([W_n^{(N)}]_t \to t\) as \(N \to \infty\). Further, since \(\tilde{H}_n, \tilde{H}_m\) are orthogonal for \(n \neq m\), we have \([W_n, W_m]_t = 0\). Since each \(W_n^{(N)}(t)\) is a martingale with jumps tending to 0 as \(N \to \infty\), it follows from the Martingale central limit theorem that \(\left(W_n^{(N)}\right)_n \overset{q}{\to} (W_n)_n\), where the \(W_n\) are independent Brownian motions.

We then have, using Itô’s formula,
\[
Z^{(N)}(t) = \pi(Z^{(N)}(t)) + (Z^{(N)}(t) - \pi(Z^{(N)}(t)))
\]
\[
= \pi(Z^{(N)}(0)) + \int_0^t (D\pi)(Z^{(N)}(s-)) dZ^{(N)}(s) + \frac{1}{2} \int_0^t (D^2\pi)(Z^{(N)}(s-))(dZ^{(N)}(s), dZ^{(N)}(s))
\]
\[
+ \eta^{(N)}(t) + (Z^{(N)}(t) - \pi(Z^{(N)}(t)))
\]
\[
= \pi(Z^{(N)}(0)) + \int_0^t N(D\pi)(Z^{(N)}(s-))\psi^{(N)}(Z^{(N)}(s-)) ds
\]
\[
+ \int_{0+}^t (D\pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)}(Z^{(N)}(s-))} dW_n^{(N)}(s) \right)
\]
\[
+ \frac{1}{2} \int_0^t (D^2\pi)(Z^{(N)}(s-))(dZ^{(N)}(s), dZ^{(N)}(s)) + \eta^{(N)}(t) + (Z^{(N)}(t) - \pi(Z^{(N)}(t)))
\]
\[
= Z^{(N)}(0) + (\pi(Z^{(N)}(0)) - Z^{(N)}(0))
\]
\[
+ \int_0^t (D\pi)(Z^{(N)}(s-)) \left( NF(Z^{(N)}(s-)) + \nu^{(N)}(Z^{(N)}(s-)) \right) ds
\]
\[
+ \int_{0+}^t (D\pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)}(Z^{(N)}(s-))} dW_n^{(N)}(s) \right)
\]
\[
+ \frac{1}{2} \int_0^t (D^2\pi)(Z^{(N)}(s-))(dZ^{(N)}(s), dZ^{(N)}(s)) + \eta^{(N)}(t) + (Z^{(N)}(t) - \pi(Z^{(N)}(t)))
\]
(4.76)
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Thus,

\[ \eta^{(N)}(t) := \sum_{s \leq t} \pi(Z^{(N)}(s)) - \pi(Z^{(N)}(s-)) - (D \pi)(Z^{(N)}(s-)) \Delta Z^{(N)}(s) \]

\[ - \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle \Delta Z^{(N)}(s), \Delta Z^{(N)}(s) \rangle \quad (4.77) \]

Thus,

\[ Z^{(N)}(t) = Z^{(N)}(0) + \int_{0^+}^{t} (D \pi)(Z^{(N)}(s-)) \nu(Z^{(N)}(s-)) \]

\[ + \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s)) \langle n, n \rangle \lambda_n(Z^{(N)}(s-)) \, ds \]

\[ + (D \pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} n \int_{0^+}^{t} \sqrt{\lambda_n(Z^{(N)}(s-))} \, dW_n^{(N)}(s) \right) + \varepsilon^{(N)}(t) \quad (4.78) \]

where

\[ \varepsilon^{(N)}(t) := \frac{(\pi(Z^{(N)}(0)) - Z^{(N)}(0))}{1} + \int_{0}^{t} N(D \pi)(Z^{(N)}(s-)) F(Z^{(N)}(s-)) \, ds \]

\[ + \int_{0}^{t} (D \pi)(Z^{(N)}(s-)) \left( \nu^{(N)}(Z^{(N)}(s-)) - \nu(Z^{(N)}(s-)) \right) \, ds \]

\[ + \int_{0^+}^{t} (D \pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)}(Z^{(N)}(s-))} - \sqrt{\lambda_n(Z^{(N)}(s-))} \right) \, dW_n^{(N)}(s) \]

\[ + \frac{1}{2} \int_{0}^{t} (D^2 \pi)(Z^{(N)}(s-)) \langle dZ^{(N)}(s), dZ^{(N)}(s) \rangle - \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s)) \langle n, n \rangle \lambda_n(Z^{(N)}(s-)) \, ds \]

\[ + \eta^{(N)}(t) + (Z^{(N)}(t) - \pi(Z^{(N)}(t))) \quad (4.79) \]
Fix $B > 0$ and let

$$T_B^{(N)} := \inf\{ t > 0 : \|Z^{(N)}(t)\| > B \}. \quad (4.80)$$

Then, using Theorem 5.4 in [120] (we use the theorem as it is stated in [115]), provided $\varepsilon^{(N)}(t \wedge T_B^{(N)}) \xrightarrow{D} 0$, $Z^{(N)}(t \wedge T_B^{(N)})$ converges weakly to a local solution of (4.67) stopped at

$$T_C := \inf\{ t > 0 : \|Z(t)\| > C \}, \quad (4.81)$$

for any $C < B$. Moreover, if (4.67) has a unique global solution $Z$, then $Z^{(N)} \xrightarrow{D} Z$. Thus, our result follows upon showing that $\varepsilon^{(N)}(t \wedge T_B^{(N)}) \xrightarrow{D} 0$. We will show that the terms individually converge weakly to 0, and thus in probability also, from which we can conclude the sum converges weakly to 0 as well.

We begin by observing that $\top \xrightarrow{D} 0$ by assumption.

Next, observe that by definition, $\pi(\psi_t x) = \pi(x)$, whence

$$0 = \frac{d}{dt} \pi(\psi_t x) = (D\pi)(\psi_t x)F(\psi_t x) \quad (4.82)$$

for all $t$. In particular, $(D\pi)(x) \cdot F(x) = 0$ and thus, $\top$ is identically zero.

For $t < T_B^{(N)}$, $Z^{(N)}(t)$ is compactly contained, so $\top$ converges uniformly to 0 by Assumptions 2.1 and 2.2.

Using Doob’s inequality, we have

$$\mathbb{E} \left[ \sup_{t \leq T} \int_{0+}^{t \wedge T_B^{(N)}} (D\pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)} (Z^{(N)}(s-))} - \sqrt{\lambda_n(Z^{(N)}(s-))} \right) dW_n^{(N)}(s) \right]$$

$$\leq \mathbb{E} \left[ \left( \int_{0+}^{T_B^{(N)}} (D\pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)} (Z^{(N)}(s-))} - \sqrt{\lambda_n(Z^{(N)}(s-))} \right) dW_n^{(N)}(s) \right)^2 \right]$$

$$\leq \mathbb{E} \left[ \int_{0+}^{T} (D\pi)(Z^{(N)}(s-)) \left( \sum_{n \in \mathbb{Z}^K} \sqrt{\lambda_n^{(N)} (Z^{(N)}(s-))} - \sqrt{\lambda_n(Z^{(N)}(s-))} \right)^2 d[W_n^{(N)}]_s \right]. \quad (4.83)$$
We observed above that \([W_n^{(N)}]_t \xrightarrow{p} t\), whilst the integrand converges uniformly to 0 on compact sets, so \(\odot\) converges to 0.

Next, we observe that

\[
\int_0^t (D^2 \pi_k)(Z^{(N)}(s-)) \langle dZ^{(N)}(s), dZ^{(N)}(s) \rangle \\
= \frac{1}{N^2} \int_0^t \sum_{n \in \mathbb{Z}^K} \sum_{i=1}^K \sum_{j=1}^K (\partial_i \partial_j \pi_k)(Z^{(N)}(s-)) n_i n_j d \left[ \bar{H}^{(N)}_n \right]_{Ns} \\
= \frac{1}{N^2} \int_0^t \sum_{n \in \mathbb{Z}^K} (D^2 \pi_k)(Z^{(N)}(s-)) \langle n, n \rangle d \left[ \bar{H}^{(N)}_n \right]_{Ns}
\]

(4.84)

whilst

\[
\frac{1}{N^2} \left[ \bar{H}^{(N)}_n \right]_{Nt} = \int_0^t \lambda^{(N)}_n(Z^{(N)}(s-)) \, ds + \frac{1}{N^2} \bar{H}^{(N)}_n(Nt).
\]

(4.85)

Thus

\[
\odot = \frac{1}{N^2} \int_0^t \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle n, n \rangle d \bar{H}^{(N)}_n(Ns) \\
+ \int_0^t \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle n, n \rangle \left( \lambda^{(N)}_n(Z^{(N)}(s-)) - \lambda_n(Z^{(N)}(s-)) \right) \, ds.
\]

(4.86)

Now, \(D^2 \pi\) is bounded on compact sets, so

\[
\frac{1}{N^2} \sup_{t \leq T} \left| \int_0^{t \wedge T_B^{(N)}} \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle n, n \rangle d \bar{H}^{(N)}_n(Ns) \right| \\
\leq \sup_{\{z : \|z\|_2 \leq B\}} (D^2 \pi)(z) \sum_{n \in \mathbb{Z}^K} \|n\|^2_2 \sup_{t \leq T} \left| \bar{H}^{(N)}_n(N(t \wedge T_B^{(N)})) \right| \\
\leq \frac{1}{N} \sup_{\{z : \|z\|_2 \leq B\}} (D^2 \pi)(z) \\
\times \sum_{n \in \mathbb{Z}^K} \|n\|^2_2 \sup_{t \leq T} \left( \left| \frac{1}{N} H^{(N)}_n(N(t \wedge T_B^{(N)})) \right| + \int_0^{t \wedge T_B^{(N)}} \lambda^{(N)}_n(Z^{(N)}(s-)) \, ds \right) \].
\]

(4.87)
We are unable to use Doob’s inequality here without making stronger assumptions on the summability of the $\lambda_n^{(N)}$. Instead, we adapt the approach of Theorem 11.2.1 in [50], and use the functional Law of Large Numbers for the counting process:

$$\lim_{N \to \infty} \sup_{t \leq T} \left| \frac{1}{N} H_n^{(N)}(N(t \wedge T_B^{(N)})) - \int_0^{t \wedge T_B^{(N)}} \lambda_n^{(N)}(Z^{(N)}(s-)) \, ds \right| = 0. \quad (4.88)$$

In particular,

$$\sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \lim_{N \to \infty} \sup_{t \leq T} \left( \left| \frac{1}{N} H_n^{(N)}(N(t \wedge T_B^{(N)})) \right| + \left| \int_0^{t \wedge T_B^{(N)}} \lambda_n^{(N)}(Z^{(N)}(s-)) \, ds \right| \right)$$

$$= \sum_{n \in \mathbb{Z}^K} \|n\|_2^2 \int_0^{T_B^{(N)}} \lambda_n^{(N)}(Z^{(N)}(s-)) \, ds, \quad (4.89)$$

which is, by assumption, convergent, so we can interchange sum and limit to conclude that

$$\lim_{N \to \infty} \frac{1}{N^2} \sup_{t \leq T} \left| \int_0^{t \wedge T_B^{(N)}} \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle n, n \rangle \, dH_n^{(N)}(Ns) \right| = 0. \quad (4.90)$$

The second integral,

$$\int_0^{T_B^{(N)}} \sum_{n \in \mathbb{Z}^K} \frac{1}{2} (D^2 \pi)(Z^{(N)}(s-)) \langle n, n \rangle \left( \lambda_n^{(N)}(Z^{(N)}(s-)) - \lambda_n(Z^{(N)}(s-)) \right) \, ds, \quad (4.91)$$

vanishes since

$$\left( \lambda_n^{(N)}(z) - \lambda_n(z) \right) \to 0 \quad (4.92)$$

uniformly on compact sets. Thus $\overset{\mathcal{P}}{\to} 0$. 

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Lastly, from Taylor’s Theorem, we have

\[
\pi_k(x + \Delta x) - \pi_k(x) - \sum_{i=1}^{K} (\partial_i \pi_k)(x) \Delta x_i(s)
= \frac{1}{2} \sum_{1 \leq i, j \leq K} \Delta x_i \Delta x_j \int_0^1 (1 - t)^2 (\partial_i \partial_j \pi_k)(x + t \Delta x) \, dt
\]

(4.93)

so that

\[
\eta_k^{(N)}(t) = \sum_{0 < s \leq t} \left\{ \frac{1}{2} \sum_{1 \leq i, j \leq K} \Delta Z_i^{(N)}(s) \Delta Z_j^{(N)}(s) \right. \\
\times \left. \int_0^1 (1 - t)^2 (\partial_i \partial_j \pi_k)(Z^{(N)}(s) + t \Delta Z^{(N)}(s)) - (\partial_i \partial_j \pi_k)(Z^{(N)}(s)) \, dt \right\}
\]

(4.94)

and

\[
\left| \eta_k^{(N)}(t) \right| \leq \sum_{0 < s \leq t} \left\{ \frac{1}{2} \sum_{1 \leq i, j \leq K} \Delta Z_i^{(N)}(s) \Delta Z_j^{(N)}(s) \\
\sup_{\{h : \|h\| \leq \frac{1}{N}\}} \left| (\partial_i \partial_j \pi_k)(Z^{(N)}(s) + h) - (\partial_i \partial_j \pi_k)(Z^{(N)}(s)) \right| \right\}
\]

(4.95)

By assumption, \((\partial_i \partial_j \pi_k)(x)\) is continuously differentiable, and thus locally Lipschitz continuous, so

\[
\left| \eta_k^{(N)}(t) \right| \ll \frac{1}{N} |Z_k^{(N)}|(t) = \frac{1}{N^3} \sum_{n \in \mathbb{Z}^K} \eta_n^2[H_n^{(N)}]_{nt},
\]

(4.96)

so \(\eta_k^{(N)}(t)\) weakly converges to 0 as \(N \to \infty\), by arguments similar to those above.

Finally, \(\mathcal{D} \to 0\) as a consequence of Corollary 4.2, completing the proof.

Remark 4.4. Equivalently, if we let

\[
b(x) := (D\pi)(x)\nu(x) + \sum_{n \in \mathbb{Z}^K} \frac{1}{2}(D^2\pi)(x)\langle n, n \rangle \lambda_n(x)
\]

(4.97)

\[
\tilde{a}(x) := \sum_{n \in \mathbb{Z}^K} nn^\top \lambda_n(x)
\]

(4.98)
and

\[ a(x) := (D\pi)(x)\tilde{a}(D\pi)^\top(x) \]  \hspace{1cm} (4.99)

then, provided \( \mathbf{Z}^{(N)}(0) \xrightarrow{\mathcal{D}} \mathbf{Z}(0) \in \mathcal{C} \), \( \mathbf{Z}(t) \) has generator

\[ (\mathcal{G}\phi)(x) = \sum_{i=1}^{K} b_i(x)\partial_i\phi(p) + \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} a_{ij}(x)\partial_i\partial_j\phi(x), \]  \hspace{1cm} (4.100)

for \( \phi \in C^2(\mathcal{C}) \).

**Remark 4.5.** We refer the interested reader to \([46, 47]\) for a discussion of existence and uniqueness of solutions of the Cauchy problem for the infinitesimal generator, (4.100).

**Remark 4.6.** Note that the assumption that \( \mathbf{Z}^{(N)}(0) \xrightarrow{\mathcal{D}} \mathbf{Z}(0) \in \mathcal{C} \) is necessary to obtain weak convergence in the results above; Propositions 2.1 and Theorem 4.1 tell us that in general,

\[ \lim_{N \to \infty} \mathbf{Z}^{(N)}(0+) = \pi(\mathbf{Z}(0)) \neq \mathbf{Z}(0). \]  \hspace{1cm} (4.101)

Thus, the limiting process has a jump discontinuity at \( t = 0 \) fails to satisfy the Feller property. We may still obtain a global convergence result, by considering a variant of the original process.

**Corollary 4.3.** Let

\[ \mathbf{\tilde{Z}}^{(N)}(t) := \mathbf{Z}^{(N)}(t) - \psi_{Nt}\mathbf{Z}^{(N)}(0) + \pi(\mathbf{Z}^{(N)}(0)). \]  \hspace{1cm} (4.102)

Then \( \mathbf{\tilde{Z}}^{(N)} \xrightarrow{\mathcal{D}} \mathbf{\tilde{Z}} \), a diffusion process satisfying (4.67) above.

**Remark 4.7.** We introduce \( \mathbf{\tilde{Z}}^{(N)} \) to avoid technical difficulties arising from the discontinuity above. Intuitively \( \mathbf{\tilde{Z}}^{(N)} \) is obtained by removing the “deterministic part”, \( \psi_{Nt}x \), from \( \mathbf{Z}^{(N)} \), and then shifting the resulting process so that it starts at \( \pi(\mathbf{Z}^{(N)}(0)) \).
Proof. Let \( \varepsilon_N = \frac{1-r}{\ln N} \), where \( 0 < r' < r < s < 1 \) are as in Proposition 2.1 and Corollary 4.1. From those results, we have

\[
\mathbb{P}\{\sup_{t \leq \varepsilon_N} |Z^{(N)}(t) - \psi_{Nt}Z^{(N)}(0)| > N^{-r}\} \leq N^{-r},
\]

while

\[
\mathbb{P}\{V(Z^{(N)}(\varepsilon_N)) > N^{-r'}\} < N^{-r'}.
\]

In particular \( Z^{(N)}(\varepsilon_N) \overset{\mathcal{D}}{\to} \pi(Z(0)) \in \mathcal{C} \). Now, consider the process

\[
\hat{Z}^{(N)}(t) = Z^{(N)}(t + \varepsilon_N).
\]

By the above, \( \hat{Z}^{(N)}(0) \overset{\mathcal{D}}{\to} \hat{Z}(0) \in \mathcal{C} \), while \( \hat{Z}^{(N)} \) satisfies (4.5). Thus, we may apply Theorem 4.2 to conclude that \( \hat{Z}^{(N)} \overset{\mathcal{D}}{\to} \hat{Z} \), where the limiting process satisfies (4.67).

Moreover,

\[
\hat{Z}^{(N)}(t + \varepsilon_N) - \hat{Z}^{(N)}(t) = \psi_{Nt+\varepsilon_N}Z^{(N)}(0) - \pi(Z^{(N)}(0)).
\]

Since \( N\varepsilon_N \to \infty \) as \( N \to \infty \), the right hand side converges to 0 uniformly in \( t \), so we must have \( \hat{Z}^{(N)}(\cdot + \varepsilon_N) - \hat{Z}^{(N)} \overset{\mathcal{D}}{\to} 0 \).

Lastly, define \( \gamma^{(N)} : \mathbb{R}^+ \to \mathbb{R}^+ \) by

\[
\gamma^{(N)}(t) := \begin{cases} 
0 & 0 \leq t \leq \varepsilon_N \\
 t - \varepsilon_N & \text{otherwise}.
\end{cases}
\]

Then, \( \gamma^{(N)}(t) \to t \) uniformly in \( N \), while

\[
\hat{Z}^{(N)}(\gamma^{(N)}(t)) = \begin{cases} 
\hat{Z}^{(N)}(0) & 0 \leq t \leq \varepsilon_N \\
\hat{Z}^{(N)}(t) & \text{otherwise}.
\end{cases}
\]

Now, the map \((f, g) \to f \circ g : \mathbb{D}_C[0, \infty) \times \mathbb{D}_{\mathbb{R}^+}[0, \infty) \to \mathbb{D}_C[0, \infty)\) is continuous at points
where the pair \( f, g \) are continuous. Since \( \hat{Z} \) is continuous, we may apply the continuous mapping theorem to conclude that \( \hat{Z}^{(N)} \circ \gamma^{(N)} \xrightarrow{D} \hat{Z} \) as \( N \to \infty \); on the other hand,

\[
\sup_t \left| \tilde{Z}^{(N)}(t) - \hat{Z}^{(N)}(\gamma^{(N)}(t)) \right| = \sup_{t \leq \varepsilon_N} \left| \tilde{Z}^{(N)}(t) - \tilde{Z}^{(N)}(\varepsilon_N) \right| \tag{4.109}
\]

which converges uniformly to 0. Thus \( \tilde{Z}^{(N)} - \hat{Z}^{(N)} \xrightarrow{D} 0 \), and the result follows. \( \square \)

We will henceforth focus on the process \( \tilde{Z} \).

