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On Quasi-stationary Distributions of Stochastic SIS Epidemic Models

Boyoung Hur

Clemson University, jbdecide@gmail.com

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ON QUASI-STATIONARY DISTRIBUTIONS OF STOCHASTIC SIS
EPIDEMIC MODELS

A Thesis
Presented to
the Graduate School of
Clemson University

In Partial Fulfillment
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Master of Science
Mathematics

by
Boyoung Hur
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Dr. Xin Liu, Committee Chair
Dr. Peter Kiessler
Dr. Brian Fralix

Abstract

We study a stochastic SIS (Susceptible-Infected-Susceptible) epidemic model, in which individuals in a population are divided into two classes: “Susceptible” to the infection of a disease, and “Infected” by the disease. We assume the population size N is fixed. The state process, which measures the number of infected individuals, is modeled as a continuous time Markov chain (CTMC). The CTMC has an absorbing state 0, and it will eventually die out by reaching the absorbing state. However, it appears to be persistent over a long time period before extinction. Such behavior can be understood by the study of quasi-stationary distributions. In this thesis, our main results show that the CTMC SIS model has a unique quasi-stationary distribution, and when the basic reproduction number is greater than 1, as $N \rightarrow \infty$, the quasi-stationary distribution converges to a dirac probability measure concentrated at the equilibrium point of a deterministic SIS model.

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Chapter 1

Introduction

Infectious diseases have always played an important role in human history. In this thesis, we study the classical susceptible-infected-susceptible (SIS) epidemic model, in which the population is divided into two classes: susceptible and infected, and individuals start being susceptible, at some stage get infected by the disease, and after some infectious period become susceptible again. Let N denote the population size, $S(t)$ the number of susceptible individuals, and $I(t)$ the number of infected individuals at time t . Assume that the population size N is fixed, and that the population is homogeneous and the mixing is also homogeneous. The deterministic SIS model can be formulated as follows (see also Figure 2.1 in Chapter 2). For $t \geq 0$,

$$\begin{aligned}\frac{dS(t)}{dt} &= -\frac{\beta}{N}I(t)S(t) + (b + \gamma)I(t), \\ \frac{dI(t)}{dt} &= \frac{\beta}{N}I(t)S(t) - (b + \gamma)I(t),\end{aligned}$$

where b is the equal birth and death rate, γ is the recovery rate of a typical infected individual and β is the average number of adequate contacts of an infected individual per unit time, and an adequate contact is defined to be the contact between a susceptible individual and an infected individual which is sufficient for the transmission of infection. Here it is also assumed that the birth and death of the susceptible population cancel out. The most important quantity in the analysis of epidemic models is the basic reproduction number R_0 , which measures the average number of new infections caused by a typical infected individual during its infectious period. If $R_0 < 1$, the disease will eventually die out in the long run, while if $R_0 > 1$, a major breakout is possible. In the above model, $R_0 = \beta/(b + \gamma)$. The deterministic SIS model has been used to study various real-life disease, such as gonorrhoea, tuberculosis, and pneumococcus (see [12, 16, 24]).

Weiss and Dishon [31] introduced the stochastic version of SIS epidemic model in 1971. Unlike the deterministic model, the stochastic model considers the number of individuals as a discrete state which is much closer to the real world. Besides, the stochastic model could deal with something which could not be explained in the deterministic model such as the probability of an outbreak, the quasi-stationary distribution, the final size distribution of an epidemic, and the expected duration of an epidemic (see [2]). In [1], a continuous time Markov chain (CTMC) model was established using Poisson processes with the same transition rates between compartments as in the deterministic model, and a stochastic differential equation (SDE) approximation was further developed. Another stochastic SIS model was introduced by Gray et al [13] using parameter perturbations. The current work applies the CTMC model as in [1]. The CTMC model has a finite state space with an absorbing state - the state when there is no infected population. From the fundamental CTMC theory, the chain will eventually reach the absorbing state. Such limiting behavior provides little useful information of the disease spread process. In Nåsell [25], it is shown that when $R_0 > 1$, it takes a long time for the CTMC to reach the absorbing state, and given that it has not been absorbed, a stationary distribution can be obtained, which is called the quasi-stationary distribution of the CTMC. Nåsell [25] also provides analysis and simulations of the quasi-stationary distribution. Since quasi-stationary distribution provides a good approximation of the distribution of states, conditional on non-extinction, after a suitable waiting time, it could be used to compute the expected time to extinction starting from quasi-stationary distribution. In the current work, we establish that when $R_0 > 1$, the quasi-stationary distribution of the CTMC converges in distribution to a dirac probability measure concentrated at the equilibrium point of the deterministic SIS model.