### 4.2 Computing the Derivatives

In practice, to use Theorem 4.2, it will be necessary to explicitly compute the partial derivatives of \( \pi(x) \). In this section, we consider several approaches. The first, which we present in below, uses Duhamel's principle to characterize the derivatives of \( \pi \) in terms of \( F \). While generally applicable in principle, it proves unwieldy in practice, so we conclude this section with a second approach that uses conservation laws to characterize the derivatives, which proves useful when the functional Law of Large Numbers for the process of interest is of Lotka-Volterra-Gause type.

#### 4.2.1 Variational Formulation

We begin by observing that

\[
\dot{\psi}_t x = \frac{d}{dt} F(\psi_t x) = (DF)(\psi_t x) \dot{\psi}_t x, \tag{4.110}
\]

so that

\[
(D\pi)(x) = \lim_{t \to \infty} e^{-\int_0^t (DF)(\psi_s x) ds}. \tag{4.111}
\]
In particular, if \( x^* \in C, \) then \( \psi_t x^* = x^* \) for all \( t \) and

\[
(D\pi)(x^*) = \lim_{t \to \infty} e^{-t(DF)(x^*)}.
\] (4.112)

Let \( P_{x^*} \) be an invertible matrix such that \((DF)(x^*)\) is in real Jordan canonical form i.e., \((DF)(x^*) = P_{x^*} A P_{x^*}^{-1}\), for

\[
A = \begin{bmatrix}
J_0 & & \\
& J_1 & \\
& & \ddots \\
& & & J_p
\end{bmatrix}
\] (4.113)

where, as in the proof of Proposition 4.1, \( J_0 = 0_{d \times d} \) and \( J_i \) is a \( d_i \times d_i \) Jordan block corresponding to the \( i^{th} \) eigenvalue. Then, \( e^{-t(DF)(\psi_s(x^*))} = P_{x^*} e^{tA} P_{x^*}^{-1} \), while

\[
e^{tA} = e^{tJ_0} \oplus \cdots e^{tJ_p},
\] (4.114)

where \( \oplus \) is the direct sum of linear operators.

Now, \( e^{tJ_0} = I_{d \times d} \), while if \( J_i \) corresponds to a real eigenvalue, then

\[
e^{tJ_i} = \begin{bmatrix}
e^{t\lambda_i} & te^{t\lambda_i} & \cdots & \frac{t^d}{d!} e^{t\lambda_i} \\
e^{t\lambda_i} & \ddots & & \\
& \ddots & \ddots & \\
& & te^{t\lambda_i} & e^{t\lambda_i}
\end{bmatrix}.
\] (4.115)

so that \( \lim_{t \to \infty} e^{tJ_i} = 0_{d_i \times d_i} \), and the same holds if \( J_i \) corresponds to a complex eigenvalue, since we have assumed that \( x^* \) is locally asymptotically stable, and thus \((DF)(x^*)\) is a stable matrix. Then,

\[
\lim_{t \to \infty} e^{tA} = I_{d \times d} \oplus 0_{K-d \times K-d},
\] (4.116)
i.e., $(D\pi)(x^*)$ is a projection onto $T_{x^*}C$ and may be computed explicitly:

**Lemma 4.1.** Let $P_{x^*}$ be a change of basis matrix such that $P_{x^*}^{-1}(DF)(\psi_s(x^*))P_{x^*}$ is in real Jordan canonical form. Then $(D\pi)(x^*) = P_{x^*}(I_{d \times d} \oplus 0_{K-d \times K-d})P_{x^*}^{-1}$.

Equivalently, writing $(DF)(x^*)^\dagger$ for the matrix with

$$(DF)(x^*)^\dagger|_{\text{Im}((DF)(x^*))} = ((DF)(x^*)|_{\text{Im}((DF)(x^*))})^{-1}$$

and

$$(DF)(x^*)^\dagger|_{\text{Ker}((DF)(x^*))} = 0,$$

we have

$$(D\pi)(x^*) = I - (DF)(x^*)^\dagger(DF)(x^*).$$

In a similar manner, we can find the second derivatives. As before,

$$\frac{d}{dt}(D_{ij}\psi_t)(x) = (D^2F)(\psi_t x)\langle(D_i \psi_t)(x), (D_j \psi_t)(x)\rangle + (DF)(\psi_t x)(D_{ij} \psi_t)(x).$$

Taking $t \to \infty$ gives

$$0 = (D^2F)(\pi(x))\langle(D_i \pi)(\pi(x)), (D_j \pi)(\pi(x))\rangle + (DF)(\pi(x))(D_{ij} \pi)(\pi(x)),$$

from which we conclude that $(D^2F)(\pi(x))\langle(D_i \pi)(\pi(x)), (D_j \pi)(\pi(x))\rangle$ is in $\text{Im}((DF)(\pi(x)))$, and

$$(D_{ij} \pi)(\pi(x)) - (DF)(\pi(x))^\dagger(D^2F)(\pi(x))\langle(D_i \pi)(\pi(x)), (D_j \pi)(\pi(x))\rangle$$

$$\in \text{Ker}((DF)(\pi(x))).$$

To determine the component in $\text{Ker}((DF)(\pi(x)))$, we apply Duhamel's principle to
(4.120), to obtain

$$
(D_{ij} \psi_t)(x) = \int_0^t e^{\int_0^t (DF)(\psi_u(x)) \, du} (D^2 F)(\psi_s x) \langle (D_i \psi_s)(x), (D_j \psi_s)(x) \rangle \, ds.
$$

(4.123)

As before, we wish to find the derivatives at points $x^* \in C$, for which

$$
(D_{ij} \psi_t)(x^*) = \int_0^t e^{\int_0^t (DF)(x^*(t-s)) (D^2 F)(x^*) \langle e^{(DF)(x^*)} s e_i, e^{(DF)(x^*)} s e_j \rangle \, ds.
$$

(4.124)

Now, $(D \pi)(x^*)$ is a projection onto $\text{Ker}((DF)(\pi(x)))$, so the quantity we seek is

$$
(D \pi)(x^*) \int_0^t e^{(DF)(x^*(t-s)) (D^2 F)(x^*) \langle e^{(DF)(x^*)} s e_i, e^{(DF)(x^*)} s e_j \rangle \, ds
$$

$$
= \int_0^t (D \pi)(x^*) (D^2 F)(x^*) \langle e^{(DF)(x^*)} s e_i, e^{(DF)(x^*)} s e_j \rangle \, ds
$$

(4.125)

since $e^{(DF)(x^*(t-s))}$ acts as the identity on $\text{Ker}((DF)(\pi(x)))$. This in turn is equal to

$$
\int_0^t (D \pi)(x^*) (D^2 F)(x^*) \langle e^{(DF)(x^*)} s e_i, e^{(DF)(x^*)} s e_j \rangle \, ds
$$

$$
- (D^2 F)(x^*) \langle (D_i \pi)(x^*), (D_j \pi)(x^*) \rangle \, ds
$$

(4.126)

which, using the bilinearity of the Hessian, is equal to

$$
= \int_0^t (D \pi)(x^*) (D^2 F)(x^*) \langle (e^{(DF)(x^*)} s - (D \pi)(x^*)) e_i, (e^{(DF)(x^*)} s - (D \pi)(x^*)) e_j \rangle
$$

$$
+ (D^2 F)(x^*) \langle (e^{(DF)(x^*)} s - (D \pi)(x^*)) e_i, (D_j \pi)(x^*) \rangle
$$

$$
+ (D^2 F)(x^*) \langle (D_i \pi)(x^*), (e^{(DF)(x^*)} s - (D \pi)(x^*)) e_j \rangle \, ds.
$$

(4.127)

We now consider the three terms in the integral separately. For the latter two, we may
use the bilinearity of the Hessian to interchanging the form and the integral. Then,

\[
\int_0^t e^{(D\mathbf{F})(\mathbf{x}^*)s} - (D\pi)(\mathbf{x}^*) \, ds = P_{\mathbf{x}^*} \left( \int_0^t e^{As} - I_{d\times d} \oplus 0_{K-d\times K-d} \, ds \right) P_{\mathbf{x}^*}^{-1}
\]

\[
= P_{\mathbf{x}^*} \left( \int_0^t 0_{d\times d} \oplus e^{J_1s} \oplus \cdots \oplus e^{J_ps} \, ds \right) P_{\mathbf{x}^*}^{-1}
\]

\[
= P_{\mathbf{x}^*} \left( 0_{d\times d} \oplus J_1^{-1} (e^{J_1t} - I_{d_1\times d_1}) \oplus \cdots \oplus J_p^{-1} (e^{J_pt} - I_{d_p\times d_p}) \right) P_{\mathbf{x}^*}^{-1} \quad (4.128)
\]

which, taking \( t \to \infty \), yields

\[
-P_{\mathbf{x}^*} \left( 0_{d\times d} \oplus J_1^{-1} \oplus \cdots \oplus J_p^{-1} \right) P_{\mathbf{x}^*}^{-1} = -(D\mathbf{F})(\mathbf{x}^*)\dagger. \quad (4.129)
\]

Thus in the limit, the second and third terms yield

\[
-(D^2\mathbf{F})(\mathbf{x}^*)((D\mathbf{F})(\mathbf{x}^*)\dagger \mathbf{e}_i, (D\pi)(\mathbf{x}^*)) - (D^2\mathbf{F})(\mathbf{x}^*)((D_i\pi)(\mathbf{x}^*), (D\mathbf{F})(\mathbf{x}^*)\dagger \mathbf{e}_j). \quad (4.130)
\]

For the remaining term, we are left with computing

\[
\int_0^t (D^2\mathbf{F})(\mathbf{x}^*)((e^{(D\mathbf{F})(\mathbf{x}^*)s} - (D\pi)(\mathbf{x}^*)) \mathbf{e}_i, (e^{(D\mathbf{F})(\mathbf{x}^*)s} - (D\pi)(\mathbf{x}^*)) \mathbf{e}_j) \, ds \quad (4.131)
\]

For conciseness, let \( \tilde{A} = J_1 \oplus \cdots \oplus J_p \), so that \( (D\mathbf{F})(\mathbf{x}^*) = P_{\mathbf{x}^*} \left( 0_{d\times d} \oplus \tilde{A} \right) P_{\mathbf{x}^*}^{-1} \) and \( e^{(D\mathbf{F})(\mathbf{x}^*)s} - (D\pi)(\mathbf{x}^*) = P_{\mathbf{x}^*} \left( 0_{d\times d} \oplus e^{\tilde{A}s} \right) P_{\mathbf{x}^*}^{-1} \). Then, the \( k \)th component of the Hessian above is the \( ij \)th entry of

\[
(P_{\mathbf{x}^*}^\top)^{-1} \left( \int_0^t (0_{d\times d} \oplus e^{\tilde{A}^Ts}) P_{\mathbf{x}^*}^\top (D^2 F_k)(\mathbf{x}^*) P_{\mathbf{x}^*} \left( 0_{d\times d} \oplus e^{\tilde{A}^Ts} \right) \, ds \right) P_{\mathbf{x}^*}^{-1}
\]

\[
= (P_{\mathbf{x}^*}^\top)^{-1} \left( \int_0^t e^{\tilde{A}^Ts} B_k e^{\tilde{A}s} \, ds \right) P_{\mathbf{x}^*}^{-1} \quad (4.132)
\]
where
\[
(0_{d \times d} \oplus B_k) = (0_{d \times d} \oplus I_{K-d \times K-d})P^\top_{x^*}(D^2F_k)(x^*)P_{x^*}(0_{d \times d} \oplus I_{K-d \times K-d}).
\] (4.133)
i.e.,
\[
(P^\top_{x^*})^{-1}(0_{d \times d} \oplus B_k)P_{x^*-1} = (I - (D\pi)(x^*))^\top(D^2F_k)(x^*)^{-1}(I - (D\pi)(x^*)).
\] (4.134)

Now, \(\tilde{A}\) is a negative definite matrix, so
\[
X_k = \lim_{t \to \infty} \int_0^t e^{\tilde{A}^\top s}B_k e^{\tilde{A}s} \, ds
\] (4.135)
exists and is the unique solution to
\[
\tilde{A}^\top X_k + X_k \tilde{A} = -B_k,
\] (4.136)
which may be obtained by solving the linear system
\[
(\tilde{A} \otimes I_{d \times d} + I_{d \times d} \otimes \tilde{A})\text{vec}(X_k) = -\text{vec}(B_k),
\] (4.137)
where \(\otimes\) denotes the Kronecker product, and \(\text{vec}(X)\) is the vector in \(\mathbb{R}^{d^2}\) with \(\text{vec}(X)_{(i-1)d+j} = X_{ij}\) [16].

Writing \(H^{ij}_k\) for the vector with
\[
H^{ij}_k = e^\top_i (P^\top_{x^*})^{-1} (X_k \oplus 0_{d \times d}) P_{x^*-1} e_j,
\] (4.138)
we then have,

\[
\lim_{t \to \infty} \int_0^t (D^2F)(x^*)(e^{(DF)(x^*)s} - (D\pi)(x^*)) e_i, (e^{(DF)(x^*)s} - (D\pi)(x^*)) e_j \, ds = H_{ij}.
\]

(4.139)

Summarizing the above, we have

**Lemma 4.2.** Using the notation above, for \( x^* \in \mathcal{C} \), we have

\[
(D_{ij}\pi)(x^*) = \langle (D\pi)(x^*), (D^2F)(x^*) e_i, (D_{ij}\pi)(x^*) \rangle - (D^2F)(x^*) \langle (D_i\pi)(x^*), (DF)(x^*) e_j \rangle.
\]

(4.140)

### 4.2.2 Explicit Expressions in Co-dimension One

Here, we consider the case where \( \mathcal{C} = \{ x : f(x) = 0 \} \) for a \( C^2 \) function \( f : \mathbb{R}^K_+ \to \mathbb{R} \) for which \( (Df)(x) \neq 0 \) for all \( x \in \mathbb{R}^K \). Fix \( x^* \in \mathcal{C} \), and, without loss of generality, assume that \( (\partial_K f)(x^*) \neq 0 \). Then, recalling the proof of Proposition 4.1 and the remarks following,

\[
\Phi_{x^*}(x) = (x_1 - x_1^*, \ldots, x_{K-1} - x_{K-1}^*, f(x))
\]

(4.141)

is a slice chart for \( \mathcal{C} \) in a neighbourhood \( U_{x^*} \) of \( x^* \). Then, \( \Phi_{x^*}(U_{x^*} \cap \mathcal{C}) \subseteq \{ x : x_K = 0 \} \), and if

\[
G(x) = (D\Phi_{x^*})(\Phi_{x^*}^{-1}(x)) F(\Phi_{x^*}^{-1}(x)),
\]

(4.142)

is the vector field topologically conjugate to \( F \) under \( \Phi_{x^*} \), then \( G(x_1, \ldots, x_{K-1}, 0) = 0 \), \textit{i.e.}, \( G(x) = x_K H(x) \) for some \( H \), and writing

\[
r(x) = (D\Phi_{x^*})(x)^{-1} H(\Phi_{x^*}(x))
\]

(4.143)
we see, that, provided \( f \) is at least \( C^2 \), \( r \) is at least \( C^1 \), and

\[
F(x) = f(x)r(x) \tag{4.144}
\]

near \( x^* \). Moreover, since \( x^* \) is arbitrary and \( f(x) \) is globally defined, \( r : \mathbb{R}_+^K \to \mathbb{R}^K \) is globally defined \( (r(x) = \frac{1}{f(x)}F(x)) \) and is \( C^1 \).

Thus,

\[
(DF)(x) = f(x)(Dr)(x) + (Df)(x) \otimes r(x), \tag{4.145}
\]

where \( u \otimes v \) is the rank-one linear operator defined by

\[
(u \otimes v)X = (u \cdot X)v \tag{4.146}
\]

for \( X \in \mathbb{R}^K \). If \( x^* \in C \), \( (DF)(x^*) = (Df)(x^*) \otimes r(x^*) \), and \( (DF)(x^*) \) has two distinct eigenvalues, 0 and \( \lambda(x^*) \), where

\[
\lambda(x) := (Df)(x) \cdot r(x). \tag{4.147}
\]

The former has corresponding eigenspace \( (Df)(x^*)^\perp = T_{x^*}C \), whilst the latter corresponds to the single eigenvector \( r(x^*) \). Thus, the projection onto \( \text{Im}((DF)(x^*)) \) is

\[
\frac{1}{\lambda(x^*)}(DF)(x^*) = \frac{1}{\lambda(x^*)}(Df)(x^*) \otimes r(x^*) \tag{4.148}
\]

and

\[
(DF)(x^*)^\dagger = \frac{1}{\lambda^2(x^*)}(Df)(x^*) \otimes r(x^*), \tag{4.149}
\]

(which is simply multiplication by \( \frac{1}{\lambda(x^*)} \) when restricted to \( \text{Im}((DF)(x^*)) \)), so that

\[
(D\pi)(x^*) = I - \frac{1}{\lambda(x^*)}(DF)(x^*). \tag{4.150}
\]
To compute the second derivatives, we begin by observing that

\[
(D^2 F_k)(x^\star) = (D^2 f)(x^\star) r_k + (D f)(x^\star)^\top (D r_k)(x^\star) + (D r_k)(x^\star)^\top (D f)(x^\star) \quad (4.151)
\]

and \((D f)(x^\star)(D \pi)(x^\star) = 0\), so that

\[
(D \pi)(x^\star)^\top (D^2 F_k)(x^\star)(D \pi)(x^\star) = (D \pi)(x^\star)^\top (D^2 f)(x^\star)(D \pi)(x^\star) r_k
\]

and

\[
(D F)(\pi(x^\star))^\dagger (D^2 F)(\pi(x^\star))\langle (D_i \pi)(\pi(x^\star)), (D_j \pi)(\pi(x^\star)) \rangle = \frac{1}{\lambda(x^\star)} (D^2 f)(x^\star)\langle (D_i \pi)(x^\star), (D_j \pi)(x^\star) \rangle r(x^\star). \quad (4.153)
\]

Proceeding as above, we also have

\[
(D^2 F)(x^\star)\langle r(x^\star), r(x^\star) \rangle = (D^2 f)(x^\star)\langle r(x^\star), r(x^\star) \rangle r(x^\star) + 2\lambda(x^\star)(D r)(x^\star) r(x^\star) \quad (4.154)
\]

and

\[
(D^2 F)(x^\star)\langle r(x^\star), e_i \rangle = (D^2 f)(x^\star)\langle r(x^\star), e_i \rangle r(x^\star) + \lambda(x^\star)(D r)(x^\star) e_i + (\partial_i f)(x^\star)(D r)(x^\star) r(x^\star) \quad (4.155)
\]

whereas

\[
(D^2 F)(x^\star)\langle (D F)(x^\star)^\dagger e_i, (D_j \pi)(x^\star) \rangle = \frac{1}{\lambda(x^\star)} \left( \frac{(D_i f)(x^\star)}{\lambda(x^\star)} (D^2 F)(r(x^\star), e_j) + \frac{(D_i f)(x^\star)(D_j f)(x^\star)}{\lambda^2(x^\star)} (D^2 F)(r(x^\star), r(x^\star)) \right). \quad (4.156)
\]
Finally, for all $X \in \mathbb{R}^K$,

\[ (DF)(x^*)X = ((Df)(x^*) \cdot X) r(x^*) \]

(4.157)

and thus

\[ (DF)(x^*)^n X = ((Df)(x^*) \cdot X) \lambda^{n-1}(x^*) r(x^*) \]

(4.158)

and

\[
e^{(DF)(x^*)t} X = \sum_{n=0}^{\infty} \frac{t^n (DF)(x^*)^n X}{n!}
\]

(4.159)

\[
= X + ((Df)(x^*) \cdot X) r(x^*) \sum_{n=1}^{\infty} \frac{\lambda^{n-1}(x^*) t^n}{n!}
\]

(4.160)

\[
= \frac{((Df)(x^*) \cdot X)}{\lambda(x^*)} (e^{\lambda(x^*)t} - 1) r(x^*).
\]

(4.161)

Further,

\[ (D\pi)(x^*) X = X - \frac{1}{\lambda(x^*)} ((Df)(x^*) \cdot X) r(x^*) \]

(4.162)

so that

\[ (e^{(DF)(x^*)t} - (D\pi)(x^*)) X = \frac{((Df)(x^*) \cdot X)}{\lambda(x^*)} e^{\lambda(x^*)t} r(x^*), \]

(4.163)

and

\[
H^{ij} = \lim_{t \to \infty} \int_0^t (D^2F)(x^*) \left( (e^{(DF)(x^*)s} - (D\pi)(x^*)) e_i, (e^{(DF)(x^*)s} - (D\pi)(x^*)) e_j \right) ds
\]

\[
= -\frac{(D_i f)(x^*)(D_j f)(x^*)}{2\lambda^3(x^*)} (D^2F)(r(x^*), r(x^*)). \]

(4.164)
Inserting the above terms into Lemma 4.2, with some calculations we find

\[
(D_{ij} \pi)(x^*) = \frac{1}{\lambda(x^*)} (D^2 f)(x^*)/(D_i \pi)(x^*) + (D_j \pi)(x^*) \nu(x) \left( \frac{1}{\lambda(x^*)} (D \pi)(x^*) (D \pi)(x^*) - \frac{1}{\lambda(x^*)} (D \pi)(x^*) (D r)(x^*) \right) \cdot (4.165)
\]

Finally, we can use the derivatives (4.165) in (4.97) to obtain the following corollary to Theorem 4.2, giving an explicit expression for the generator of \( Z(t) \) in co-dimension one:

**Corollary 4.4.** Suppose \( F(x) = f(x) r(x) \) with \( (D f)(x) \leq 0 \) and \( r(x) > 0 \). Then, \( C = f^{-1}(0) \) and

\[
(D \pi)(x^*) = I - \frac{1}{\lambda(x^*)} (D F)(x^*) = I - \frac{1}{\lambda(x^*)} (D f)(x^*) \otimes r(x^*). \quad (4.166)
\]

Recall that

\[
\bar{a}(x) := \sum_{n \in \mathbb{Z}^K} m n^\top \lambda_n(x). \quad (4.167)
\]

If we set

\[
a(x) := (D \pi)(x) \bar{a}(x)(D \pi)^\top(x) \quad (4.168)
\]

and

\[
b(x) = (D \pi)(x) \nu(x) - \frac{1}{\lambda(x)} \text{tr} \left( (D^2 f)(x) a(x) \right) r(x) - \frac{1}{\lambda(x)} (D \pi)(x) (D r)(x) (I + (D \pi)(x)) \bar{a}(x)(D f)^\top(x), \quad (4.169)
\]
then $\tilde{Z}$ has generator

$$
(\mathcal{G}\phi)(\mathbf{x}) = \sum_{i=1}^{K} b_i(\mathbf{x}) \partial_i \phi(\mathbf{x}) + \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} a_{ij}(\mathbf{x}) \partial_i \partial_j \phi(\mathbf{x}).
$$

(4.170)

In the next section, we will apply this to several density dependent birth-death-mutation processes, but first we consider an alternative approach to computing the derivatives of $\pi(\mathbf{x})$, which is considerably more tractable, when the Law of Large numbers is of Lotka-Volterra-Gause type.

### 4.2.3 Energy-based Approaches

Consider the case when

$$
F_i(\mathbf{x}) = x_i \left( b_i - \sum_{j=1}^{K} a_{ij} x_j \right) = x_i (b - A\mathbf{x})_i,
$$

(4.171)

so the set of interior equilibria consists of the set of points $\mathcal{C} = \{ \mathbf{x} \in \mathbb{R}_+^K : A\mathbf{x} = b \}$. We are thus in the weak selection regime if $\text{rank}(A|b) = K - d$ for some $d > 0$. Thus, there exist $d$ linearly independent vectors $\mathbf{c}^{(j)} \in \mathbb{R}^K$ such that

$$
(\mathbf{c}^{(j)})^\top A = (\mathbf{c}^{(j)})^\top b = 0.
$$

(4.172)

Let

$$
\mathcal{E}_j(\mathbf{x}) = \sum_{i=1}^{d} c_i^{(j)} \ln x_i.
$$

(4.173)

Then, for all $\mathbf{x} \in \mathbb{R}_+^K$

$$
\dot{\mathcal{E}}_j(\mathbf{x}) = \sum_{i=1}^{d} c_i^{(j)} \left( b_i - \sum_{j=1}^{K} a_{ij} x_j \right) = (\mathbf{c}^{(j)})^\top b - (\mathbf{c}^{(j)})^\top A\mathbf{x} = 0,
$$

(4.174)

so $\mathcal{E}_j$ is an invariant of motion for the system.
In particular, we have
\[ E_j(\pi(x)) = E_j(x), \]  
for \( j = 1, \ldots, d \), which, together with the rank \( K - d \) system
\[ \sum_{j=1}^{K} a_{ij} \pi_j(x) = b_i, \quad i = 1, \ldots, K \]  
allows us to compute \( \pi(x) \) and it’s derivatives. For the latter, differentiating both sets of equations with respect to \( x_k \) yields
\[ \sum_{i=1}^{K} c_i^{(j)} \frac{\partial \pi_i}{\pi_i(x) \partial x_k} = \frac{c_k^{(j)}}{x_k}, \]  
and
\[ \sum_{j=1}^{K} a_{ij} \frac{\partial \pi_j}{\partial x_k} = 0, \quad i = 1, \ldots, K, \]
which is generically a rank \( n \) system of linear equations that may be solved for the unknown derivatives in terms of \( \pi(x) \). The second derivatives may be obtained in a similar fashion.

**Example 4.1** (The Co-dimension One Lotka-Volterra-Gause Model). In co-dimension one, \( C \) is a hyperplane, and there exist scalars \( \beta, \alpha_1, \ldots, \alpha_K \) and \( \gamma_1, \ldots, \gamma_K \) such that
\[ b_i = \gamma_i \beta \quad \text{and} \quad a_{ij} = \gamma_i \alpha_j \]  
(4.179)
for all $i$, so that $r_i(x) = \gamma_i x_i$ and $f(x) = \beta - \sum_{j=1}^{K} \alpha_j x_j$. Thus,

$$ (D_i f)(x) = \alpha_i, \quad (D_{ij} f)(x) = 0, \quad \lambda(x) = \sum_{l=1}^{K} \gamma_l \alpha_l x_l, $$

and

$$ (D\lambda)(x) = \begin{bmatrix} \gamma_1 \alpha_1 \\ \vdots \\ \gamma_K \alpha_K \end{bmatrix}, $$

$$ (Dr)(x) = \begin{bmatrix} \gamma_1 \\ \vdots \\ \gamma_K \end{bmatrix}. $$

It may be readily verified that here we may take $c^{(j)} = \gamma_1 e_1 - \gamma_j e_j$, so that

$$ E_j(x) = \gamma_1 \ln x_1 - \gamma_j \ln x_j. \quad (4.180) $$

We omit the calculations, but note that, together with the requirement that

$$ \sum_{i=1}^{K} \alpha_i \pi_i(x) = \beta, \quad (4.181) $$

these invariants may be used to show that for $x^* \in C$,

$$ (D_i \pi_k)(x^*) = \delta_{ik} - \frac{\alpha_i \gamma_k x^*_k}{\sum_{l=1}^{K} \gamma_l \alpha_l x^*_l} \quad (4.182) $$
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and

$$(D_{ij} \pi_k)(x^*) = \frac{\gamma_k}{\sum_{l=1}^K \gamma_l \alpha_l x_l^*} (-\alpha_i \delta_{jk} - \alpha_j \delta_{ik})$$
$$+ \frac{\alpha_i \alpha_j x_k^*}{\sum_{l=1}^K \gamma_l \alpha_l x_l^*} \left( \gamma_i + \gamma_j + \gamma_k - \frac{\sum_{l=1}^K \gamma_l^2 \alpha_l x_l^*}{\sum_{l=1}^K \gamma_l \alpha_l x_l^*} \right), \quad (4.183)$$

which may be verified using the variational approach given previously.

We will return to this approach in the next chapter, where it will allow us to calculate the first and second derivatives in an example where $C$ has co-dimension 2.

4.3 Weakly Selected Density Dependent Birth-Death-Mutation Processes

In this section, we apply the results of the previous sections to the Birth-Death-Mutation processes discussed in Chapter 2. In particular, we consider the special case of weak selection when $C$ is a co-dimension one submanifold, $C = f^{-1}(0)$. We can then use the explicit forms of the first and second partial derivatives of $\pi(x)$ computed in Section 4.2.2 to state the generator of the limiting process. Unfortunately, even under this strong assumption, the generator of the limiting process defies easy biological interpretation, so we will take the approach of classical population genetics, and begin by analyzing the exchangeable case, and then consider the consequences of relaxing exchangeability.

We begin by introducing some notation that will allow a more easy comparison to classical population genetics. Let

$$\tilde{\beta}_1^{(N)}(x) := \sum_{n \in \mathbb{N}_0^K} \|n\|_1 \beta_{1,n}^{(N)}(x)$$
$$\tilde{\beta}_1^{(N)}(x) := \sum_{n \in \mathbb{N}_0^K} \|n\|_2^2 \beta_{1,n}^{(N)}(x),$$
and

\[
\mu_{ij}^{(N)}(x) := \begin{cases} 
\frac{1}{\bar{\beta}_i(x)} \sum_{n \in N_0^K} n_j \beta_{i,n}^{(N)}(x) & \text{if } i \neq j \\
0 & \text{otherwise}
\end{cases}
\]

\(\bar{\beta}_i^{(N)}(x)\) is thus the expected total reproductive output of an individual of type \(i\) per unit time in environment \(x\), \(\hat{\beta}_i^{(N)}(x) - \left(\bar{\beta}_i^{(N)}(x)\right)^2\) is the variance in total reproductive output per unit time, and \(\mu_{ij}^{(N)}(x)\) is the fraction of the expected number of offspring which are of type \(j\). By assumption,

\[
\mu_{ij}^{(N)}(x) = O\left(\frac{1}{N}\right). \tag{4.184}
\]

for \(i \neq j\). Let

\[
\theta_{ij}(x) := \lim_{N \to \infty} N \mu_{ij}^{(N)}(x) \tag{4.185}
\]

be the rescaled rate of mutation,

\[
s_i^{(N)}(x) = \frac{\left(\bar{\beta}_i^{(N)}(x) - \bar{\beta}_i(x)\right) - \left(\delta_i^{(N)}(x) - \delta_i(x)\right)}{\bar{\beta}_i^{(N)}(x)}, \tag{4.186}
\]

and let

\[
\alpha_i(x) := \lim_{N \to \infty} N s_i^{(N)}(x), \tag{4.187}
\]

i.e., \(\alpha_i(x)\) is the \(O\left(\frac{1}{N}\right)\) component of the net reproductive rate (that the limit exists is guaranteed by Assumption (2.3)). With this notation, we have

\[
F_i^{(N)}(x) - F_i(x) = -\sum_{j=1}^K \mu_{ij}^{(N)}(x)\bar{\beta}_i^{(N)}(x)x_i + \sum_{j=1}^K \mu_{ji}^{(N)}(x)\bar{\beta}_j^{(N)}(x)x_j + \bar{\beta}_i^{(N)}(x)s_i^{(N)}(x)x_i. \tag{4.188}
\]
so that

\[
\nu_i(x) = \lim_{N \to \infty} N \left( F_i^{(N)}(x) - F_i(x) \right) = -\sum_{j=1}^{K} \theta_{ij}(x) \bar{\beta}_i(x)x_i + \sum_{j=1}^{K} \theta_{ji}(x) \bar{\beta}_j(x)x_j + \bar{\beta}_i(x) \alpha_i(x)x_i.
\]

Further, by Assumptions 2.1 and 2.3, we have

\[
\bar{\beta}_i^{(N)}(x) \to \bar{\beta}_i(x)
\]

and

\[
\hat{\beta}_i^{(N)}(x) \to \hat{\beta}_i(x) := \sum_{n=1}^{\infty} n^2 \beta_i(x)
\]

as \(N \to \infty\), uniformly on compact sets.

Thus, using the notation of Theorem 4.2,

\[
\nu(x) = \tilde{a}_{ij}(x) = \begin{cases} 
\hat{\beta}_i(x)x_i + \delta_i(x)x_i & \text{if } i = j, \\
0 & \text{otherwise.} 
\end{cases}
\]

In particular, at points \(x^* \in \mathcal{C}\), \(\bar{\beta}_i(x^*) = \delta_i(x^*)\), so \(\tilde{a}_{ij}(x^*) = \delta_{ij}(\hat{\beta}_i(x^*) + \bar{\beta}_i(x^*))x_i\).

### 4.3.1 The Relative Frequency Process and Projection to the Standard Simplex

In keeping with the convention in population genetics, we will focus on the relative frequency of types, rather than their absolute density. As we discuss below, this will be useful in interpreting the process, in particular in considering fixation probabilities. To that end, we introduce a second projection map,

\[
\rho(x) = \frac{1}{\sum_{i=1}^{K} x_i} x.
\]
with partial derivatives

\[(D\rho)(x) = \frac{1}{\sum_{i=1}^{K} x_i} (I - 1 \otimes \rho(x)) \quad (4.194)\]

and

\[(D_{ij}\rho)(x) = -\frac{1}{(\sum_{i=1}^{K} x_i)^2} (e_i + e_j - 2\rho(x)), \quad (4.195)\]

where

\[1 = \begin{pmatrix} 1 \\ \vdots \\ 1 \end{pmatrix} \quad (4.196)\]

is the vector with all entries equal to 1. \( \rho \) is thus a differentiable map from \( C \) to the standard simplex \( \Delta_1 = \left\{ p \in \mathbb{R}_+^K : \sum_{i=1}^{K} p_i = 1 \right\} \). In fact, if we assume that the origin is a source, then \( \rho \) is a diffeomorphism. We begin with a lemma:

**Lemma 4.3.** If the dynamical system generated by the vector field \( F(x) = r(x)f(x) \) is dissipative and totally competitive, then the set \( \{ x : f(x) \geq 0 \} \) is compact.

**Proof.** Suppose the contrary; then given any \( M > 0 \), there exist a point \( x_0 \) such that \( f(x) > 0 \) and \( \|x\| > M \). Then, either \( f > 0 \) on the complement of the ball of radius \( M \), \( B_M(0)^c \), in which case \( \gamma_+(x) \) is unbounded for any \( x \in B_M(0)^c \), or there exists \( x_1 \in B_M(0)^c \) such that \( f(x_1) \leq 0 \). In the latter case, we must also have \( x^* \in B_M(0)^c \) such that \( f(x^*) = 0 \) (indeed, there exists \( x^* \) which is a convex combination of \( x_0 \) and \( x_1 \)) so that the dynamical system has an equilibrium point in \( B_M(0)^c \). Since the system is totally competitive, this fixed point must be a locally asymptotically stable attractor. Since \( M \) was arbitrary, the dynamical system must have an attractor outside of any compact set. Thus, in either case, the system fails to be dissipative.

**Remark 4.8.** We briefly remark that the analogous result doesn’t hold for the general Kolmogorov system i.e., we can have a system \( \dot{x}_i = f_i(x)x_i \) which is competitive and
dissipative, but for which the set \( \{ x : f_i(x) > 0 \} \) need not be compact for all \( i \). For example,

\[
\begin{align*}
\dot{x}_1 &= (1 - (1 + x_1)x_2)x_1 \\
\dot{x}_2 &= (2 - x_1 - x_2)x_2
\end{align*}
\] (4.197)

has saddle nodes at \((0, 2)\) and \((1, 0)\), and a unique fixed interior point, \( \left( \frac{1+\sqrt{5}}{2}, \frac{3-\sqrt{5}}{2} \right) \) that is globally attracting on \( \mathbb{R}_+^2 \), whereas

\[
\{ x : f_1(x) > 0 \} = \left\{ x : x_2 \leq \frac{1}{1+x_1} \right\}
\] (4.199)

is unbounded.

We now have

**Proposition 4.2.** Assume that the system with vector field \( F(x) = r(x)f(x) \) is dissipative and totally competitive and that \( f(0) > 0 \). Then, \( \rho : \mathcal{C} \to \Delta_1 \) is a diffeomorphism.

**Proof.** First, note that \( p \in \rho(\mathcal{C}) \) if and only if there exists \( n(p) \geq 0 \) such that \( f(n(p)p) = 0 \). If \( p = \rho(x^*) \), then

\[
n(p) = \sum_{i=1}^{K} x^*_i.
\] (4.200)

Let \( g_{p}(t) := f(tp) \), so \( g \) is continuous, and by assumption \( g_p(0) > 0 \). From the lemma, we see that \( g_p(t) < 0 \) for \( t \) sufficiently large. By the intermediate value theorem, \( g_p(n(p)) = 0 \) for some \( n(p) > 0 \), so \( \rho \) is onto.

Now, suppose that there exist \( x^*_1 \neq x^*_2 \in \mathcal{C} \) such that \( \rho(x^*_1) = \rho(x^*_2) = p \). Then, without loss of generality,

\[
x^*_2 - x^*_1 = cp
\] (4.201)

for some \( c > 0 \). Let \( \gamma(t) \) be a geodesic in \( \mathcal{C} \) such that there exist \( t_2 > t_1 \) with \( \gamma(t_i) = x_i \).
Then, by the mean value theorem, there exists $t_3 \in [t_1, t_2]$ such that

$$\dot{\gamma}(t_3) = \frac{\gamma(t_2) - \gamma(t_1)}{t_2 - t_1} = \frac{c}{t_2 - t_1} p. \tag{4.202}$$

On the other hand, $\gamma(t)$ lies in $C$, so we must have $f(\gamma(t)) = 0$ for all $t$ and

$$0 = \frac{d}{dt} \bigg|_{t=t_3} = (Df)(\gamma(t_3)) \cdot \dot{\gamma}(t_3) = \frac{c}{t_2 - t_1} (Df)(\gamma(t_3)) \cdot p, \tag{4.203}$$

i.e., $(Df)(\gamma(t_3)) \cdot p = 0$, contradicting the assumption of total competitiveness. Hence $\rho$ is injective.

Lastly, let $G(x, t) = (x, g_x(t))$, $p \in \Delta_1$ and let $n(p)$ be the unique $t > 0$ such that $tp \in C$. Then,

$$\det ((DG)(x, t)) = (\partial_t g_x)(t) = (Df)(tx) \cdot x, \tag{4.204}$$

which, by assumption is strictly positive in a neighbourhood of $(p, n(p))$. By the inverse function theorem, $G^{-1}$ exists and is differentiable near $(p, n(p))$. In particular, $g_p^{-1}(0)$ exists and is singly valued – it is equal to $n(p)$ – and differentiable in $p$, so $p \mapsto g_p^{-1}(0)x : \Delta_1 \to C$ is a differentiable injection. 