The study of epidemic models has a long history. The first mathematical model in epidemiology is due to Daniel Bernoulli [5, 6] in 1760s on inoculation against smallpox. The basic compartmental epidemic models are introduced by Kermack and Mckendrick in a sequence of papers [19, 20, 18]. These early models were mostly deterministic models. However, the deterministic models have a fatal problem that it considers the number of individuals in population as a continuous variable but actually it is not true in real world. This led to development of stochastic epidemic models (see [25]). An extensive literature exists performing to stochastic models of epidemiology. Multivariate Markov jump models are commonly employed to stochastic epidemic models (see [1, 4, 22]). Researchers have studied numerous stochastic phenomena such as the distribution of final size of an epidemic (see [14]), stochastically sustained oscillations to explain the semi-regular recurrence of outbreaks (see [23]), quasi-stationary distributions, which capture variances in endemic states (see [2, 8, 9, 17, 26, 30]), time to extinction of the disease (see [3, 7, 28]), etc.

We introduce the stochastic SIS model in Section 2.1. In Section 2.2, we summarize some important asymptotic properties of the stochastic SIS model (see Theorem 2.2.1 and Theorem 2.2.3). More precisely, Theorem 2.2.1 says that the proportion of infected population in the stochastic model approaches the solution of a deterministic SIS model as the population size goes to infinity, and in Theorem 2.2.3 the stability of this deterministic model is established. In Theorem 2.2.4, we establish the main result that the proportion of infected population has a unique quasi-stationary distribution and it converges to the dirac probability measure concentrated at the stable equilibrium point of the deterministic model when $R_0 > 1$.

Chapter 2

SIS Epidemic model

2.1 Stochastic SIS Model

We study an SIS epidemic model (cf.[2]). In this model, individuals in the population are classified according to their health status as either “susceptible” to the infection of a disease or “infected” by the disease. We assume the total population size N is fixed and let $S^N(t)$ denote the number of susceptible individual at time t , and $I^N(t)$ the number of infected individual at time t . Noting that $S^N(t) + I^N(t) = N$, it suffices to focus on the study of the 1-dimensional process $\{I^N(t); t \geq 0\}$. We assume each individual spends exponentially distributed time in “susceptible” status, and then move to “infected” status. Once infected, the individual gets recovered (i.e, susceptible) after another exponentially distributed time. The disease spreads through contacts between susceptible individuals and infected individuals. We assume that when a contact occurs, it involves each pair of individuals equally likely. Let $\tilde{\beta}$ denote the average number of contacts for one typical individual within the unit time, and p the probability of getting infected per contact between a susceptible individual and an infectious individual. Thus, for a susceptible individual, $\frac{I^N}{N} \cdot \tilde{\beta}$ gives the average number of contacts from all infectious individuals, and $\frac{I^N}{N} \cdot \tilde{\beta} \cdot p$ gives the infection rate. Finally, $\frac{I^N}{N} \cdot \tilde{\beta} \cdot p \cdot S^N$ is the total infection rate for all susceptible individuals. Furthermore, we assume all newborns are susceptible. For simplicity, the newborns and the deaths of susceptible individuals cancel out. We summarize all transitions in Figure 2.1. Therefore, we model $\{I^N(t); t \geq 0\}$ as a continuous time Markov chain (CTMC) with state space $E = \{0, 1, 2, \dots, N\}$. The infinitesimal generator $Q = (Q_{ij})_{i,j=0}^N$ is given as follows.