We will henceforth refer to $P(t) := \rho(\tilde{Z}(t))$ as the relative frequency process corresponding to $\tilde{Z}(t)$. If $\tilde{Z}(t)$ has generator

$$(G\phi)(x) = \sum_{i=1}^{K} b_i(x) \partial_i \phi(x) + \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} a_{ij}(x) \partial_i \partial_j \phi(x), \tag{4.205}$$
then, using Itô’s formula, it is readily shown that $P(t)$ has generator

$$(\mathcal{G}_p \phi)(p) = \frac{1}{n(p)} \sum_{i=1}^{K} \left[ b_i(n(p)p) \right] - \frac{1}{n(p)} \sum_{n=1}^{K} a_n(n(p)p)

- p_i \sum_{j=1}^{K} \left( b_j(n(p)p) \right) \delta_{ij} - \frac{1}{n(p)} \sum_{m=1}^{K} a_{mj}(n(p)p)

+ \frac{1}{2n(p)} \sum_{i=1}^{K} \sum_{j=1}^{K} \left( a_{ij}(n(p)p) \delta_{ij} - p_i \sum_{m=1}^{K} a_{mj}(n(p)p) - p_j \sum_{n=1}^{K} a_{in}(n(p)p)

+ p_i p_j \sum_{m=1}^{K} \sum_{n=1}^{K} a_{mn}(n(p)p) \right] \partial_i \partial_j \phi(p). \quad (4.206)$$

In the next two sections, we will consider a few examples of density-dependent birth-death-mutation processes in the weak selection regime and their corresponding limiting relative frequency processes, with the intent of gleaning some biological insight and identify points of departure from the classical theory. As with Cannings’ approach, we start with exchangeable birth-death-mutation processes, which have Kimura’s diffusion as their invariance principle. We then consider a few biologically interesting examples of “nearby” processes which depart from Kimura’s diffusion. In the final section, we revisit the Generalized Moran model as a means of understanding the population genetic consequences of fecundity/mortality tradeoffs.

### 4.3.2 Exchangeable Processes, Neutrality and Kimura’s Diffusion

We begin by considering the case when all types are exchangeable, so that $\beta_i^{(N)}(x) = \beta_j^{(N)}(x)$ and $\delta_i^{(N)}(x) = \delta_j^{(N)}(x)$ for all $i, j$ and all $x$. Then, $\beta_i(x) \equiv \beta_i(x)$, $\delta_i(x) \equiv \delta(x)$, and we may thus take $f(x) = \beta(x) - \delta(x)$ and $r = x$. Moreover, to ensure exchangeability, $f$ must be invariant under permutations of its arguments, so we must have $\partial_i f = \partial_j f$ for all $i, j$. This largely characterizes $f$, as is shown by the following simple lemma.
Lemma 4.4. Suppose $f : \mathbb{R}^K \to \mathbb{R}$ is differentiable. Then $\partial_i f = \partial_j f$ for all $i, j$ if and only if there exists a differentiable $\tilde{f}$ such that $f(x) = \tilde{f}(\sum_{i=1}^K x_i)$.

Proof. If $f(x) = \tilde{f}(\sum_{i=1}^K x_i)$, then $\partial_i f = \partial_j f$ for all $i, j$.

Conversely, suppose $f$ satisfies $\partial_i f = \partial_j f$ for all $i, j$. Given $x \in \mathbb{R}^K$, let

$$g(t) = f(x_1 + t \sum_{i=2}^K x_i, (1-t)x_2, \ldots, (1-t)x_K)$$

so that

$$g'(t) = \sum_{i=2}^K x_i (\partial_1 f - \partial_i f) = 0,$$

and

$$f(x) = g(0) = g(1) = f(\sum_{i=1}^K x_i, 0, \ldots, 0).$$

The result follows taking $\tilde{f}(t) = f(t, 0, \ldots, 0)$. \hfill \Box

We thus have $f(x) = \tilde{f}(\sum_{i=1}^K x_i)$. In a slight abuse of notation, we will use $f$ and $\tilde{f}$ interchangeably. By assumption, our process is competitive, so $\partial_i f < 0$ for all $i$, and thus $f' < 0$. In particular, $f$ can has exactly one zero, $n^*$, and $\mathcal{C}$ is the simplex

$$\left\{ x : \sum_{i=1}^K x_i = n^* \right\}.$$ 

Moreover, for all $x^* \in \mathcal{C}$, $T_{x^*}\mathcal{C}$ is the hyperplane perpendicular to $\mathbb{1}$, $\lambda(x^*) = f'(n^*)n^*$, and $(Df)(x) = f'(\sum_{i=1}^K x_i)\mathbb{1}$. Direct calculation then shows that on $\mathcal{C}$ the derivatives of $\pi(x)$, (4.150) and (4.165), simplify to

$$(D\pi)(x^*) = I - \frac{1}{n^*} \mathbb{1} \otimes x^*$$

and

$$(D_{ij}\pi)(x^*) = -\frac{1}{n^*} \left( e_i + e_j - \frac{2}{n^*} x^* \right).$$
whilst $P(t) = \frac{1}{n^*} \tilde{Z}(t)$.

In this case, we have

$$G\phi(p) = \sum_{i=1}^{K} \left( - \sum_{j=1}^{K} \theta_{ij}(n^*p) \tilde{\beta}(n^*p) p_i + \sum_{j=1}^{K} \theta_{ji}(n^*p) \tilde{\beta}(n^*p) p_j \right) \partial_i \phi(p)$$

$$+ \frac{1}{n^*} \sum_{i=1}^{K} \sum_{j=1}^{K} \tilde{\beta}(n^*p) p_i (\delta_{ij} - p_j) \partial_i \partial_j \phi(p). \quad (4.213)$$

Moreover, since $\tilde{\beta} \geq 0$,

$$\gamma(t) := \inf\left\{ u : \int_{0}^{u} \tilde{\beta}(n^*P(s)) ds > t \right\}, \quad (4.214)$$

is non-decreasing and we can apply Theorem 6.1.4 in [50] (Random Time Change), to conclude that the time-rescaled process, $\tilde{P}(t) := P(\gamma(t))$, satisfies

$$\tilde{G}\phi(p) = \sum_{i=1}^{K} \left( - \sum_{j=1}^{K} \theta_{ij}(n^*p) p_i + \sum_{j=1}^{K} \theta_{ji}(n^*p) p_j \right) \partial_i \phi(p)$$

$$+ \frac{1}{n^*} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i (\delta_{ij} - p_j) \partial_i \partial_j \phi(p). \quad (4.215)$$

which is essentially the generator for Kimura’s diffusion, (1.12), except that we have allowed for frequency-dependent mutation. Notice that the time rescaling is equivalent to measuring time in units of $\frac{1}{\tilde{\beta}(x)}$, the per-individual expected time to first reproduction. In particular, the process $\tilde{P}(t)$ is obtained from $X^{(N)}(t)$ via (among other things) a time rescaling of $\frac{N}{\tilde{\beta}(x)}$, which is the generation time for the original process i.e., the expected time for all individuals to have reproduced at least once. The census population size at equilibrium is approximately $n^*N$, so we may regard $n^*$ as analogous to an effective population size.

**Remark 4.9.** In fact, to obtain Kimura’s diffusion, (1.12) as a limit, we did not require the processes $X^{(N)}(t)$ to be exchangeable, only the weaker conditions
(i) \( \bar{\beta}_i(x) \equiv \beta(x) \) and \( \delta_i(x) \equiv \delta(x) \) for all \( i \) and all \( x \),

(ii) \( \hat{\beta}_i(x) \equiv \hat{\beta}(x) \) for all \( i \) and all \( x \),

(iii) \( \partial_i f(x) = \partial_j f(x) \) for all \( i, j \) and all \( x \), for \( f(x) = \beta(x) - \delta(x) \), and

(iv) \( \alpha_i(x) = 0 \) for all \( x \).

We investigate the consequences of relaxing these assumptions in the sequel.

**Classical Weak Selection**

If we allow the individual total reproductive rate, \( \bar{\beta}(N)(x) \) and death rate \( \delta(N)(x) \) (and thus expected total lifetime reproductive output) to differ to order \( O\left( \frac{1}{N} \right) \), then \( \alpha_i(x) \neq 0 \), and we obtain a diffusion analogous to Kimura’s diffusion under weak selection. Rescaling time, as above, by \( \gamma(t) = \inf \{ u : \int_0^u \bar{\beta}(n^s \mathbf{P}) \, ds > t \} \), we have

\[
\tilde{G}\phi(p) = \sum_{i=1}^{K} \left[ -\sum_{j=1}^{K} \theta_{ij}(n^s \mathbf{p})p_i + \sum_{j=1}^{K} \theta_{ji}(n^s \mathbf{p})p_j \right. \\
+ p_i \left( \alpha_i(n^s \mathbf{p}) - \sum_{j=1}^{K} \alpha_j(n^s \mathbf{p})p_j \right) \left. \right] \partial_i \phi(p) \\
+ \frac{1}{n^s} \sum_{i=1}^{K} \sum_{j=1}^{K} p_i(\delta_{ij} - p_j)\partial_i \partial_j \phi(p). \quad (4.216)
\]

Again, when the \( \theta_{ij} \) and \( \alpha_i \) are constant, we recover Kimura’s generator for processes under weak selection. As in the classical case, if, without loss of generality, \( \alpha_1 > \alpha_i \) for all \( i > 1 \), then

\[
\mathbb{E}_p[P_1(t)] = p_i + \int_0^t \mathbb{E} \left[ P_i(s) \left( \sum_{j=1}^{K} (\alpha_i - \alpha_j)P_j(s) \right) \right] \, ds > p_i, \quad (4.217)
\]
and there is selection favouring type 1. More generally, when the $\alpha_i$ are frequency dependent, i.e., depend on $p$, then

$$p_i \left( \alpha_i(n^*p) - \sum_{j=1}^{K} \alpha_j(n^*p)p_j \right)$$  \hspace{1cm} (4.218)

is simply the projection onto $\Delta_0 = \{ x \in \mathbb{R}^K : \sum_{i=1}^{K} x_i = 0 \}$ of the essentially arbitrary vector field $\alpha(x)$, and we can only conclude that frequency dependent selection occurs: that $E[P_i(t)]$ will increase at those times when $P_i(t)$ is non-zero and $\alpha_i(n^*P(t))$ is greater than the population average value $\bar{\alpha}(n^*P(t)) = \sum_{j=1}^{K} \alpha_j(n^*P(t))P_j(t)$.

**Fecundity Variance Polymorphism**

Among the most extensively studied departures from exchangeability is when $\bar{\beta}_i \equiv \beta$, $\delta_i \equiv \delta$, and $\partial_i f(x) = \partial_j f(x)$, but $\hat{\beta}_i \neq \hat{\beta}_j$ for $i \neq j$, so that all types have the same mean reproductive output, but may differ in the variance in the number of offspring per reproductive event. This is referred to as *fecundity variance polymorphism* (see e.g., [66, 171, 67, 68, 61, 176] etc.). In this case, $P(t)$ has generator

$$\mathcal{G}\phi(p) = \sum_{i=1}^{K} \left[ -\sum_{j=1}^{K} \theta_{ij}(n^*p)\bar{\beta}(n^*p)p_i + \sum_{j=1}^{K} \theta_{ji}(n^*p)\bar{\beta}(n^*p)p_j \right]$$

$$-\frac{1}{n^*}p_i \left( \hat{\beta}_i(n^*p) - \sum_{j=1}^{K} \hat{\beta}_j(n^*p)p_j \right) \partial_i\phi(p) + \frac{1}{n^*} \sum_{i=1}^{K} \sum_{j=1}^{K} \left[ p_i \left( (\hat{\beta}_i + \bar{\beta})(n^*p)\delta_{ij} \right) \right. \partial_i\partial_j\phi(p) \hspace{1cm} (4.219)$$

or, again, rescaling time by

$$\gamma(t) := \inf \left\{ u : \int_0^u \bar{\beta}(n^*P(s)) \, ds > t \right\} ,$$  \hspace{1cm} (4.220)
the generator takes the form

\[
\tilde{G}\phi(p) = \sum_{i=1}^{K} \left[ -\sum_{j=1}^{K} \theta_{ij}(n^*p)p_i + \sum_{j=1}^{K} \theta_{ji}(n^*p)p_j - \frac{1}{n^*} \left( \sigma_i^2(n^*p) - \sum_{j=1}^{K} \sigma_j^2(n^*p)p_j \right) \right] \partial_i \phi(p) \\
+ \frac{1}{n^*} \sum_{i=1}^{K} \sum_{j=1}^{K} \left[ p_i \left( \sigma_i^2(n^*p)\delta_{ij} - \left( \sigma_i^2(n^*p) + \sigma_j^2(n^*p) - \sum_{n=1}^{K} \sigma_i^2(n^*p)p_n \right) p_j \right) \right] \partial_i \partial_j \phi(p)
\]

(4.221)

where

\[
\sigma_i^2(p) := \frac{\beta_i(p)}{\beta(p)} + 1
\]

(4.222)

was shown in Corollary 2.1 to be the variance in total lifetime reproductive output for type \(i\) when the population has reached the manifold of fixed points \(C\). For \(K = 2\) and constant \(\sigma_i^2\), this generator was derived via a heuristic argument in [66]. Under the assumption of constant \(\sigma_i^2\), this shows that \textit{ceteris paribus}, among types with the same equilibrium expected lifetime reproductive success, the one with the lowest variance in fecundity is selectively favoured.

**Resource Competition**

We now consider relaxing the third condition, \(\partial_i f(x) = \partial_j f(x)\) for all \(i, j\), while retaining the first two. Unlike our previous examples, here we depart from the realm of classical population genetics to consider questions more traditionally within the purview of population ecology.

As in the previous cases, we have \(r(x) = x\), so that \((Dr)(x) = I\), \(\lambda(x) = (Df)(x) \cdot x\),

\[
(D\pi)(x^*) = I - \frac{1}{\lambda(x^*)} (Df)(x^*) \otimes x^*
\]

(4.223)
and

\begin{equation}
(D_{ij}\pi)(x^*) = \frac{1}{\lambda(x^*)}(D^2 f)(x^*) - (D_i\pi)(x^*) \left( (\partial_i f)(x^*) e_j + (\partial_j f)(x^*) e_i - \frac{(\partial_i f)(x^*) (\partial_j f)(x^*)}{\lambda(x^*)} x^* \right). \tag{4.224}
\end{equation}

Moreover,

\begin{equation}
(D\rho)(x^*)(D\pi)(x^*) = (D\rho)(x^*), \tag{4.225}
\end{equation}

which greatly simplifies calculations. Here, we use the time rescaling

\begin{equation}
\gamma(t) := \inf \left\{ u : \int_0^u (\tilde{\beta} + \hat{\beta})(n^*P(s)) \, ds > t \right\}, \tag{4.226}
\end{equation}

and under which the process \( \tilde{P}(t) := \rho(\tilde{Z}(\gamma(t))) \) has generator

\begin{equation}
G\phi(p) = \sum_{i=1}^K \left( -\sum_{j=1}^K \theta_{ij}(n^*p)p_i + \sum_{j=1}^K \theta_{ji}(n^*p)p_j \right) + p_i \left( (\partial_i f)(n^*p) - \sum_{j=1}^K (\partial_j f)(n^*p)p_j \right) \partial_i\phi(p)
+ \frac{1}{n^*} \sum_{i=1}^K \sum_{j=1}^K p_i(\delta_{ij} - p_j)(\partial_i \partial_j \phi(p)). \tag{4.227}
\end{equation}

Comparing with our expression for the generator under Classical Weak Selection, we see that this is formally equivalent to local selection favouring any type for which \( \partial_j f \) is below the population mean.

This result has an interesting interpretation under the aegis of consumer resource theory; \( f \) is asymptotically equal to the per-capita net growth rate of all individuals of all types, which, under the assumption of total competition, is, at least in a neighbourhood of \( C \) a strictly decreasing function of the density of all types. \( f \) can thus be considered a measure of the degradation of the environment, by the depletion of essential resources.
or the accumulation of wastes. $\partial_i f$ is then the marginal degradation of the environment with an increase of type $i$. We thus see that selection favours the type with the highest marginal degradation per capita. This might be considered a “second-order” analogue of a result of Volterra’s, popularized by Tilman as $R^*$ theory [177]: in $R^*$ theory, when species compete for a single limiting resource, it is the type that can most deplete the resource, and survive in the most degraded environment that will exclude the others, here we see that among species which share a common lowest viable resource level, the type that most efficiently depletes the resource will exclude all others.

### 4.3.3 The Generalized Moran Model

To conclude this chapter, we return to our prototypical model, the Generalized Moran Model, Example 2.1 which, at least when $K = 2$, is sufficiently specific that we may obtain analytical results for the fixation probabilities, fixation and absorption times, and for the quasi-stationary distribution. In this case we have

- $\bar{\beta}_i^{(N)}(x) = \bar{\beta}_i(x) = \beta_i$ and $\hat{\beta}_i^{(N)}(x) = \hat{\beta}_i(x) = \beta_i$,
- $\delta_i(x) = \delta_i \left(1 + \sum_{j=1}^{K} x_j\right)$,
- $\mu_{ij}^{(N)}(x) = \frac{\theta_{ij}}{N}$ and $\theta_{ij}(x) = \theta_{ij}$,
- $s_i^{(N)}(x) = \alpha_i(x) = 0$.

For the Generalized Moran model, the existence of a submanifold of attracting fixed points is equivalent to the existence of multiplicative tradeoff between mortality and fecundity, \( \text{i.e.,} \) when there exists a constant $\tau$ such that

$$\frac{\bar{\beta}_i}{\delta_i} = \tau > 1,$$  \hspace{1cm} (4.228)

independently of $i$. As we observed in Proposition 2.2, this corresponds to the case when all types have the same expected lifetime reproductive success at equilibrium. Although
one type may have an elevated birth rate, this is compensated by a correspondingly elevated death rate. Assuming (4.228),

\[ C = \left\{ \mathbf{x} \in \mathbb{R}^K_+ : \sum_{i=1}^K x_i = \tau - 1 \right\} \quad (4.229) \]

is a linear submanifold, so as before, \( \rho \) is a bijection from \( C \) onto \( \Delta_1 \).

After rescaling time by \( \gamma(t) = \frac{\tau - 1}{2} t \), the relative frequency process corresponding to the Generalized Moran model has generator

\[
G\phi(p) = \sum_{i=1}^K \left( -\sum_{j=1}^K \theta_{ij} \beta_i p_i + \sum_{j=1}^K \theta_{ji} \beta_j p_j \right.
\]

\[
+ \frac{1}{2} \left( \sum_{k=1}^K \beta_k p_k \right)^2 \sum_{k=1}^K (\beta_k - \beta_i) \beta_k p_k \right) \partial_i \phi(p)
\]

\[
+ \frac{1}{2} \sum_{i=1}^{K-1} \sum_{j=1}^K \beta_i p_i \left( \delta_{ij} - \frac{\beta_j p_j}{\sum_{k=1}^K \beta_k p_k} \right) \partial_i \partial_j \phi(p). \quad (4.230)
\]

for \( K = 2 \), we have \( \mathbf{P}(t) = (P_1(t), 1 - P_1(t)) \), and the generator of \( P_1 \) is

\[
G\phi(p) = \left( -\theta_{12} \beta_1 p + \theta_{21} \beta_2 (1 - p) + \frac{1}{2} \frac{\beta_1 \beta_2 (\beta_2 - \beta_1)}{\beta_1 p + \beta_2 (1 - p)} p(1 - p) \right) \phi'(p)
\]

\[
+ \frac{1}{2} \frac{\beta_1 \beta_2}{\beta_1 p + \beta_2 (1 - p)} p(1 - p) \phi''(p) \quad (4.231)
\]

Setting \( \theta_{12} = \theta_{21} = 0 \) and solving the Dirichlet problems

\[ \mathcal{G}h = 0 \]

\[ h(0) = 0, h(1) = 1, \]

\[ \mathcal{G}g_{abs} = -1 \]

\[ t_{abs}(0) = g_{abs}(1) = 0, \]
and

\[ \mathcal{G} g_{fix} = -h \]

\[ h(0)g_{fix}(0) = h(1)g_{fix}(1) = 0 \]

give the fixation probability, absorption time, and fixation time for type 1 respectively, while the gradient solution to \( \mathcal{G}^* \nu = 0 \), gives, up to a normalizing constant, the density for the stationary distribution of \( P_1 \) when \( \theta_{12}, \theta_{21} > 0 \). These are summarized in Table 4.1, along with the corresponding solutions (when closed forms are available) for the Wright-Fisher model, with and without selection for the sake of contrast. The latter processes have generator

\[ \mathcal{G}\phi(p) = (-\theta_{12}p + \theta_{21}(1-p) + \alpha p(1-p))\phi'(p) + \frac{1}{2}p(1-p)\phi''(p) \]  

(4.232)

with \( \alpha = 0 \) giving the neutral model.