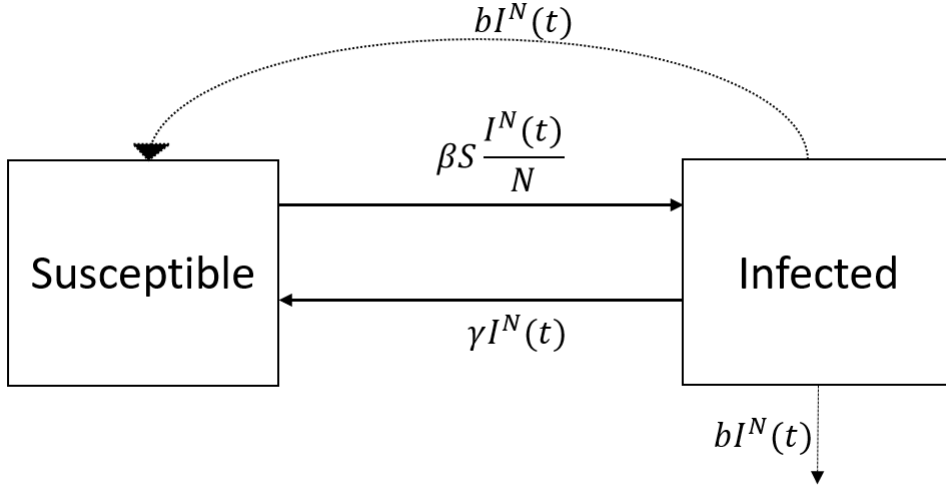


Figure 2.1: SIS compartmental diagram at time t

For $i, j = 0, \dots, N$,

$$Q_{i,j} = \begin{cases} (b + \gamma)i, & j = i - 1, \quad i \geq 1; \\ \frac{i}{N}\beta(N - i), & j = i + 1, \quad i \geq 0; \\ 1 - \{\frac{i}{N}\beta(N - i) + (b + \gamma)i\}, & i = j, \quad i \geq 0; \end{cases}$$

where $\beta = \tilde{\beta} \cdot p$ is the contact rate, γ is the recovery rate, and b is the equal birth and death rate.

We next introduce the basic reproduction number R_0 , which determines whether or not an infectious disease can spread through a population: If $R_0 < 1$, then the infection will die out in the long run, while if $R_0 > 1$, then a large outbreak and endemic is possible. For the SIS model, the basic reproduction number $R_0 = \frac{\beta}{b + \gamma}$, which measures the expected number of secondary infections caused by an infected individual during its infection period.

In CTMC SIS model, the state space $E = \{0, 1, \dots, N\}$ can be written as $\{0\} \cup \{1, 2, \dots, N\}$, where $\{0\}$ is the absorbing state and $\{1, 2, \dots, N\}$ is the irreducible transient class. Since there is an absorbing state, the stationary distribution of this model approaches to this disease-free state asymptotically in long run. Although simple, the stationary distribution provides little information of the epidemic model. Instead, we study the extinction time and the quasi stationary distribution of the process I^N . The extinction time is defined to be the time when the process I^N reaches the absorbing state 0. Under the condition that $R_0 > 1$, it can be shown that it takes a rather long time period for I^N to extinct, (cf.[25]). This makes it reasonable to study the long-time behavior of I^N given that absorption

has not occurred which brings about the quasi-stationary distribution. More precisely, from [29], a sequence $\{q_j\}_{j=1}^N$ with $q_j \geq 0$, and $\sum_{j=1}^N q_j = 1$ is a quasi-stationary distribution if $p_j(t)/(1 - p_0(t)) = q_j$, for $j = 1, \dots, N$, and $t \geq 0$, where $p_j(t) = P(X(t) = j)$, $j = 0, 1, \dots, N$, and $P(X(0) = j) = q_j$, $j = 1, \dots, N$. Unfortunately, the quasi-stationary distribution doesn't have an explicit form, and one needs to develop appropriate approximation. In this work, we will study the limiting behavior of the quasi-stationary distribution. We will show that the quasi-stationary distribution converges to the dirac probability measure concentrated at the equilibrium point of the deterministic SIS model when $R_0 > 1$.

2.2 Main results

In this section, we first summarize some asymptotic results for I^N as $N \rightarrow \infty$ and/or $t \rightarrow \infty$. Our eventual goal is to establish the convergence of the quasi-stationary distribution as $N \rightarrow \infty$.

We first note that the CTMC mentioned above can be modeled by the independent unit-rate Poisson processes Y_1 and Y_2 (see Theorem 4.1 of Chapter 6 in [11]). More precisely, for $t \geq 0$,

$$I^N(t) = I^N(0) + Y_1 \left(\int_0^t \frac{\beta}{N} I^N(u)(N - I^N(u)) du \right) - Y_2 \left(\int_0^t (b + \gamma) I^N(u) du \right).$$

In the following, we define a scaled process $\bar{I}^N(t) = \frac{I^N(t)}{N}$, $t \geq 0$, which can be interpreted as the density of the infected individuals at time t . We first let $N \rightarrow \infty$, and derive a deterministic limit of \bar{I}^N (see [21] for a similar convergence of a stochastic SIR model).

Theorem 2.2.1. *Assume that $\bar{I}^N(0)$ converges to some deterministic i_0 in probability. Then for each $T \geq 0$,*

$$\sup_{t \leq T} |\bar{I}^N(t) - i_t| \rightarrow 0, \quad \text{as } N \rightarrow \infty,$$

where i_t is the solution of the following ODE with initial value i_0 .

$$\frac{di_t}{dt} = \beta(1 - i_t)i_t - (b + \gamma)i_t, \tag{2.2.1}$$

The ODE in (2.2.1) gives the well-known deterministic SIS model, which has been well studied, (see [2, 10, 27]). In particular, it can be analytically solved as in the following theorem.