Under the Wright-Fisher model without mutation, a neutral allele will fix with probability given by its initial frequency. In the Generalized Moran model, however, the fixation probability differs qualitatively from the Wright-Fisher expectation (Table 4.1). Starting from a population at carrying capacity, the fixation probability of a mutant has a quadratic dependence on the mutant’s initial frequency, and it favours fixation of the type with low birth and death rates (Figure 4.1a). Differences in generation time induce a form of apparent selection favouring one type over another – despite the fact that the two types might superficially appear to be strictly neutral variants under a Wright-Fisher model with \( N_e = N(\tau - 1) \).

A similar result holds for the mean time before a mutant allele fixes or goes extinct. The behaviour of the Generalized Moran process is skewed relative to the neutral Wright-
Table 4.1: A comparison of the neutral Wright-Fisher model and the Generalized Moran model. The table summarizes our analytical, asymptotic results for the Generalized Moran model, which are derived in the main text. Absorption and fixation times are given in generations. For the Generalized Moran model the generation time is the average time to reproduction, \( \frac{1}{β_1 + β_2} \), and the carrying simplex is \( C = \left\{ x \in \mathbb{R}_+^K : \sum_{i=1}^{K} x_i = τ - 1 \right\} \). \( p \) is the proportion of type one.

<table>
<thead>
<tr>
<th>Model</th>
<th>Fixation probability, ( h(p) )</th>
<th>Absorption time, ( g_{abs}(p) )</th>
<th>Fixation time, ( g_{fix}(p) )</th>
<th>Stationary distribution, ( ν(p) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright-Fisher (neutral)</td>
<td>( \frac{p}{1 - e^{-2αp}} ) ( \approx p + o(p)(1 - p) )</td>
<td>( \frac{τ - 1}{β_1 + β_2} \left[ \frac{(β_1 + β_2) p (1 - p) ln(1 - p) - (β_1 - β_2)^2 p (1 - p)}{p (1 - p) ln(1 - p)} \right] )</td>
<td>( \frac{1}{p} \left[ \frac{(β_1 + β_2) p (1 - p) ln(1 - p) - (β_1 - β_2)^2 p (1 - p)}{p (1 - p) ln(1 - p)} \right] )</td>
<td>( \frac{p^{β_1 + β_2 - 2α} - 1}{β_1 + β_2} )</td>
</tr>
</tbody>
</table>
Chapter 4. Weak Selection

Figure 4.1: (a) The probability that type 1 fixes, as a function of its initial proportion, for the Wright-Fisher model (blue) and the Generalized Moran model (exact numerical results, dashed black; analytical results from Table 4.1, solid red) starting at carrying capacity. (b) The absorption time of type one under the Wright-Fisher model (blue) and the Generalized Moran model (exact numerical results, solid red; analytical results from Table 4.1, dashed red). Parameter values: $\beta_1 = 2$, $\beta_2 = 1$, $\tau = 2$ and $N = 1000$ (reproduced from [151], originally prepared by Christopher Quince).

Fisher prediction: the mean absorption time is longer than the classical expectation when the type with higher birth rate forms a larger initial proportion of the population (Figure 4.1b). The conditional mean time before fixation of an allele is also skewed: the type with low vital rates fixes more quickly than a type with high vital rates. Again, the Generalized Moran model exhibits a form of selection that favours one type over another, despite the fact that the two types would have the same expected lifetime reproductive output were the population size held exogenously fixed.

When mutations are permitted between the two types, the stationary allele frequency distribution of the Generalized Moran process is very similar to that of a Wright-Fisher model with selection favouring the type with low birth rate. The results above potentially have practical consequences for practitioners who wish to make inferences about natural selection based on samples from wild or laboratory populations. When life-history traits are under genetic control, inference based on standard assumptions (i.e. Kimura’s diffusion) may yield erroneous and even contradictory conclusions: at small population
densities one allele will appear superior, whereas at large densities the other allele will dominate.

In Figure 4.2) we analyze polymorphism “data” generated by simulating the Generalized Moran processes of competing, quasi-neutral types. We sampled 100 individuals from a large population near carrying capacity, and we recorded the polymorphism frequency spectrum across 1000 independent sites. The observed spectrum, which describes the number of sites at which the type-one allele segregates at different frequencies, is typical of the polymorphism data observed in field studies of microbes and higher eukaryotes (e.g. [75, 76]). If we analyze the simulated polymorphism data using standard inference techniques based on the Wright-Fisher diffusion [166, 22, 30], we would infer directional selection favouring the type with low birth rate.

Alternative approaches to inferring selection pressures from data would reach the opposite conclusion. Selection coefficients are often quantified by competing two types in a nutrient-rich laboratory environment, and measuring the difference in their initial exponential growth rates [126, 125]. Under the Generalized Moran model starting from a small population, type one will grow at exponential rate $\beta_1 - \delta_1 = \beta_1(1 - \alpha)$ and type two at exponential rate $\beta_2 - \delta_2 = \beta_2(1 - \alpha)$, yielding an apparent selective advantage to the type with high birth rate. Thus, the selection coefficient inferred from a laboratory competition experiment will have the opposite sign as the selection coefficient inferred from the stationary polymorphism frequency spectrum, as would be sampled in the field. Thus, the interpretation of such a competition experiment depends on the trade-offs that occur between birth rate and other life history traits, and also on assumptions about the underlying demographic process.
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Figure 4.2: The stationary distribution of allele frequencies under reversible mutation. Bars show results from Monte-Carlo simulations of the quasi-neutral Generalized Moran process ($N = 1000, \tau = 2, \beta_1 = 1.6, \beta_2 = 2, \mu = 0.0005$), in frequency bins of size 10%. Dots show our analytic approximation to the Generalized Moran process, taken from the equation in Table 4.1. The analytical approximation closely matches the numerical simulation. In addition, the quasi-neutral frequency spectrum is very similar to the spectrum produced by a Wright-Fisher model with selection (triangles). The parameters of a best-fit Wright-Fisher model ($\hat{\theta} = 0.512, \hat{N}_e s = 0.252$) were obtained by applying standard maximum-likelihood inference techniques [166, 22, 30] to the simulated data, and they would indicate selection favoring the type with low birth rate (reproduced from [151], originally prepared by Joshua B. Plotkin).

4.4 Summary

In this chapter, we considered the appropriate density-dependent analogue of the weak selection regime of classical population genetics, in which the deterministic approximation to the birth-death mutation process given by the functional Law of Large Numbers (Proposition 2.1) has an attracting submanifold of fixed points $C$; these points correspond to equilibria at which two or more species can coexist deterministically. Theorems 4.1 and 4.2 tell us that the rescaled stochastic process $Z^{(N)}(t) = N^{-1}X^{(N)}(t)$ is also attracted
to $C$. Unlike the deterministic process, which arrives at some point $x \in C$ and then remains there indefinitely, $Z^{(N)}(t)$ converges to a diffusion process $Z(t)$ on $C$. $Z(t)$ may be explicitly characterized using the projection map

$$\pi(x) = \lim_{t \to \infty} \psi_t x,$$

which gives the equilibrium density of each type, assuming that type $i$ initially has density $i$, and the derivatives of $\pi(x)$. Section 4.2 shows how these may be computed in any specific example.

As in classical population genetics, we find that the Wright-Fisher diffusion is a robust description of neutral population dynamics (Section 4.3.2). To be precise, for any population consisting of types that all have the same mean per-capita birth rates and death rates, i.e., $\hat{\beta}_i(x) = \hat{\beta}_j(x)$ and $\delta_i(x) = \delta_j(x)$ for all $i, j$ and all $x$, the same variance in reproductive output, so $\hat{\beta}_i(x) = \hat{\beta}_j(x)$ or all $i, j$ and all $x$, and the same strength of interspecific competition, i.e.,

$$\partial_j (\hat{\beta}_i(x) - \delta_i(x)) = \partial_l (\hat{\beta}_k(x) - \delta_k(x))$$

for all $i, j, k, l$ and all $x$, the relative abundances of each type will, with an appropriate rescaling of time, converge to the Wright-Fisher diffusion, which has generator

$$(\mathcal{G} f)(p) = \frac{1}{2} \sum_{i,j=1}^{K} p_i (\delta_{ij} - p_j) (\partial_i \partial_j f)(p).$$

Relaxing any of these assumptions leads to a qualitatively different behaviours, which can include frequency-dependent selection (Section 4.3.2), selection for minimal fecundity variance (Section 4.3.2), selection for maximal efficiency in resource consumption (Section 4.3.2), or $r$ vs. $K$ selection in a model incorporating fecundity/mortality tradeoffs (Section 4.3.3). The last example provides a cautionary tale for recent efforts to infer the
presence of strength of selection from site frequency spectra, such as the Poisson Random Field approach [166, 76, 22]: many qualitatively models can lead to an allele-frequency distribution with the same functional form, but the parameters must be interpreted in a model-specific manner. In particular, without \textit{a priori} biological reasons to favour one model over all others, inferred values of the selection coefficient, effective population size, or per-site mutation rates can have ambiguous, and even contradictory interpretations.
Chapter 5

An Application to Evolution in the SIR Epidemic Model

In this chapter, we illustrate that the results of the previous chapters are applicable beyond the scope of single population genetics. We will use a stochastic version of a simple epidemic model, a multi-strain SIR model of host-parasitoid interactions, to illustrate the use of our approach in a multi-trophic model involving interspecies interactions. The crucial bifurcation parameter for the SIR and related epidemic model is the basic reproduction number, $R_{0,i}$, the expected total number of infections caused by a single individual infected with strain $i$ introduced into a population composed entirely of susceptible individuals. Similar to our previous examples, we will find that strain 1 is strongly selected if $R_{0,1} > R_{0,j}$ for all $j > 1$, whereas weak selection corresponds to the case $R_{0,i} = R_{0,j}$ for all $i, j$.

We will focus our efforts on the case of two strains, $K = 2$. In the strong selection case, we get a simple and appealing expression for the fixation probability of a novel strain invading a population in which the ancestral strain is at its endemic equilibrium, while the weak selection case will provides a biologically interesting example of a birth-death-mutation process that concentrates on a co-dimension two submanifold. Our analysis
has some interesting implications: among strains with the same basic reproduction number, those that have the lowest virulence have a higher probability of fixation, and will outcompete more virulent strains with the same $R_0$.

The models in this chapter differ slightly from those of the previous two, as we will consider processes with immigration from an external source and processes in which individuals may change their type during their lifetime, which we will call transmutation, in honour of its Lamarckian historical use. We discuss how such processes fit into our previous framework in the next section, before turning our focus to the SIR model for the balance of the chapter.

5.1 Birth-Death-Mutation Processes with Immigration and Transmutation

As previously, immigration and transmutation events occur as counting processes with Markovian rates that may depend on the current density of all species. Thus, we assume that groups of immigrants, with $n_i \geq 0$ individuals of type $i$, arrive according to a counting process $I^{(N)}_i(t)$ with intensity $N_{i_0}^{(N)}(X^{(N)}(t))$, and that individuals of type $i$ change to type $j$ according to the process $T^{(N)}_{ij}(t)$ with rate $N_{ij}^{(N)}(X^{(N)}(t))$. Thus

$$X^{(N)}(t) = X^{(N)}(0) + \sum_{i=1}^K \sum_{n \in \mathbb{N}_0^K} n B^{(N)}_{i,n}(t) - \sum_{i=1}^K e_i D^{(N)}_i(t) + \sum_{n \in \mathbb{N}_0^K} n I^{(N)}_n(t) + \sum_{j=1}^K (e_j - e_i) T^{(N)}_{ij}(t),$$

(5.1)

We will assume that for all compact sets $\mathcal{K}$ that

$$\lim_{N \to \infty} \sup_{x \in \mathcal{X}} \sum_{n \in \mathbb{N}_0^K} \|n\|_2^2 I^{(N)}_n(x) < \infty \quad \text{and} \quad \lim_{N \to \infty} \sup_{x \in \mathcal{X}} \sum_{n \in \mathbb{N}_0^K} \|n\|_2^2 I^{(N)}_n(x) < \infty,$$

(5.2)
and that there exists functions $\iota_n(x)$ such that
\[
\lim_{N \to \infty} \iota_n^{(N)}(x) = \iota_n(x) \quad \text{and} \quad \lim_{N \to \infty} \tau_{ij}^{(N)}(x) = \tau_{ij}(x)
\]
uniformly on compacts, so that such birth-death-mutation processes with immigration or transmutation are again a density dependent family with rates
\[
\lambda_n^{(N)}(x) = \sum_{i=1}^{K} \beta_{i,n}^{(N)}(x)x_i + \iota_n^{(N)}(x), \quad \lambda_{-e_i}^{(N)}(x)x_i, \quad \text{and} \quad \lambda_{e_j-e_i}^{(N)} = \tau_{ij}^{(N)}(x).
\]
Thus, the Law of Large Numbers, Proposition 2.1, continues to apply, as do Theorems 4.1 and 4.2 on the existence of diffusion limits under weak selection.

**Definition 5.1.** We will say immigration or transmutation is rare if $\iota_n(x) \equiv 0$ for all $n \in \mathbb{N}_0^K$, but
\[
\lim_{N \to \infty} N\iota_n^{(N)}(x)
\]
is nonzero for at least one $n \in \mathbb{N}_0^K$ and similarly for $\tau_{ij}(x)$ and $\tau_{ij}^{(N)}(x)$.

In the next sections, we will discuss an important example of a birth-death-mutation processes with immigration and transmutation, applying our previous results to the study of viral evolution in a two-strain SIR epidemic.

## 5.2 The SIR Model with Host Demography

In this section we consider a two-strain SIR epidemic model with host demography (see e.g., [4] and references therein). We assume that the population is subdivided into groups of susceptibles, infectives who may spread the disease to susceptible individuals, and removed individuals who have either died or recovered from the illness and attained immunity (for our purposes we will not distinguish between recovery and death, as in either case the individual no longer affects the epidemic). Departing slightly from our
previous notational convention, we will write $X_0^N(t)$ for the number of susceptible hosts at time $t$, and $X_i^N(t)$ for the number of individuals infected with strain $i$.

We will consider a simple, Markovian version of the model, with a well-mixed population: each infective has contacts with other individuals a constant rate, with the contacted individual chosen uniformly at random from the entire population. Encounters between a susceptible and an infective results in transmission (i.e., the transmutation of a susceptible to an infective) with a fixed probability i.e., there exist contact rates $\beta_i$ such that

$$\tau_{0i}^{(N)}(x) = \beta_i x_0 x_i.$$  \hfill (5.6)

We will further assume that all individuals have intrinsic per-capita mortality rate $\delta$, and individuals infected with strain $i$ recover or experience excess mortality (virulence) at rate $\alpha_i$, so that

$$\delta_{i}^{(N)}(x) = \begin{cases} 
\delta & \text{if } i = 0, \\
\delta + \alpha_i & \text{if } i = 1, 2.
\end{cases}$$ \hfill (5.7)

Finally, we assume that new individuals immigrate at rate $N\lambda$, so that

$$\iota_{e_i}^{(N)} = \lambda.$$ \hfill (5.8)

These transitions are summarized in Figure 5.1.

### 5.2.1 Law of Large Numbers

As before, we let

$$Y^{(N)}(t) = \frac{1}{N}X^{(N)}(t)$$ \hfill (5.10)
and suppose that as $N \to \infty$, $Y^{(N)}(0) \to x$. Then, by Proposition 2.1, $Y^{(N)}$ converges almost surely to a deterministic limit $Y$ satisfying

$$\dot{Y}(t) = F(Y(t))$$ \hfill (5.11)

where

$$F(x_0, x_1, x_2) = \begin{pmatrix} \lambda - (\beta_1 x_1 + \beta_2 x_2 + \delta) x_0 \\ (\beta_1 x_0 - (\delta + \alpha_1)) x_1 \\ (\beta_2 x_0 - (\delta + \alpha_2)) x_2 \end{pmatrix}. \hfill (5.12)$$

and $Y(0) = x$.

This deterministic dynamical system has equilibria at

$$x^{*,0} := \left( \frac{\lambda}{\delta}, 0, 0 \right), \quad x^{*,1} := \left( \frac{\delta + \alpha_1}{\beta_1}, \frac{\lambda}{\delta + \alpha_1} - \frac{\delta}{\beta_1}, 0 \right), \quad \text{and} \quad x^{*,2} := \left( \frac{\delta + \alpha_2}{\beta_2}, 0, \frac{\lambda}{\delta + \alpha_2} - \frac{\delta}{\beta_2} \right). \hfill (5.13)$$

$(DF)(x^{*,0})$ has eigenvalues $\delta$ and

$$\beta_i \left( \frac{\lambda}{\delta} - \frac{\delta + \alpha_i}{\beta_i} \right) \hfill (5.14)$$
for $i = 1, 2$. $(DF)(x^{*1})$ has eigenvalues

$$\frac{\beta_2}{\beta_1} \left( \frac{\delta + \alpha_1}{\beta_1 - \frac{\delta + \alpha_2}{\beta_2}} \right)$$

(5.15)

and

$$-\frac{1}{2} \frac{\lambda \beta_1}{\delta + \alpha_1} \pm \frac{1}{2} \sqrt{\left( \frac{\lambda \beta_1}{\delta + \alpha_1} \right)^2 + 4\lambda(\delta + \alpha_1) \left( \frac{\delta}{\lambda} - \frac{\beta_1}{\delta + \alpha_1} \right)},$$

(5.16)

while the eigenvalues of $(DF)(x^{*2})$ can be obtained by interchanging indices 1 and 2 in those of $(DF)(x^{*1})$. Thus the first of these equilibria is locally stable if and only if

$$\frac{\beta_i}{\delta + \alpha_i} < \frac{\delta}{\lambda} \quad i = 1, 2,$$

(5.17)

the second is locally stable if

$$\frac{\delta}{\lambda} < \frac{\beta_1}{\delta + \alpha_1} \quad \text{and} \quad \frac{\beta_2}{\delta + \alpha_2} < \frac{\beta_1}{\delta + \alpha_1},$$

(5.18)

while the third is locally stable if the preceding inequalities hold with 1 and 2 interchanged.

Of particular interest to us is the degenerate case, where

$$\frac{\delta}{\lambda} < \frac{\beta_1}{\delta + \alpha_1} = \frac{\beta_2}{\delta + \alpha_2}$$

(5.19)

In this case, letting

$$x_0^* = \frac{\delta + \alpha_1}{\beta_1} = \frac{\delta + \alpha_2}{\beta_2},$$

(5.20)

every point in the attracting submanifold

$$C := \{(x_0^*, x_1^*, x_2^*) \in \mathbb{R}_+^3 : \beta_1 x_1^* + \beta_2 x_2^* = \frac{\lambda}{x_0^*} - \delta\}$$

(5.21)

is an equilibrium, i.e., both strains can coexist stably, and we are in the weak selection
regime.

Recall that the basic reproduction number for strain $i$ is the expected total number of infections caused by a single individual infected with strain $i$ introduced into a population composed entirely of susceptible individuals. For our model, this is

$$R_{0,i} := \frac{\beta_i}{\delta + \alpha_i},$$

whereas the density of susceptibles at the fixed point $x^{*,i}$ is $x^{*,i}_0 = \frac{1}{R_{0,i}}$. The above analysis shows that $x^{*,i}$ is locally asymptotically stable if and only if $R_{0,i} > R_{0,j}$ for all $j \neq i$.

In fact, the basic reproductive number is sufficient to determine global stability. In the strong selection case, we have

**Proposition 5.1** (Bremermann & Thieme [21]). *(i)* Suppose

$$\frac{\delta}{\lambda} < R_{0,1} \quad \text{and} \quad R_{0,1} > R_{0,2},$$

then $x^{*,1}$ is globally asymptotically stable.

*(ii)* If on the other hand,

$$\frac{\delta}{\lambda} < R_{0,2} \quad \text{and} \quad R_{0,1} < R_{0,2},$$

then $x^{*,2}$ is globally asymptotically stable.

In the weakly selected case we have

**Proposition 5.2.** If

$$\frac{\delta}{\lambda} < R_0 = R_{0,1} = R_{0,2},$$

then the linear submanifold $C$ is globally asymptotically stable.
Proof. We use a family of Lyapunov functions inspired by [113]. First, recall that

\[ x_0^* = \frac{\delta + \alpha_1}{\beta_1} = \frac{\delta + \alpha_2}{\beta_2}, \]  

and let

\[ x_0^\sigma := \sigma \frac{\delta + \alpha_1}{\beta_1} + (1 - \sigma) \frac{\delta + \alpha_2}{\beta_2} = x_0^*, \]

\[ x_1^\sigma := \sigma \frac{\lambda}{x_0^\sigma} - \delta, \]

and

\[ x_2^\sigma := \frac{1 - \sigma}{\beta_2} \left( \frac{\lambda}{x_0^\sigma} - \delta \right). \]

For \(0 < \sigma < 1\), let

\[
V_\sigma(x_0, x_1, x_2) = x_0^\sigma \left( \frac{x_0}{x_0^\sigma} - x_0^\sigma \ln \frac{x_0}{x_0^\sigma} \right) \\
+ x_1^\sigma \left( \frac{x_1}{x_1^\sigma} - x_1^\sigma \ln \frac{x_1}{x_1^\sigma} \right) + x_2^\sigma \left( \frac{x_2}{x_2^\sigma} - x_2^\sigma \ln \frac{x_2}{x_2^\sigma} \right). \]  

A calculation shows that

\[
\dot{V}_\sigma(x_0, x_1, x_2) = -\frac{x_0}{x_0^\sigma} \left( 1 - \frac{x_0^\sigma}{x_0} \right)^2 \leq 0. \]  

Hence \(\dot{V}_0(x_0, x_1, x_2) \leq 0\), and vanishes only at those points with \(x_0 = x_0^*\). The only positive invariant subset of \(\{ x_0 = x_0^* \}\) for the dynamical system is \(C\), so global asymptotic stability then follows by LaSalle’s Invariance Principle [70].

Henceforth, we will restrict ourselves to the case when \((\delta, 0, 0)\) is unstable i.e., when at least one of the strains will persist indefinitely in the absence of demographic stochasticity.
5.2.2 Strong Results

Suppose that $R_{0,1} > R_{0,2}$, so that the limiting deterministic system, $Y(t)$, has a unique global attractor at $x^{*1}$ and a saddle node at $x^{*2}$. In this case, a straightforward modification of Proposition 3.9 (we omit the details) allows us to consider a small number of individuals infected with strain 1 entering a population where strain 2 is endemic, by coupling with the non-autonomous branching process with transition rates

$$\beta_{i,e_i}(t) = \beta_i Y_0(t) \quad \text{and} \quad \delta_i(t) = (\delta + \alpha_i). \quad (5.29)$$

In particular, we can apply Corollary 3.1 to obtain an asymptotic estimate of the probability that strain 1 eventually outcompetes strain 2. Unfortunately, unlike the Generalized Moran/SIS model, Example 2.1, there is no simple closed form for the extinction probability across all initial conditions. We do, however, get an appealingly simple expression for the fixation probability when the resident population starts in equilibrium:

**Corollary 5.1.** Consider a single individual infected with strain 1 entering a population where strain 2 is endemic, i.e., $X_1(0) = 1$. Then the probability strain 1 eventually goes extinct is

$$q_{x^{*2}}(t) = \frac{\int_0^t e^{-\int_0^s \beta_1 Y_0(u) - (\delta + \alpha_1)} du (\delta + \alpha_1) ds}{1 + \int_0^t e^{-\int_0^s \beta_1 Y_0(u) - (\delta + \alpha_1)} du (\delta + \alpha_1) ds}. \quad (5.30)$$

When the resident population is initially at equilibrium, $Y(t) = x^{*2}$ for all $t$, then

$$q_{x^{*2}}(t) = \frac{\int_0^t e^{-\int_0^s \beta_1 x_0^{*2} - (\delta + \alpha_1)} du (\delta + \alpha_1) ds}{1 + \int_0^t e^{-\int_0^s \beta_1 x_0^{*2} - (\delta + \alpha_1)} du (\delta + \alpha_1) ds} \quad (5.31)$$

$$= \frac{\delta + \alpha_1}{\beta_1 x_0^{*2} - (\delta + \alpha_1)} \left( 1 - e^{-\beta_1 x_0^{*2} - (\delta + \alpha_1)t} \right). \quad (5.32)$$

Recalling that $x_0^{*2} = \frac{1}{R_{0,2}}$, we see that assuming the resident is at equilibrium, the probability that strain 1 eventually fixes is asymptotically $\frac{R_{0,2}}{R_{0,1}}$ if $R_{0,1} > R_{0,2}$, and 0 otherwise.
5.2.3 Weak Results

Throughout this section, we assume that $R_{0,1} = R_{0,2}$, so that the limiting dynamical system (5.11) has a co-dimension two linear submanifold of fixed points, $C$. Here we apply Theorem 4.2 from the previous chapter to conclude that the two-strain SIR model converges weakly to a diffusion process on $C$, but first, we adapt the methods of §4.2.3 to compute the derivatives of the projection map $\pi(x)$.

The Projection Map and its Derivatives

Recall, if $Y(t, x)$ is the solution to (5.11) with $Y(0, x) = x$, then

$$\pi(x) = \lim_{t \to \infty} Y(t).$$

(5.33)

From Section 5.2.1, we see that $\pi_0(x_0, x_1, x_2) = x_0^\star$, independent of the initial condition, so that

$$\partial_i \pi_0 = \partial_{ij} \pi_0 = 0$$

(5.34)

for all $i$ and $j$. We are thus left with the task of determining the derivatives of $\pi_1$ and $\pi_2$.

We first observe that $\pi(x) \in C$, so that

$$\beta_1 \pi_1(x_0, x_1, x_2) + \beta_2 \pi_2(x_0, x_1, x_2) = \frac{\lambda}{x_0^\star} - \delta.$$  

(5.35)

We next turn to the task of determining an appropriate invariant of motion for the dynamical system. Under our assumption (5.19), $F_i(x)$, $i = 1, 2$, take the form

$$\dot{Y}_i(t) = \beta_i(Y_0(t) - x_0^\star)Y_i(t),$$

(5.36)
so that
\[
\frac{dY_1}{dY_2} = \frac{\beta_1 Y_1}{\beta_2 Y_2}.
\]
(5.37)

Solving this gives
\[
\frac{Y_2^{\beta_1}}{Y_1^{\beta_2}} = C
\]
(5.38)
for a fixed constant \(C\). Thus \(E(x) = \frac{x^{\beta_1}}{x_1^{\beta_2}}\) is an invariant by which flows of the dynamical system (5.11) may be characterized. In particular,
\[
E(x) = E(\pi(x))
\]
(5.39)

Differentiating (5.35) yields
\[
\beta_1 \frac{\partial \pi_1}{\partial x_i} = -\beta_2 \frac{\partial \pi_2}{\partial x_i},
\]
(5.40)
while implicitly differentiating (5.39) with respect to \(x_1\) yields
\[
\beta_2 x_1^{\beta_2-1} \pi_2^{\beta_1} + \beta_1 x_1^{\beta_2} x_2^{\beta_1-1} \frac{\partial \pi_2}{\partial x_1} = \beta_2 x_2^{\beta_1} x_1^{\beta_2-1} \frac{\partial \pi_1}{\partial x_1}.
\]
(5.41)

Using (5.40), we can eliminate \(\frac{\partial \pi_1}{\partial x_1}\), and thus obtain
\[
\frac{\partial \pi_2}{\partial x_1} = -\frac{\beta_1 \beta_2 x_1^{\beta_2-1} \pi_2^{\beta_1}}{\beta_1 x_1^{\beta_2} \pi_2^{\beta_1-1} + \beta_2 \pi_1^{\beta_2-1} x_2^{\beta_1}}.
\]
(5.42)

In a similar manner, we find
\[
\frac{\partial \pi_2}{\partial x_2} = \frac{\beta_2 x_2^{\beta_2-1} x_1^{\beta_1-1}}{\beta_1 x_1^{\beta_2} \pi_2^{\beta_1-1} + \beta_2 \pi_1^{\beta_2-1} x_2^{\beta_1}},
\]
(5.43)
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\[
\frac{\partial^2 \pi_2}{\partial x_1^2} = -\frac{1}{\beta_1^2 x_1^2 \pi_2^{\beta_1-2} + \beta_2^2 \pi_1^{\beta_2-2} x_2^2} \left[ \beta_1 \beta_2 (\beta_2 - 1) x_1^{\beta_2-2} \pi_2^{\beta_1-1} + 2 \beta_1^2 \beta_2 x_1^{\beta_1-1} (\pi_2)^{\beta_1-1} \left( \frac{\partial \pi_2}{\partial x_1} \right) \right] + \frac{1}{\beta_1} \left( \beta_1^3 (\beta_1 - 1) x_1^{\beta_2-2} \pi_2^{\beta_1-2} - \beta_2^3 (\beta_2 - 1) \pi_1^{\beta_2-2} x_2^2 \right) \left( \frac{\partial \pi_2}{\partial x_1} \right)^2 , \quad (5.44)
\]

\[
\frac{\partial^2 \pi_2}{\partial x_1 \partial x_2} = -\frac{1}{\beta_1^2 x_1^2 \pi_2^{\beta_1-2} + \beta_2^2 \pi_1^{\beta_2-2} x_2^2} \left[ \beta_1 \beta_2^2 \pi_1^{\beta_2-1} x_2^{\beta_1-1} \left( \frac{\partial \pi_2}{\partial x_1} \right) + \beta_1^2 \beta_2^2 \pi_1^{\beta_2-1} (\pi_2)^{\beta_1-1} \left( \frac{\partial \pi_2}{\partial x_2} \right) \right] + \frac{1}{\beta_1} \left( \beta_1^3 (\beta_1 - 1) x_1^{\beta_2-2} \pi_2^{\beta_1-2} - \beta_2^3 (\beta_2 - 1) \pi_1^{\beta_2-2} x_2^2 \right) \left( \frac{\partial \pi_2}{\partial x_1} \right) \left( \frac{\partial \pi_2}{\partial x_2} \right) \left( \frac{\partial \pi_2}{\partial x_1} \right)^2 , \quad (5.45)
\]

and

\[
\frac{\partial^2 \pi_2}{\partial x_2^2} = \frac{1}{\beta_1^2 x_1^2 \pi_2^{\beta_1-2} + \beta_2^2 \pi_1^{\beta_2-2} x_2^2} \left[ \beta_2^2 (\beta_1 - 1) x_1^{\beta_2-2} \pi_2^{\beta_1-2} - 2 \beta_1 \beta_2^2 \pi_1^{\beta_2-1} x_2^{\beta_1-1} \left( \frac{\partial \pi_2}{\partial x_2} \right) \right] - \frac{1}{\beta_1} \left( \beta_1^3 (\beta_1 - 1) x_1^{\beta_2-2} \pi_2^{\beta_1-2} - \beta_2^3 (\beta_2 - 1) \pi_1^{\beta_2-2} x_2^2 \right) \left( \frac{\partial \pi_2}{\partial x_2} \right)^2 . \quad (5.46)
\]

The corresponding derivatives for \( \pi_1 \) can be obtained from these via (5.40) and its higher derivatives.

At points \((x_0^*, x_1^*, x_2^*) \in C\), these simplify to

\[
\left. \frac{\partial \pi_2}{\partial x_1} \right|_{(x_0, x_1, x_2)=(x_0^*, x_1^*, x_2^*)} = -\frac{\beta_1 \beta_2 x_2^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} ,
\]

\[
\left. \frac{\partial \pi_2}{\partial x_1} \right|_{(x_0, x_1, x_2)=(x_0^*, x_1^*, x_2^*)} = \frac{\beta_1^2 x_1^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} ,
\]

\[
\left. \frac{\partial^2 \pi_2}{\partial x_1^2} \right|_{(x_0, x_1, x_2)=(x_0^*, x_1^*, x_2^*)} = -\frac{\beta_1 \beta_2 x_2^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \left[ \frac{\beta_2 - 1}{x_1^*} - 2 \frac{\beta_1^2 \beta_2}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \right] + \left( \beta_1^3 (\beta_1 - 1) \frac{x_1^*}{x_2^*} - \beta_2^3 (\beta_2 - 1) \frac{x_2^*}{x_1^*} \right) \frac{\beta_2 x_2^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} , \quad (5.47)
\]
\[
\frac{\partial^2 \pi_2}{\partial x_1 \partial x_2} \bigg|_{(x_0,x_1,x_2)=(x_0^*,x_1^*,x_2^*)} = \frac{\beta_1^2 \beta_2}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \left[ \beta_2^2 x_2^* - \beta_1^2 x_1^* + \left( \beta_1 (\beta_2 - 1) \frac{x_1^*}{x_2^*} - \beta_1 (\beta_2 - 1) \frac{x_2^*}{x_1^*} \right) \frac{x_1^* x_2^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \right], \quad (5.48)
\]

and

\[
\frac{\partial^2 \pi_2}{\partial x_2^2} \bigg|_{(x_0,x_1,x_2)=(x_0^*,x_1^*,x_2^*)} = \frac{\beta_1^2 x_1^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \left[ \frac{\beta_1}{x_2^*} - 2 \frac{\beta_1 \beta_2}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \right] - \left( \beta_1 (\beta_2 - 1) \frac{x_1^*}{x_2^*} - \beta_1 (\beta_2 - 1) \frac{x_2^*}{x_1^*} \right) \frac{\beta_1 x_1^*}{\beta_1^2 x_1^* + \beta_2^2 x_2^*} \right]. \quad (5.49)
\]

**Diffusion Limit**

As before, we will be interested in the time rescaled process

\[
\mathbf{Z}^{(N)}(t) := \frac{1}{N} \mathbf{X}^{(N)}(Nt)
\]

and its modification \(\tilde{\mathbf{Z}}^{(N)}(t)\), which coincides with \(\mathbf{Z}^{(N)}(t)\) whenever the latter begins in \(\mathcal{C}\).

Applying Theorem 4.2, using the derivatives calculated above, we have

\[
d\tilde{Z}_2(t) = x_0^* \frac{\beta_1 \beta_2 \tilde{Z}_1 \tilde{Z}_2}{(\beta_1^2 \tilde{Z}_1 + \beta_2^2 \tilde{Z}_2)^2} (\beta_1 - \beta_2) \left[ \frac{\beta_1 + \beta_2}{\beta_1^2 \tilde{Z}_1 + \beta_2^2 \tilde{Z}_2} \right] dt + \sqrt{x_0^*} \frac{\beta_1}{(\beta_1^2 \tilde{Z}_1 + \beta_2^2 \tilde{Z}_2)} \left[ -\beta_2 \tilde{Z}_2 \sqrt{\beta_1} \tilde{Z}_1 dB_1(t) + \beta_1 \tilde{Z}_1 \sqrt{\beta_2} \tilde{Z}_2 dB_2(t) \right]
\]

Finally, letting

\[
P(\tilde{Z}_1, \tilde{Z}_2) = \frac{\tilde{Z}_1}{\tilde{Z}_1 + \tilde{Z}_2}, \quad (5.52)
\]
we have, via Itô’s formula,

\[
\begin{align*}
\frac{dP(t)}{dt} &= x_0^* \frac{\beta_1 \beta_2}{n_e(P)(\beta_1^2 P + \beta_2^2(1 - P))^2} P(1 - P)(\beta_2 - \beta_1) \\
& \quad \times \left[ \beta_1 (1 - P) + \beta_2 P + \frac{\beta_1 \beta_2 (\beta_1 P + \beta_2 (1 - P))}{\beta_1^2 P + \beta_2^2 (1 - P)} \right] dt \\
& \quad - \frac{\sqrt{x_0}}{\sqrt{n_e(P)(\beta_1^2 P + \beta_2^2 (1 - P))}} \left[ \beta_2 (1 - P) \sqrt{\beta_1 P} dB_1(t) + \beta_1 P \sqrt{\beta_2 (1 - P)} dB_2(t) \right]
\end{align*}
\]

(5.53)

where

\[
n_e(P) = \pi_1 + \pi_2,
\]

(5.54)

which, given that \(\beta_1 \pi_1 + \beta_2 \pi_2 = \frac{\lambda}{x_0} - \delta\), may be written

\[
n_e(P) = \frac{\frac{\lambda}{x_0} - \delta}{\beta_1 P + \beta_2 (1 - P)}.
\]

(5.55)

We adopt the notation \(n_e(P)\) in analogy with the effective population size common in population genetics, noting that \(N_e(P) = Nn_e(P)\) is the actual number of individuals of all types when type 1 has frequency \(P\).

The corresponding infinitesimal generator takes the form

\[
\mathcal{G} \phi(p) = b(p) \phi'(p) + \frac{1}{2} a(p) \phi''(p),
\]

(5.56)

where

\[
b(p) = x_0^* \frac{\beta_1 \beta_2}{n_e(p)(\beta_1^2 p + \beta_2^2 (1 - p))^2} P(1 - P)(\beta_2 - \beta_1) \\
& \quad \times \left( \beta_1 (1 - p) + \beta_2 p + \frac{\beta_1 \beta_2 (\beta_1 p + \beta_2 (1 - p))}{\beta_1^2 p + \beta_2^2 (1 - p)} \right)
\]

(5.57)
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and

\[ a(p) = 2x_0^* \beta_1 \beta_2 \left( \beta_1 p + \beta_2(1-p) \right)^3 \frac{n_e(p)}{(\beta_1^2 p + \beta_2^2(1-p))^2} p(1-p) \]  \hspace{1cm} (5.58)

Thus, there is a drift towards the type with lower contact rate, in proportion to the difference in contact rates. Under our assumption of equal basic reproductive number \( R_0 \), this is equivalent to a drift favouring the type with longer infective period, which may be achieved by reducing either the excess mortality caused by the pathogen, or by a reduced recovery rate.

In particular, writing

\[ s(p) = e^{-2 \int \frac{b(p)}{a(p)} dp} \]  \hspace{1cm} (5.59)

\[ = \frac{\beta_1^2 p + \beta_2^2(1-p)}{(\beta_1 p + \beta_2(1-p))^2} e^{-\frac{\beta_1 + \beta_2}{\beta_1 p + \beta_2(1-p)}} \]  \hspace{1cm} (5.60)

the probability that strain 1 out-competes strain 2, given an initial frequency of \( p \) is [53]

\[ \frac{\int_0^p s(z) \, dz}{\int_0^1 s(z) \, dz} \]  \hspace{1cm} (5.61)

Unfortunately, no simple closed form is available for the above integrals. We observe, however, that writing \( \beta_2 = \beta_1 (1 + \alpha) \) the above probability admits an asymptotic series expansion

\[ p + \alpha p (1-p) + \frac{\alpha^2}{3} p(1-p)(2-p) + O(\alpha^3) \]  \hspace{1cm} (5.62)

for small values of \( \alpha \). The expected time to absorption and fixation may be computed similarly.

This result, and Corollary 5.1 above have an interesting context within the development of the theory of infectious diseases. Until fairly recently, the “conventional wisdom” [145, 1, 135], inspired by such examples as myxomatosis in Australian rabbits [58], or, more recently simian immunodeficiency virus (SIV), was that pathogens evolved towards reduced virulence, supported by such verbal arguments as, without “the early appear-
ance and dominance of strains of virus which caused a lower mortality”, “rabbits would have been eradicated or greatly reduced in numbers, and the rabbit itself would have disappeared from such localities” ([58] p. 494, as quoted in [127]). A series of theoretical studies using ordinary differential equations or game-theoretic invasion arguments (e.g., [127, 2, 3, 20, 110, 137]) indicated that tradeoffs between virulence and the length of the infectious period could support intermediate levels of virulence, and that evolution tended to maximize the basic reproduction number, $R_0$; in Corollary 5.1 we quantified the probability that a strain with a higher value of $R_0$ would successfully invade, and found that it could be expressed simply in terms of the ratio of basic reproductive numbers for the two strains, which is perhaps unsurprising, as $R_0$ is essentially the expected lifetime reproductive success rate or absolute fitness of the pathogen, and, as we observed in the introduction, Haldane first showed that the fixation probability of an invading mutant is simply its relative fitness [71].