Theorem 2.2.2. *Given an initial condition i_0 , the solution of (2.2.1) is given by*

$$i_t = \begin{cases} \frac{e^{(\beta-(b+\gamma))t}}{\frac{\beta(e^{(\beta-(b+\gamma))t}-1)}{\beta-(b+\gamma)} + \frac{1}{i_0}}, & \beta \neq b + \gamma, \\ \frac{1}{\beta t + \frac{1}{i_0}}, & \beta = b + \gamma. \end{cases}$$

We next study the stability of the equilibrium points of (2.2.1).

Definition 2.2.1 (Stability). Consider a differential equation $\dot{x} = f(x)$, where $f : \mathbb{R}^n \rightarrow \mathbb{R}^n$. A point $x_e \in \mathbb{R}^n$ is an equilibrium point of the system if $f(x_e) = 0$. An equilibrium point x_e is said to be stable if given $\epsilon > 0$, there is a $\delta > 0$ such that for every solution x , when $|x(0) - x_e| < \delta$, we have $|x(t) - x_e| < \epsilon$ for all t ; it is said to be locally asymptotically stable (L.A.S) if there is an $R > 0$ such that when $\|x(0) - x_e\| \leq R$, $x(t) \rightarrow x_e$ as $t \rightarrow \infty$; it is said to be globally asymptotically stable (G.A.S) if for every trajectory $x(t)$, we have $x(t) \rightarrow x_e$ as $t \rightarrow \infty$; it is said to be unstable if it is not stable.

The equilibrium points and their stability properties are summarized in the following theorem (see [15]).

Theorem 2.2.3. *The ODE (2.2.1) has two equilibrium points $E_0 = 0$ and $E_1 = 1 - \frac{1}{R_0}$. Furthermore,*

- (i) E_0 is globally asymptotically stable (g.a.s) when $R_0 \leq 1$;
- (ii) E_0 is unstable when $R_0 > 1$;
- (iii) E_1 is locally asymptotically stable (l.a.s) when $R_0 > 1$;
- (iv) E_1 is globally asymptotically stable (g.a.s) when $i_0 > 0$ and $R_0 > 1$.

The main contribution of this thesis is to establish the following limit theorem for the quasi-stationary distribution of the stochastic SIS model to the equilibrium point of the deterministic SIS model.

Theorem 2.2.4. *When $R_0 > 1$, \bar{I}^N has a unique quasi-stationary distribution for each N .*

Denote by q_N^* the quasi-stationary distribution of \bar{I}^N . The following is our main result.

Theorem 2.2.5. *When $R_0 > 1$, q_N^* converges to δ_{E_1} as $N \rightarrow \infty$, where $E_1 = 1 - \frac{1}{R_0}$ is the endemic equilibrium point of the deterministic SIS model.*

2.3 Proofs

Proof of Theorem 2.2.1. Recall that Y_1 and Y_2 are independent unit rate Poisson Processes. For $t \geq 0$, let $\bar{Y}_i^N(t) = \frac{Y_i(Nt)}{N}$, $i = 1, 2$. Then, for $t \geq 0$, we have

$$\bar{I}^N(t) = \frac{I^N(t)}{N} = \bar{I}^N(0) + \bar{Y}_1^N \left(\int_0^t \beta \bar{I}^N(u) (1 - \bar{I}^N(u)) du \right) - \bar{Y}_2^N \left(\int_0^t (b + \gamma) \bar{I}^N(u) du \right).$$

Let i_t be the solution of the deterministic equation (2.2.1). We derive the following equation. For $t \geq 0$,

$$\begin{aligned} \bar{I}^N(t) - i_t &= \bar{I}^N(0) + \bar{Y}_1^N \left(\int_0^t \alpha^1(\bar{I}^N(u)) du \right) - \bar{Y}_2^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) - \left(i_0 + \int_0^t \alpha^1(i_u) du - \int_0^t \alpha^2(i_u) du \right) \\ &= \bar{I}^N(0) - i_0 + \bar{Y}_1^N \left(\int_0^t \alpha^1(\bar{I}^N(u)) du \right) - \bar{Y}_2^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) - \int_0^t \alpha^1(i_u) du + \int_0^t \alpha^2(i_u) du \\ &= \bar{I}^N(0) - i_0 + \tilde{Y}_1^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) - \tilde{Y}_2^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) + \int_0^t [\alpha^1(\bar{I}^N(u)) - \alpha^1(i_u)] du \\ &\quad - \int_0^t [\alpha^2(\bar{I}^N(u)) - \alpha^2(i_u)] du, \end{aligned}$$

where $\tilde{Y}_i^N(t) = \bar{Y}_i^N(t) - t$, $i = 1, 2$, are the centered and scaled Poisson process and for $x \geq 0$, $\alpha^1(x) = \beta x(1 - x)$ and $\alpha^2(x) = (b + \gamma)x$. It follows that

$$\begin{aligned} |\bar{I}^N(t) - i_t| &\leq |\bar{I}^N(0) - i_0| + \left| \tilde{Y}_1^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) - \tilde{Y}_2^N \left(\int_0^t \alpha^2(\bar{I}^N(u)) du \right) \right| + \int_0^t |\alpha^1(\bar{I}^N(u)) - \alpha^1(i_u)| du \\ &\quad + \int_0^t |\alpha^2(\bar{I}^N(u)) - \alpha^2(i_u)| du. \end{aligned}$$

Let $\epsilon_i^N(t) = \left| \tilde{Y}_i^N \left(\int_0^t \alpha^i(\bar{I}^N(u)) du \right) \right|$ for $i = 1, 2$. From the Strong Law of Large numbers (SLLN) for a Poisson process, we have for $0 \leq v < \infty$ and $i = 1, 2$ such that

$$\lim_{N \rightarrow \infty} \sup_{u \leq v} |\tilde{Y}_i^N(u)| = 0, \quad a.s.$$

Noting that $\alpha^i(x) \leq \beta + b + \gamma + 1$ for all $x \geq 0$, it follows that for $T \geq 0$,

$$\lim_{N \rightarrow \infty} \sup_{t \leq T} \epsilon_i^N(t) = 0, \quad a.s. \quad for \quad i = 1, 2.$$

Because the α^i functions are Lipschitz continuous, there exists $M > 0$ such that

$$\sup_{0 \leq t \leq T} |\bar{I}^N(t) - i_t| \leq |\bar{I}^N(0) - i_0| + \max_{i=1,2} \sup_{t \leq T} \epsilon_i^N(t) + M \int_0^T |\bar{I}^N(u) - i_u| du.$$

Therefore, by Gronwall's inequality,

$$\sup_{0 \leq t \leq T} |\bar{I}^N(t) - i_t| \leq \left(|\bar{I}^N(0) - i_0| + \max_{i=1,2} \sup_{t \leq T} \epsilon_i^N(t) \right) e^{MT}.$$

Letting $N \rightarrow \infty$, we have $\sup_{t \leq T} |\bar{I}^N(t) - i_t| \rightarrow 0$ a.s. □

Proof of Theorem 2.2.3. First, let the ODE (2.2.1) be zero to see that there exists the equilibrium points. That is, $\beta(1 - i_t)i_t - (b + \gamma)i_t = 0$, then, we can find two equilibrium points $i_t = 0$ and $i_t = 1 - \frac{b+\gamma}{\beta}$. Next, for (ii) and (iii), we note that the Jacobian matrix for the model (2.2.1) is given by

$$J = \begin{bmatrix} -\beta i_t & -\beta s_t + (b + \gamma) \\ \beta i_t & \beta s_t - (b + \gamma) \end{bmatrix},$$

where $s_t = 1 - i_t$. If we plug E_0 into J , then we can get the eigenvalues $\lambda_1 = 0$ and $\lambda_2 = \beta - (b + \gamma)$, and if we plug E_1 , then we can get the eigenvalues $\lambda_1 = 0$ and $\lambda_2 = (b + \gamma) - \beta$. Since λ_1 's for each cases are zero, if $\lambda_2 < 0$, then it is locally asymptotically stable, and if $\lambda_2 > 0$, then it is unstable. When $R_0 > 1$, λ_2 at E_0 is greater than zero, and thus it is unstable, while, λ_2 at E_1 is less than zero, and so it is locally asymptotically stable. For (i) and (iv), from Theorem 2.2.2, we know that when $\beta \leq b + \gamma$, $i_t \rightarrow 0$, and when $\beta > b + \gamma$, $i_0 > 0$, $i_t \rightarrow 1 - \frac{b+\gamma}{\beta} = 1 - \frac{1}{R_0}$ as $t \rightarrow \infty$. By Definition 2.2.1, they show that $E_0 = 0$ is globally asymptotically stable when $R_0 \leq 1$ and $E_1 = 1 - \frac{1}{R_0}$ is globally asymptotically stable when $R_0 > 1$, respectively. □