More interesting is the fixation probability for the diffusive limit, when the two strains have the same $R_0$: here, we see that “conventional wisdom” is not completely lacking, and that if we account for the common association between increased pathogenicity and enhanced rates of production for the pathogen [19, 135, 62] as a tradeoff holding $R_0$ asymptotically fixed (a mathematical idealization, but one that may approximate the very long term evolutionary dynamics of pathogens which have exhausted most big benefit mutations) then we do see evolution towards reduced virulence. Recall that the basic reproduction number for strain $i$ is

$$R_{0,i} = \frac{\beta_i}{\delta + \alpha_i},$$

where the virulence (the rate excess host mortality) was incorporated together with the rate of host recovery into the parameter $\alpha_i$. The expression for the approximate fixation probability (5.62) shows selection favouring types with higher transmissibility, which
must be balanced either by an increase in the duration of the hosts’ infectious period or a decrease in virulence. We thus recover the original hypothesis on the evolution of pathogenicity as a “second–order” consequence of stochastic dynamics (see also [173] which obtained a similar finding using numerical and heuristic analyses of a related model for meningococcal disease in which pathogenic strains competed against a benign resident strain) which may be relevant to long persisting viral pathogens like myxomatosis or SIV.

5.3 Summary

Here, we saw that the results of the previous chapters have applications beyond traditional population genetics, as illustrated by a study of viral evolution in a multi-strain SIR epidemic with host demography. Interestingly, the introduction of stochasticity resurrected the out-of-favour hypothesis that pathogens become less virulent over time. This is a small effect relative to the advantage of a higher basic reproductive number, but we believe it merits further study in more realistic epidemic models.

Most significantly, the SIR model here shows that our methods have applicability well beyond the purview of classical population genetics, which tends to consider populations and their evolution in isolation, and allow us to consider co-evolution between hosts and parasitoids, hosts and prey, and similar collections of species interacting at multiple trophic levels. As such, we believe it is an interesting first step from population genetics to a theory of “community genetics” that considers evolution in the context of a plurality of interacting species.
Chapter 6

Conclusion: Towards a
Mathematical Framework for
Density Dependent Population
Genetics

It borders upon absurdity to attempt to write a conclusion when we have only obtained the most preliminary results on the density-dependent birth-death-mutation processes that have been the object of study. This chapter then, rather than reflecting upon what has been done, will identify some of the many tasks that remain to be done.

Thus far, all results we have obtained have been in the context of specific asymptotic dynamics in the associated functional law of large numbers, Proposition 2.1. Depending on one’s perspective, this is either a blessing or curse – as we saw in Example 1.1, there are an unlimited supply of limiting dynamics, and thus no end of questions to ponder. With no other, more general, strategy apparent, we began by considering two examples with obvious precedents in classical population genetics, and for which previously applied strategies could be adapted. In Chapters 3 and 4, we set about generaliz-
ing the classical single-population, single-locus theory of population genetics to include more mechanistic population dynamics, in particular, allowing variable population sizes and density-dependent regulation. In the first of these chapters, we considered a novel mutant successfully invading an established wild-type population and found that birth-death-mutation processes could be coupled to time-inhomogeneous branching processes (Proposition 3.9) in such a way that a successful invasion was equivalent to non-extinction of the approximating branching process. In particular, under the assumption of strong selection – that is, deterministic fixation in the functional Law of Large numbers – we could explicitly compute fixation probabilities (Corollary 3.4) and fixation times (Proposition 3.11). In Chapter 4, we showed that when the deterministic dynamics of the functional Law of Large Numbers allow stationary coexistence of multiple types at all points of an attracting submanifold of phase space, we obtained a generalization of the weakly selected population genetics. Under this assumption, the abundances of types could be described by a diffusion (Theorem 4.2) that included the Wright-Fisher diffusion as a special case (Section 4.3.2). Moreover, our results also apply to models incorporating frequency-dependent selection, fecundity variance polymorphism, resource-ratio theory, and life-history strategies, such as fecundity/mortality tradeoffs. At least in the case of two alleotypes, we could obtain explicit expressions for the fixation probabilities and times, and thus explore which strategies were selectively favoured and thus expected to persist. Finally, in Chapter 5, we took a tentative step beyond single-population genetics into the realm of multi-trophic interactions, analyzing simple host-parasitoid dynamics and finding new theoretical support for selection favouring reduced virulence (Equation 5.62).

Given our stated goal of building bridges between well established traditions of mathematical population genetics and population ecology, the obvious next step would be a more profound interaction with mathematical ecology. In particular, there are a number of well-established models – with well-understood deterministic dynamics – for which a
stochastic analogue should be available.

The most obvious example is one that should already be here, but for the limits of time and the interests of brevity, which is the case of a single asymptotically stable or unstable interior fixed point in $\mathbb{R}^K_+$ or, more generally, a heteroclinic cycle consisting of several hyperbolic fixed points. Such dynamics have been frequently proposed as a mechanism underlying stable coexistence in the ecological literature, but have been largely neglected in population genetics, where the prevailing model for coexistence is neutrality or near neutrality. Given sufficient care to deal with degeneracies at the boundary, these cases are essentially the classical exit problem, and should be easily approached by the large deviation principle of Freidlin and Wentzell [63] or the more recent “path-based” approach of Bakhtin [11, 12, 13], which is closer in spirit to the approach taken here. The latter also suggest the possibility of obtaining results that depend only on the topological equivalence class of the law of large numbers.

The other obvious, and perhaps unforgivable lacuna is the complete absence of coalescent theory in the preceding chapters. Just as the “forward-time” theory of population genetics considerably preceded Kingman’s coalescent, similarly coalescents for density-dependent birth-death-mutation processes remain work in progress. A preliminary investigation with Jesse Taylor suggests that the approaches in [15, 176] may be adapted to obtain the genealogy of a neutral locus linked to one that is weakly selected. The analogous case of a neutral allele linked to a strongly selected allele should be able to be approached similarly to [40, 41, 167]. The true analogue of Kingman’s coalescent and the corresponding infinite-sites or infinite alleles model, describing the genealogy of an arbitrary collection of linked alleles, each potentially under selection, remains an elusive goal.

Other extensions that would greatly extend the population-genetic relevance of our approach would involve moving beyond populations of haploid organisms to diploid organisms, and from single to multiple loci, and with these the complications of recombi-
From a more ecologically inspired perspective, natural next steps would be to consider explicit consumer resource models, with one or more limiting resources and explicit functional responses, which could be more readily compared to experiments in the chemostat. Preliminary work with Christopher Quince suggests this is a profitable direction – we have been particularly interested to discover competition experiments between strains of *E. coli* by Hansen and Hubbell [72] in which they observed qualitative dynamics very similar to those exhibited by our Generalized Moran model, (Example 2.1). We hope to have results available soon.

Further afield, but much more interesting, is to consider more complicated food webs with more trophic levels (e.g. competition among predators for prey which in turn forage on a basal species, or between prey subject to top-down control by a predator). The dynamics of such systems are increasingly complicated, with periodic or even chaotic attractors, and as such will demand considerably more mathematical sophistication than has been presented here, but would be essential steps in any honest effort at bridging population ecology and population genetics.

Finally, we note that the work presented here has largely attempted to incorporate insights from population ecology into population genetics, to understand how more biologically realistic dynamics would alter fixation probabilities and gene frequencies, and how these might complicate the detection and understanding of selection pressures. It is equally important, however, that the exchange flow in both directions, and this opens up entirely new avenues of research. Among the most significant of these will be to introduce the finite population perspective of population genetics, with its awareness of drift, together with the density dependent dynamics considered herein, into the framework of conservation biology. Current methods of population viability analysis, an essential tool in species preservation, often neglect density dependence and are limited in their consideration of small effective population sizes. An extension of the approach to population
dynamics and population genetics presented herein could provide a valuable correction to current methods.

Almost one hundred years ago, R. A. Fisher, J. B. S. Haldane, and Sewall Wright provided mathematical insights invaluable to the creation of the modern evolutionary synthesis. In doing so, they opened up new directions of mathematical inquiry which would influence the study of stochastic processes. From our present vantage point, it is exciting to realize that they were making the first forays into what remains largely uncharted territory, and that there is still a significant role for mathematics to play in forging an “extended evolutionary synthesis” [157, 158, 159] that will bring together insights from population genetics, population ecology, evolutionary developmental biology, genomics, and beyond. It is equally exciting to imagine how participating in a new synthesis will inform new developments in probability theory. In the preceding pages, we have attempted to make a small contribution at the interface between population dynamics and population genetics. With luck, they have also been the point of departure for more significant contributions to both biology and mathematics.
Appendix A

Probability Glossary

Here, we give a quick and informal survey – without proofs – of the essential definitions and results we shall need from the theory of probability and stochastic processes. Details on random variables and stochastic processes can be found in any standard text on measure-theoretic probability, e.g. [18, 37] ([164] is an excellent introductory text). Results on convergence of random variables may be found in [17, 50, 86]. Results on martingales, semi-martingales and stochastic integration can be found in [140, 161]. [95] includes a particularly readable account of Markov processes and diffusions for the applied practitioner. [129] is an excellent text on coupling, whilst [14] is a very good introduction for those interested in biological applications.

Throughout, we will implicitly assume a probability space $(\Omega, \mathcal{F}, \mathbb{P})$: $\mathbb{P}$ is a probability measure on an underlying space of outcomes $\Omega$ i.e. $\mathbb{P}(\Omega) = 1$, and $\mathcal{F}$ is a $\sigma$-algebra of events i.e. measurable subsets of $\Omega$. We will assume throughout that $(\Omega, \mathcal{F}, \mathbb{P})$ is complete, i.e. if $B \in \mathcal{F}$, $A \subseteq B$, and $\mathbb{P}(B) = 0$, then $A \in \mathcal{F}$ (and, necessarily, $\mathbb{P}(A) = 0$ also).

We will use $\mathbb{E}$ for the expectation (i.e. the integral) with respect to $\mathbb{P}$.
A.1 Random Variables and Stochastic Processes

Let \((S, \mathcal{S})\) be a measurable space, i.e., \(S\) is a \(\sigma\)-algebra of measurable subsets of \(S\). A random variable \(X\) with state space \(S\) is a measurable function \(X : \Omega \to S\).

A random variable \(X\) is uniformly integrable if for all \(\varepsilon > 0\), there exists \(\delta > 0\) such that if \(\mathbb{P}(A) < \varepsilon\) for some \(A \in \mathcal{F}\), then \(\mathbb{E}[X \mathbb{1}_A] < \delta\). Here, \(\mathbb{1}_A\) is the indicator function of the set \(A\), so

\[
\mathbb{1}_A(x) := \begin{cases} 
1 & \text{if } x \in A, \text{ and} \\
0 & \text{otherwise}
\end{cases} \tag{A.1}
\]

There are a number of notions of equivalence for random variables. We give them in order of increasing stringency:

(i) We say that two random variables \(X\) and \(Y\) taking values in \(S\) are equal in distribution if they have the same distribution, i.e.,

\[
\mathbb{E}[f(X)] = \mathbb{E}[f(Y)]. \tag{A.2}
\]

for all continuous and bounded functions \(f\) on \(S\). We write this as \(X \overset{d}{=} Y\).

(ii) They are equal almost surely if

\[
\mathbb{P}\{X = Y\} = 1. \tag{A.3}
\]

(iii) \(X\) and \(Y\) are equal if they are equal as functions on \(\Omega\), i.e., \(X(\omega) = Y(\omega)\) for all \(\omega \in \Omega\).

A stochastic process is a collection of \(S\)-valued random variables, \(\{X(t)\}_{t \in \mathcal{T}}\), indexed by a totally ordered set \(\mathcal{T}\) – for our purposes, \(\mathcal{T}\) is time, and will either be a compact set \([0, T]\) for some fixed \(T\) or \([0, \infty)\). For ease of notation, we will frequently abbreviate \(\{X(t)\}_{t \in \mathcal{T}}\) by \(X(t)\) or \(X\) when the set \(\mathcal{T}\) is clear.
We will regard stochastic processes taking values in a metric space \((S,d)\) as random variables taking values in the set of càdlàg functions – functions that are continuous from the right and have left-hand limits – endowed with the Skorokhod topology. With this topology the càdlàg functions form a complete, separable metric space, which we denote \(\mathbb{D}_S[0,T]\) or \(\mathbb{D}_S[0,\infty)\) according to our set of times, \(\mathcal{T}\). While the Skorokhod topology can be described via an explicit metric, more insight is gained from defining the topology by sequential convergence: we say that \(X^{(N)}(t)\) converges to \(X(t)\) in the Skorokhod topology if there exists a sequence of strictly increasing continuous functions \(\lambda^{(N)} : \mathbb{R}_+ \to \mathbb{R}_+\) such that

- \(\lambda^{(N)}(0) = 0,\)
- \(\lim_{t \to \infty} \lambda^{(N)}(t) = \infty,\)
- For all \(T > 0, \lim_{N \to \infty} \sup_{0 \leq s \leq t} \left| \ln \frac{\lambda^{(N)}(t) - \lambda^{(N)}(s)}{t - s} \right| = 0 \) \((N. B. this is a technical condition to require that the \(\lambda^{(N)}(t)\) not change too rapidly; a consequence of this condition is that \(\lim_{N \to \infty} \sup_{0 \leq t \leq T} |\lambda^{(N)}(t) - t| = 0\), and
- \(\lim_{N \to \infty} \sup_{0 \leq t \leq T} d(X^{(N)}(\lambda^{(N)}(t)), X(t)) = 0.\)

Intuitively, for two processes to be close in the Skorokhod topology, we require them to be close in the topology on \(S\) at all points of continuity, as in the usual topology on continuous functions, but also that the times at which their discontinuities occur must also be close. Standard references on convergence in \(\mathbb{D}_S\) are [17, 50, 86].

A filtration, \(\{\mathcal{F}_t\}_{t \in \mathcal{T}}\), is an increasing set of sub-\(\sigma\)-algebras of \(\mathcal{F}\) indexed by a totally ordered set \(\mathcal{T}\), i.e. if \(s, t \in \mathcal{T}\) and \(s \leq t\), then \(\mathcal{F}_s \subseteq \mathcal{F}_t \subseteq \mathcal{F}\). A process \(X\) is adapted with respect to \(\mathcal{F}\) (\(\mathcal{F}\)-adapted) if \(X(t)\) is a \(\mathcal{F}_t\)-measurable function for all \(t\). The natural filtration associated to a stochastic process \(\{X(t)\}_{t \in \mathcal{T}}\) is the filtration

\[
\mathcal{F}_t = \sigma(X(t)) := \sigma \left( \{ X(t)^{-1}(B) : B \in \mathcal{S} \} \right),
\]

\((A.4)\)
i.e. the $\sigma$-algebra generated by the pre-image of all measurable sets in $S$ under $X(t)$ (since $X(t)$ is assumed to be measurable for all $t \in T$, $X(t)^{-1}(B)$ is a measurable set for all $B \in S$). Intuitively, $\mathcal{F}_t$ is the available information up to time $t$. Whenever a filtration is not explicitly given, we will adopt the convention that we are using the natural filtration.

A random variable $T$ taking values in $\mathcal{T} \cup \{\infty\}$ is a stopping time with respect to a filtration $\{\mathcal{F}_t\}_{t \in \mathcal{T}}$ if $\{T < t\} \in \mathcal{F}_t$ for all $t \in \mathcal{T}$. We explain the origin of the term in the discussion of martingales below. Note that a fixed time is trivially a stopping time.

### A.2 Coupling

We say that random variables $X_1$ and $X_2$ on probability spaces $(\Omega_1, \mathcal{F}_1, \mathbb{P}_1)$ and $(\Omega_2, \mathcal{F}_2, \mathbb{P}_2)$ are coupled if there exists a third probability space $(\Omega, \mathcal{F}, \mathbb{P})$ and random variables $\tilde{X}_1$ and $\tilde{X}_2$ both defined on $(\Omega, \mathcal{F}, \mathbb{P})$ such that $X_1 \overset{D}{=} \tilde{X}_1$ and $X_2 \overset{D}{=} \tilde{X}_2$.

Suppose $S$ is a totally ordered set with order relation $>$. If $X_1$ and $X_2$ are random variables taking values in $S$, we say that $X$ stochastically dominates $Y$ if for all $x \in S$,

$$\mathbb{P}\{X_1 > x\} \geq \mathbb{P}\{X_2 > x\}. \quad (A.5)$$

We write this as $X_1 \succ X_2$.

We say that there is a monotone coupling between $X_1$ and $X_2$ if there exists a probability space $(\Omega, \mathcal{F}, \mathbb{P})$ and random variables $\tilde{X}_1$ and $\tilde{X}_2$ both defined on $(\Omega, \mathcal{F}, \mathbb{P})$ such that $X_1 \overset{D}{=} \tilde{X}_2$ and $X_2 \overset{D}{=} \tilde{X}_2$ and $X_1 > X_2$ almost surely.

*Strassen's theorem* states that $X_1 \succ X_2$ if and only if there is a monotone coupling between $X_1$ and $X_2$. We will use Strassen's theorem extensively, albeit implicitly – on several occasions, we will construct a monotone coupling between random variables and use this to conclude that one stochastically dominates the other.
A.3 Convergence of Random Variables

Just as there are multiple notions of equivalence for random variables, there are also a number of notions of convergence considered for random variables. We shall make use of four common topologies of convergence, which are described below. For the latter three, we require that the state space $S$ to be a metric space, with metric $d$. To avoid technicalities, we assume that $(S, d)$ is complete and separable i.e. a Polish space. This will be sufficient for all spaces that we consider.

**Almost sure convergence** a collection of random variables $\{X^{(N)}\}_{N \in \mathbb{N}}$ converges to $X$ almost surely (abbreviated a.s.) if

$$
P \left\{ \lim_{N \to \infty} X^{(N)} = X \right\} = 1. \quad (A.6)$$

We will sometimes write this as $X^{(N)} \xrightarrow{\text{a.s.}} X$.

**Convergence in probability** $X^{(N)}$ converges to $X$ in probability $(X^{(N)} \xrightarrow{P} X)$ if for all $\varepsilon > 0$,

$$
P \left\{ d(X^{(N)}, X) > \varepsilon \right\} \to 0 \quad (A.7)$$

as $N \to \infty$.

**Convergence in distribution** $X^{(N)}$ converges to $X$ in distribution (also referred to as weakly or in law) if for all continuous, bounded functions $f : S \to \mathbb{R}$,

$$
\mathbb{E} \left[ f(X^{(N)}) \right] \to \mathbb{E} \left[ f(X) \right] \quad (A.8)
$$

as $N \to \infty$. We will write this as $X^{(N)} \xrightarrow{D} X$.

**$L^p$ convergence** $X^{(N)}$ converges to $X$ in $L^p$ ($p \geq 1$) if

$$
\mathbb{E} \left[ d(X^{(N)}, X)^p \right] \to 0 \quad (A.9)
$$
as \(N \to \infty\). We will sometimes write this as \(X^{(N)} \overset{L^p}{\to} X\).

The first of these topologies are relatively coarser:

\[
X^{(N)} \overset{a.s.}{\to} X \Rightarrow X^{(N)} \overset{P}{\to} X \Rightarrow X^{(N)} \overset{D}{\to} X.
\] (A.10)

Almost sure convergence and convergence in \(L^p\) are not directly comparable, but

\[
X^{(N)} \overset{L^p}{\to} X \Rightarrow X^{(N)} \overset{P}{\to} X.
\] (A.11)

Finally, \(\Omega\) is a finite measure space, so

\[
X^{(N)} \overset{L^r}{\to} X \Rightarrow X^{(N)} \overset{L^p}{\to} X
\] (A.12)

for \(r \geq p \geq 1\).