Proof of Theorem 2.2.4. From Theorem 3.2 (ii) in [29], it suffices to show that $\sum_{n=0}^{\infty} (\lambda_n \rho_n)^{-1} \sum_{i=n+1}^{\infty} \rho_i <$

∞ , where $\lambda_n = \beta(n(N-n))/N$ and $\mu_n = (b + \gamma)n$. We observe that

$$\begin{aligned} \sum_{i=n+1}^{\infty} \rho_i &= \sum_{i=n+1}^{\infty} \frac{\lambda_1 \lambda_2 \cdots \lambda_i}{\mu_2 \mu_3 \cdots \mu_{i+1}} \quad \text{since } \lambda_N = \lambda_{N+1} = \cdots = 0 \quad \text{and} \quad \mu_{N+1} = \mu_{N+2} = \cdots = 0, \\ &= \sum_{i=n+1}^{N-1} \frac{\lambda_1 \lambda_2 \cdots \lambda_i}{\mu_2 \mu_3 \cdots \mu_{i+1}}. \end{aligned}$$

Therefore,

$$\sum_{n=0}^{\infty} (\lambda_n \rho_n)^{-1} \sum_{i=n+1}^{\infty} \rho_i = \sum_{n=1}^{N-2} (\lambda_n \rho_n)^{-1} \sum_{i=n+1}^{N-1} \rho_i < \infty.$$

Thus there is a unique quasi-stationary distribution. \square

To show the main theorem, we introduce the Portmanteau Theorem.

Theorem 2.3.1 (Portmanteau Theorem). *Let p_n, p be the probability measures on S . The following conditions are equivalent.*

- (i) $p_n \rightarrow p$, in distribution.
- (ii) $\lim_{n \rightarrow \infty} \int_S f dp_n = \int_S f dp$ for all bounded, uniformly continuous real f on S .
- (iii) $\limsup_n p_n(F) \leq p(F)$ for all closed set $F \subseteq S$.
- (iv) $\liminf_n p_n(G) \geq p(G)$ for all open set $G \subseteq S$.
- (v) $\lim_{n \rightarrow \infty} p_n(A) = p(A)$ for all p -continuity sets $A \in S$.

Proof of Theorem 2.2.5. Let $q_N^* = \lim_{t \rightarrow \infty} P(\bar{I}^N(t) | \bar{I}^N(t) \neq 0)$ be a quasi-stationary distribution of \bar{I}^N . As in [25], we consider an auxiliary process $\{X(t); t \geq 0\}$ with the same state space E , which is a birth-death process with birth rate $\lambda_i, i = 0, 1, \dots, N-1$ and death rate $\mu_i, i = 0, 1, \dots, N-1$ and the stationary distribution of the process X is $\pi_n = \rho_n \pi_1$ where $n = 1, 2, \dots, N, \pi_1 = \frac{1}{\sum_{n=1}^N \rho_n}$, and $\rho_n = \frac{\lambda_1 \lambda_2 \cdots \lambda_{n-1}}{\mu_1 \mu_2 \cdots \mu_{n-1}}, n = 2, 3, \dots, N, \rho_1 = 1$. First, we collect the results on ρ_n from [25].

$$\begin{aligned}
\rho_n &= \frac{\lambda_1 \cdot \lambda_2 \cdots \lambda_{n-1}}{\mu_1 \cdot \mu_2 \cdots \mu_{n-1}}, \quad \text{where } \lambda_i = \lambda(1 - i/N)i, \quad \text{and } \mu_i = i\mu, \\
&= \frac{\lambda(1 - 1/N) \cdot \lambda(1 - 2/N)2 \cdot \lambda(1 - 3/N)3 \cdots \lambda(1 - (n-1)/N)(n-1)}{\mu \cdot 2\mu \cdot 3\mu \cdots (n-1)\mu} \\
&= \frac{\lambda^{n-1}(N-1)(N-2) \cdots (N-(n-1))}{\mu^{n-1}N^{n-1}} \\
&= (N-1)(N-2) \cdots (N-(n-1)) \left(\frac{R_0}{N}\right)^n \\
&= \frac{1}{R_0} \cdot \frac{N}{N-n} \cdot \frac{\Gamma(N)}{\Gamma(N-n)} \cdot \left(\frac{R_0}{N}\right)^n \quad \text{for } n = 2, 3, \dots, N-1,
\end{aligned}$$