\section*{A.4 Markov Processes}

A stochastic process \(\{X(t)\}_{t \in T}\) is a Markov process if

\[
\mathbb{E} [X(t)|\mathcal{F}_s] = \mathbb{E} [X(t)|X(s)]
\] (A.13)

for all \(s \leq t\) \(i.e.\) the process is “memoryless”, so that knowing \(X(s)\) is equivalent to knowing the entire history up to time \(s\), \(\mathcal{F}_s\).

When considering Markov processes, we will frequently use the notational shorthands

\[
\mathbb{P}_x \{\cdot\} := \mathbb{P} \{\cdot|X_0 = x\}, \quad (A.14)
\]

\[
\mathbb{E}_x [\cdot] := \mathbb{E} [\cdot|X_0 = x]. \quad (A.15)
\]

The \textit{infinitesimal generator} (\textit{generator}, for short) of a Markov process is the linear
operator $\mathcal{G}$ defined by

$$(\mathcal{G}\phi)(x) = \lim_{h \downarrow 0} \frac{\mathbb{E}_x[\phi(X(h))] - \phi(x)}{h}. \quad (A.16)$$

for the set of functions, $\mathcal{D}(\mathcal{G})$, for which this limit exists. $\mathcal{D}(\mathcal{G})$ is the domain of $\mathcal{G}$.

*Dynkin’s formula* states that if $T$ is a stopping time, then

$$\mathbb{E}_x[\phi(X(T))] = \phi(x) + \mathbb{E}_x\left[\int_0^T (\mathcal{G}\phi)(X(s)) \, ds\right]. \quad (A.17)$$

We can use Dynkin’s formula to analyze quantities related to the *exit distribution*. Let $X(t)$ be a Markov process with state space $S$, and let $A \subseteq S$. Then,

$$T_{\text{exit}} := \inf\{t \geq 0 : X(t) \notin A\} \quad (A.18)$$

is the *time of first exit* from $A$. Suppose $X(t)$ is a Markov process with continuous sample paths. Let $\Gamma \subseteq \partial A$, and suppose that we have a solution to the Dirichlet problem

$$(\mathcal{G}h_{\Gamma})(x) = 0 \quad (A.19)$$

$$h_{\Gamma}(x)|_{\partial A} = \begin{cases} 1 & \text{if } x \in \Gamma \\ 0 & \text{otherwise}. \end{cases} \quad (A.20)$$

Then

$$h_{\Gamma}(x) = \mathbb{E}_x[f(X(T_{\text{exit}}))] = \mathbb{P}_x\{X(T_{\text{exit}}) \in \Gamma\} \quad (A.21)$$

gives the probability of exit through $\Gamma$. Similarly, if $g_{\text{exit}}$ is the solution to

$$(\mathcal{G}g_{\text{exit}})(x) = -1 \quad (A.22)$$

$$g_{\text{exit}}(x)|_{\partial A} \equiv 0, \quad (A.23)$$
then
\[ g_{\text{exit}}(x) = \mathbb{E}_x [T_{\text{exit}}]. \] (A.24)

Let \( h \) be a harmonic function with respect to \( G \) (i.e. \( G h = 0 \)). The Doob \( h \)-transform of \( \mathbb{P} \) is the measure \( \tilde{\mathbb{P}} \) defined by
\[ \tilde{\mathbb{P}}_x(A) := \mathbb{E}_x \left[ \mathbb{1}_A \frac{h(X(t))}{h(x)} \right], \] (A.25)
with corresponding generator
\[ (\tilde{G} f)(x) = \frac{1}{h(x)} G(hf)(x). \] (A.26)

In particular, if \( h_\Gamma \) solves (A.19), then \( h_\Gamma \) is harmonic, and \( \tilde{\mathbb{P}} \) is the probability conditioned on the first exit through \( \Gamma \). Similarly to (A.22), if \( f \) solves
\[ (G h_\Gamma g_\Gamma)(x) = -h(x) \] (A.27)
\[ (h_\Gamma g_\Gamma)(x)|_{\partial A} \equiv 0, \] (A.28)
then
\[ g_\Gamma(x) = \mathbb{E}_x [T_{\text{exit}}|X(T_{\text{exit}}) \in \Gamma]. \] (A.29)

We will use this to compute expected times to fixation.

We can also use the infinitesimal generator to find the stationary distribution for a Markov process \( X(t) \). Suppose that a stationary measure \( \mu \) exists. Then,
\[ \frac{d}{dt} \int_S \mathbb{E}_x [f(X(t))] \mu(dx) = 0, \] (A.30)
so that
\[ \int_S (\mathcal{G} f)(x), \mu(dx) = 0 \] (A.31)
also. Using the duality between continuous bounded functions and measures, we can write this as
\[ \int_S f(x)(G^*\mu)(dx) = 0, \] (A.32)

where \( G^* \) is the adjoint of \( G \). Now, \( f \) is an arbitrary function, so we must have \((G^*\mu)(dx) \equiv 0\). In particular, if \( \mu \) has a density \( u \), then \( G^* \) may be regarded as a linear operator acting on \( u \) and \( G^*u = 0 \).

We will be particularly interested in the case for a \( K \)-dimensional diffusion process, given by
\[
X(t) = X(0) + \int_0^t b(X(s)) ds + \int_0^t \sigma(X(s)) dW(s),
\] (A.33)

where \( b : \mathbb{R}^K \to \mathbb{R}^K \), \( \sigma : \mathbb{R}^K \to M_{K \times K}(\mathbb{R}) \), and \( W \) is \( K \)-dimensional Brownian motion. The generator of \( X \) is
\[
(Gf)(x) = \sum_{i=1}^K b_i(x)(\partial_i f)(x) + \frac{1}{2} \sum_{i=1}^K \sum_{j=1}^K a_{ij}(x)(\partial_i \partial_j f)(x),
\] (A.34)

where \( a := \sigma \sigma^T \). The adjoint of \( G \) is
\[
(G^*f)(x) = -\sum_{i=1}^K \partial_i(b_i f)(x) + \frac{1}{2} \sum_{i=1}^K \sum_{j=1}^K \partial_i \partial_j(a_{ij} f)(x).
\] (A.35)

In particular, if \( X(t) \) is a one dimensional diffusion on an interval \([l, r]\), with generator
\[
(Gf)(x) = b(x)f'(x) + \frac{1}{2} a(x)f''(x),
\] (A.36)

the solution to the Dirichlet problems \( Gf = 0 \) and \( G^*f = 0 \) – and thus the exit probabilities and stationary distributions – can be explicitly solved. Let
\[
s(x) := e^{-\int_{x_0}^x \frac{2b(\xi)}{a(\xi)} d\xi}
\] (A.37)
for some arbitrary \( x_0 \in [l, r] \),
\[
S(x) := \int_{x_0}^{x} s(\xi) \, d\xi,
\]
(A.38)
and
\[
m(x) := \frac{1}{a(x) s(x)},
\]
(A.39)

\( S(x) \) and \( m(x) \) are referred to as the *scale function* and *speed density* respectively, and solve \( \mathcal{G} S = 0 \) and \( \mathcal{G}^* m = 0 \). In particular, when the denominator is non-zero and finite,
\[
\frac{m(x)}{\int_{l}^{x} m(x) \, dx}
\]
(A.40)
is the stationary distribution for \( X(t) \), and if the integrals
\[
\int_{l}^{x_0} (S(x) - S(l)) \, m(x) \, dx
\]
(A.41)
and
\[
\int_{x_0}^{r} (S(r) - S(x)) \, m(x) \, dx
\]
(A.42)
converge, then \( X(t) \) can reach the boundary points \( l \) and \( r \) in finite time, and
\[
\frac{S(x) - S(r)}{S(l) - S(r)}
\]
(A.43)
is the probability that \( X(t) \), started from \( X(0) = x \), hits the left endpoint \( l \) before the right endpoint \( r \).

If the probability distribution
\[
\mathbb{P} \{ X(t) \in A | X(s) = y \}
\]
(A.44)
has a density function $f$, i.e.,

$$
P \{ X(t) \in A | X(s) = y \} = \int_A f(t, x, s, y) \, dx,
$$

(A.45)

then $\partial_t f = G^* f$ and $\partial_s f = G f$. In the context of diffusions, these two partial differential equations are commonly referred to the Fokker-Planck or forward equation and the Kolmogorov backward equation, respectively, as they describe the forward-time and backward-time evolution of the process $X(t)$.

### A.5 Martingales

A stochastic process $\{M(t)\}_{t \in T}$ is a martingale/sub-martingale/super-martingale with respect to the filtration $\mathcal{F}$ ($\mathcal{F}$-martingale) if

$$
\mathbb{E}[M(t) | \mathcal{F}_s] = M(s) \quad (A.46)
$$

$$
\mathbb{E}[M(t) | \mathcal{F}_s] \geq M(s) \quad (A.47)
$$

$$
\mathbb{E}[M(t) | \mathcal{F}_s] \leq M(s) \quad (A.48)
$$

for all $s \leq t$, $s, t \in T$. In particular, if $\{M(t)\}_{t \in T}$ is a Markov martingale, then

$$
\mathbb{E}[M(t) | M(s)] = M(s), \quad (A.49)
$$

etc.

The notion of martingale and stopping time arise from probability’s origin in gambling: martingales were coin-tossing games that were popular in 18th century France. The game was fair if one’s expected holdings after a period of gambling was equal to the amount with which the player began. Stopping times emerge from betting strategies (“know when to fold ’em”): non-clairvoyant players can only rely on information up to
the present when deciding when to stop.

The optional sampling theorem or optional stopping theorem states that if $S \leq T$ are stopping times with respect to the natural filtration for a super-martingale $\{M(t)\}_{t \in T}$, then

$$\mathbb{E}[M(T)|\mathcal{F}_S] \leq M(S).$$

(A.50)

If $\{M(t)\}_{t \in T}$ is a uniformly integrable martingale, then

$$\mathbb{E}[M(T)|\mathcal{F}_S] = M(S).$$

(A.51)

The optional sampling theorem tells us that in a fair game, there is no gambling strategy that improves the players odds beyond random chance.

Doob’s martingale inequalities tell us that if $M$ is a non-negative real-valued sub-martingale then

$$\mathbb{P}\left\{\sup_{t \leq T} M(t) \geq C\right\} \leq \frac{\mathbb{E}[M(T)]}{C},$$

(A.52)

and, if $p > 1$,

$$\mathbb{E}\left[\sup_{t \leq T} M(t)^p\right] \leq \left(\frac{p}{p - 1}\right)^p \mathbb{E}[M(T)^p].$$

(A.53)

Note that if $M(t)$ is a martingale and $\varphi$ is a convex function, then $\varphi(M(t))$ is a sub-martingale. In particular, if $S$ is a normed linear space, its norm $\|\cdot\|$ is a convex function, so

$$\mathbb{P}\left\{\sup_{t \leq T} \|M(t)\| \geq C\right\} \leq \frac{\mathbb{E}[\|M(T)\|]}{C},$$

(A.54)

and, for $p > 1$,

$$\mathbb{E}\left[\sup_{t \leq T} \|M(t)\|^2\right] \leq 4\mathbb{E}\left[\|M(T)\|^2\right].$$

(A.55)

We shall make considerable use of these last two inequalities.

For simplicity, we will henceforth assume that $(S, \|\cdot\|)$ is a complete normed linear space, which is adequate for all random variables and stochastic processes contained
Doob’s *martingale convergence theorem* states that if $M(t)$ is an $L^1$-martingale, so $\sup_{t \in [0,\infty)} \mathbb{E}[\|M(t)\|] < \infty$, then

$$\lim_{t \to \infty} M(t)$$

(A.56)

exists almost surely. If in addition, $M(t)$ is a *square integrable* martingale ($L^2$-martingale), *i.e.* $\sup_{t \in [0,\infty)} \mathbb{E}[\|M(t)\|^2] < \infty$, then

$$\mathbb{E}\left[\lim_{t \to \infty} M(t)\right] = \lim_{t \to \infty} \mathbb{E}[M(t)].$$

(A.57)

In general, this need not hold, and one can construct examples using branching processes for which $\lim_{t \to \infty} M(t) \equiv 0$ whilst $\mathbb{E}[M(t)] = 1$ for all $t$.

### A.6 Quadratic Variation and Covariation

The *quadratic covariation* (or simply *covariation*) of two stochastic processes $X_1$ and $X_2$ is

$$[X_1, X_2](t) = \lim_{\mathcal{P}} \sum_{i \in \mathcal{P}} |X_1(t_{i+1}) - X_1(t_i)||X_2(t_{i+1}) - X_2(t_i)|$$

(A.58)

where the limit is over all partitions $\mathcal{P} = \{t_0 = 0 < t_1 < \cdots < t_{n-1} < t_n = t\}$ of $[0, t]$ with $\max_i |t_{i+1} - t_i| \to 0$ and is taken in probability, provided this limit exists.

The covariation of a process $X$ with itself is referred to as its *quadratic variation* and is denoted $[X]$. If $B$ is Brownian motion, then $[B](t) = t$.

If $M$ is a local martingale, then its quadratic variation exists and is right-continuous. If, in addition, $M$ is locally square integrable, then the limit defining the quadratic variation converges in $L^1$ and

$$\mathbb{E}[M(t)^2] = \mathbb{E}[\|M(t)\|].$$

(A.59)
Appendix A. Probability Glossary

Let \( \{M^{(N)}\} \) be a sequence of martingales such that

\[
\lim_{N \to \infty} \mathbb{E} \left[ \sup_{t \leq T} \left| M^{(N)}(t) - M^{(N)}(t-) \right| \right] = 0 \tag{A.60}
\]

for all \( T > 0 \), i.e., such that the jump sizes converge to 0, and suppose that

\[
\lim_{N \to \infty} \mathbb{E} \left[ \left| [M^{(N)}](t) - t \right| \right] = 0. \tag{A.61}
\]

for all \( t \). Then, the martingale Central Limit Theorem states that \( M^{(N)} \overset{D}{\to} B \), where \( B \) is Brownian motion.

A.7 Semimartingales

Recall that \( x \wedge y := \max\{x, y\} \). A process \( M(t) \) is a local martingale (resp. local square integrable martingale) if there exists a sequence of stopping times \( T^{(N)} \) such that \( T^{(N)} \to \infty \) a.s. and \( M(t \wedge T^{(N)}) \) is a martingale (resp. square integrable martingale) for all \( N \).

The total variation of a process \( V \) up to time \( t \) is

\[
T_t(V) = \sup_{\mathcal{P}} \sum_{t_i \in \mathcal{P}} |V(t_{i+1}) - V(t_i)| \tag{A.62}
\]

where the supremum is over all partitions \( \mathcal{P} = \{t_0 = 0 < t_1 < \cdots < t_{n-1} < t_n = t\} \) of \([0, t]\. V \) is a finite variation process if \( T_t(V) < \infty \) for all \( t \geq 0 \).

A stochastic process \( X \) is a semimartingale with respect to a filtration \( \mathcal{F} \) if and only if \( X = M + V \) for a local \( \mathcal{F} \)-martingale \( M \) and a \( \mathcal{F} \)-adapted finite variation process \( V \). \( M \) and \( V \) may always be chosen such that \( M \) is a local square integrable martingale. Moreover, if we require \( V(0) = 0 \), this decomposition is unique.

If \( M \) is a local martingale, then its quadratic variation \([M]\) is a submartingale and
a semimartingale, and can be decomposed as $[M] = M' + ⟨M⟩$, where $M'$ is a local martingale and $⟨M⟩$ is the unique finite variation process with $⟨M⟩(0) = 0$. $⟨M⟩$ is called the *predictable quadratic variation* or *Meyer process* associated with $M$. Note that

$$
\mathbb{E} [M(t)^2] = \mathbb{E} [[M](t)] = \mathbb{E} [⟨M⟩(t)].
$$

Given martingales $M$ and $N$, we may similarly define $⟨M, N⟩$ to be the finite variation process with $⟨M, N⟩(0) = 0$ such that $MN − ⟨M, N⟩$ is a martingale.

If $M \in \mathbb{R}^K$ is a vector-valued martingale, the *tensor quadratic variation* of $M$ is the $M_{K \times K}(\mathbb{R})$ valued process $\llbracket M \rrbracket$ with

$$\llbracket M \rrbracket_{ij} = [M_i, M_j]. \quad (A.63)$$

Similarly,

$$\llangle M \rrangle_{ij} = \langle M_i, M_j \rangle. \quad (A.64)$$

Semimartingales are the class of “good integrators” [161] in that if $Y$ is a càdlàg process and $X$ is a semimartingale, then we can define a stochastic integral

$$\int_0^t Y(s−) dX(s) = \int_0^t Y(s−) dM(s) + \int_0^t Y(s−) dV(s), \quad (A.65)$$

such that $\int_0^t Y(s−) dV(s)$ is a finite variation process. Moreover, if

$$\mathbb{E} \left[ \int_0^t Y(s−)^2 d[M](s) \right] < \infty, \quad (A.66)$$

then $\int_0^t Y(s−) dM(s)$ is a local square integrable martingale such that

$$\mathbb{E} \left[ \left( \int_0^t Y(s−) dM(s) \right)^2 \right] = \mathbb{E} \left[ \int_0^t Y(s−)^2 d[M](s) \right]. \quad (A.67)$$
When $M$ is Brownian motion, his equality is sometimes referred to as the Itô isometry.

Let $X = (X_1, \ldots, X_K)$ be a $\mathbb{R}^K$-valued semimartingale. Itô’s formula states that for any $f \in C^2(\mathbb{R}^K)$,

\[
\begin{align*}
    f(X(t)) &= f(X(0)) + \sum_{i=1}^{K} (\partial_i f)(X(s-)) \, dX_i(s) + \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} (\partial_i \partial_j f)(X(s-)) \, d[X_i, X_j](s) \\
    &\quad + \sum_{s \leq t} \left\{ f(X(s-)) - f(X(s)) - \sum_{i=1}^{K} (\partial_i f)(X(s-)) \Delta X_i(s) \\
    &\quad \quad - \frac{1}{2} \sum_{i=1}^{K} \sum_{j=1}^{K} (\partial_i \partial_j f)(X(s-)) \Delta X_i(s) \Delta X_j(s) \right\}, \quad (A.68)
\end{align*}
\]

where

\[\Delta X_i(s) := X_i(s) - X_i(s-).\]  

(A.69)

Itô’s formula is the analogue of the chain rule for a semimartingale.

## A.8 Counting Processes

A random variable $N(t)$ taking values in $\mathbb{N}_0$ is a counting process if

(i) $N$ is increasing: $N(s) \leq N(t)$ for $s < t$,

(ii) $\Delta N(t) = N(t) - N(t-)$ is equal to 0 or 1, and

(iii) $\mathbb{E}[N(t)] < \infty$ for all $t > 0$.

A counting process is a semimartingale, and can be decomposed into local martingale and finite variation components: $N(t) = M(t) + V(t)$. $V$ is always be an increasing process, and is commonly referred to as the compensator or cumulative intensity of $N$, whilst $M$ is referred to as the compensated process, and is sometimes written $\tilde{N}$. $V(t)$ has finite variation, so its derivative $V'(t) = \lambda(t)$ exists almost everywhere. $\lambda(t)$ is referred to as the intensity of the counting process. Intuitively, $N(t) - N(s)$ is the number of
“events” occurring in the interval $(s, t]$, whilst $\lambda(t)\Delta t$ is the probability an event occurs in $[t, t + \Delta t)$.

Poisson processes and renewal processes are examples of counting processes. In particular, given a Markov counting process with intensity $\lambda$, there exists a rate-one poisson process $P(t)$ such that

$$N(t) \overset{D}{=} P \left( \int_0^t \lambda(s) \, ds \right).$$

(A.70)
Bibliography