where $R_0 = \lambda/\mu$, $\Gamma(k) = (k-1)!$ for $k \in \mathbb{N}$, and $\rho_N = (N-1)!(\frac{R_0}{N})^N$. Then, we can get by Stirling's Formula

$$\begin{aligned}
\Gamma(N) &\sim (N/e)^N \sqrt{2\pi/N} \quad \text{as } N \rightarrow \infty, \\
\Gamma(N-n) &\sim ((N-n)/e)^{N-n} \sqrt{2\pi/(N-n)} \quad \text{as } N-n \rightarrow \infty,
\end{aligned}$$

where for two functions $f, g: [0, \infty) \rightarrow [0, \infty)$, $f(x) \sim g(x)$ as $x \rightarrow \infty$ if $\frac{f(x)}{g(x)} \rightarrow 1$ as $x \rightarrow \infty$. Then we have

$$\begin{aligned}
\rho_n &\sim \frac{1}{R_0} \cdot \frac{N}{N-n} \cdot \frac{(N/e)^N}{((N-n)/e)^{N-n}} \cdot \frac{\sqrt{2\pi/N}}{\sqrt{2\pi/(N-n)}} \left(\frac{R_0}{N}\right)^n \\
&= g(n) \cdot \exp(h(n)),
\end{aligned}$$

where $g(n) = \frac{1}{R_0} \cdot \frac{1}{\sqrt{1-n/N}}$ and $h(n) = \log\left(\left(\frac{1}{1-n/N}\right)^N \left(\frac{N-n}{e}\right)^n \left(\frac{R_0}{N}\right)^n\right)$. Let $f(x) = x(\log R_0 - 1) - (1-x)\log(1-x)$, then $h(n) = Nf(\frac{n}{N})$. Noting that for $x < 1$

$$\begin{aligned}
f'(x) &= \log R_0 - 1 + \frac{1}{1-x} + \log(1-x) - \frac{x}{1-x} \\
&= \log R_0 + \log(1-x), \\
f''(x) &= \frac{-1}{1-x} < 0,
\end{aligned}$$

so $f(x)$ attains its maximum at $x = 1 - \frac{1}{R_0}$. Let $x_0 = (1 - \frac{1}{R_0})$. Then, for any $x \in [0, 1]$ such that $x \neq x_0$, we observe that

$$\frac{\rho_{\lfloor Nx \rfloor}}{\rho_{\lfloor Nx_0 \rfloor}} \sim \frac{g(\lfloor Nx \rfloor) \exp\{Nf(\frac{\lfloor Nx \rfloor}{N})\}}{g(\lfloor Nx_0 \rfloor) \exp\{Nf(\frac{\lfloor Nx_0 \rfloor}{N})\}}$$

$$\begin{aligned}
&= \frac{\sqrt{1 - \frac{\lfloor Nx \rfloor}{N}}}{\sqrt{1 - \frac{\lfloor Nx_0 \rfloor}{N}}} \exp\{N(f(\frac{\lfloor Nx \rfloor}{N}) - f(\frac{\lfloor Nx_0 \rfloor}{N}))\} \quad \text{since } f(x_0) > f(x), \\
&\sim \frac{\sqrt{1-x}}{\sqrt{1-x_0}} \exp\{-N(f(x_0) - f(x))\} \rightarrow 0 \quad \text{as } N \rightarrow \infty.
\end{aligned} \tag{2.3.1}$$

Now, we are ready to see the behavior of q_N^* which is the quasi-stationary distribution of \bar{I}^N . Firstly, consider the conditional probability $q_n(t) = \frac{P(\bar{I}^N(t)=n)}{1-P(\bar{I}^N(t)=0)} = \frac{p_n(t)}{1-p_0(t)}$. We note that $\{q_n(t); n = 1, \dots, N\}$ depends on N . For convenience, we omit N from the notation. Taking derivatives, we have

$$\begin{aligned}
q_n'(t) &= \left(\frac{p_n(t)}{1-p_0(t)} \right)' \\
&= \frac{p_n'(t)(1-p_0(t))}{(1-p_0(t))^2} + \frac{p_n(t)p_0'(t)}{(1-p_0(t))^2} \\
&= \frac{p_n(t)}{1-p_0(t)} + \frac{p_n(t)p_0'(t)}{(1-p_0(t))^2} \quad \text{since } p_n'(t) = \lambda_{n-1}p_{n-1}(t) + \mu_{n+1}p_{n+1}(t) - (\lambda_n + \mu_n)p_n(t) \\
&= \frac{\mu_{n+1}p_{n+1}(t)}{1-p_0(t)} - \frac{(\lambda_n + \mu_n)p_n(t)}{1-p_0(t)} + \frac{\lambda_{n-1}p_{n-1}(t)}{1-p_0(t)} + \frac{p_n(t)\mu_1 p_1(t)}{(1-p_0(t))^2} \\
&= \mu_{n+1}q_{n+1}(t) - (\lambda_n + \mu_n)q_n(t) + \lambda_{n-1}q_{n-1}(t) + q_n(t)\mu_1 q_1(t).
\end{aligned}$$

For the quasi-stationary solution, let $q_n'(t) = 0$. Then we have

$$\mu_{n+1}q_{n+1}^* - (\lambda_n + \mu_n)q_n^* + \lambda_{n-1}q_{n-1}^* = -\mu_1 q_1^* q_n^*,$$

which yields

$$q_n^* = q_1^* \frac{\rho_n}{n} \sum_{k=1}^n \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k}, \quad n = 1, 2, \dots, N, \quad \sum_{n=1}^N q_n^* = 1.$$

Using this result, we can get the following inequalities:

$$\begin{aligned}
1 &= \sum_{j=1}^N q_j^* = q_1^* \sum_{j=1}^N \frac{\rho_n}{n} \sum_{k=1}^n \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k} \quad \text{where } \rho_1 = 1 \\
&\geq q_1^* \frac{\rho_{n_0}}{n_0} \quad \text{where } n_0 = \left\lfloor \left(1 - \frac{1}{R_0}\right) N \right\rfloor
\end{aligned}$$

and thus $q_1^* \leq \frac{n_0}{\rho_{n_0}}$. It follows that when $\frac{n}{N} < 1 - \frac{1}{R_0}$,

$$q_n^* = q_1^* \frac{\rho_n}{n} \sum_{k=1}^n \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k} \leq \frac{\rho_n}{n} \sum_{k=1}^n \frac{1}{\rho_k} q_1^*$$

$$\begin{aligned}
&\leq \frac{\rho_n}{n} \cdot \frac{n}{\rho_1} q_1^* \\
&= \frac{\rho_n}{\rho_1} q_1^* \leq \frac{\rho_n}{\rho_1} \cdot \frac{n_0}{\rho_{n_0}} = \rho_n \frac{n_0}{\rho_{n_0}},
\end{aligned} \tag{2.3.2}$$

and when $\frac{n}{N} > 1 - \frac{1}{R_0}$,

$$\begin{aligned}
q_n^* &= q_1^* \frac{\rho_n}{n} \sum_{k=1}^n \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k} = q_1^* \frac{\rho_n}{n} \left(\sum_{k=1}^{n_0} \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k} + \sum_{k=n_0+1}^n \frac{1 - \sum_{j=1}^{k-1} q_j^*}{\rho_k} \right) \\
&\leq q_1^* \frac{\rho_n}{n} \left(n_0 \frac{1}{\rho_1} + (n - n_0) \frac{1 - \sum_{j=1}^{n_0} q_j^*}{\rho_n} \right) \\
&\leq \frac{n_0}{\rho_{n_0}} \frac{\rho_n}{n} \left(n_0 + (n - n_0) \frac{1}{\rho_n} \right) \\
&= \frac{n_0^2 \rho_n + (n - n_0) n_0}{n \rho_{n_0}}.
\end{aligned} \tag{2.3.3}$$

Now, consider a closed set $A \subseteq [0, 1]$.

1. If A is on the left of $1 - \frac{1}{R_0}$, i.e., $\max_{x \in A} x < 1 - \frac{1}{R_0}$,

$$\begin{aligned}
q^*(A) &= \sum_{\frac{i}{N} \in A} q_i^* \\
&\leq \sum_{\frac{i}{N} \in A} \rho_i \frac{n_0}{\rho_{n_0}} \quad \text{by (2.3.2)} \\
&= \frac{n_0}{\rho_{n_0}} \sum_{\frac{i}{N} \in A} \rho_i.
\end{aligned}$$

Let a_0 be the largest value in A and $\lambda(A)$ the Lebesgue measure of A . Then

$$q^*(A) \leq \frac{n_0}{\rho_{n_0}} \sum_{\frac{i}{N} \in A} \rho_i = \frac{n_0}{\rho_{n_0}} N \lambda(A) \rho_{\lceil Na_0 \rceil} \sim \frac{n_0}{\rho_{n_0}} N \lambda(A) \rho_{\lfloor Na_0 \rfloor} \rightarrow 0 \quad \text{as } N \rightarrow \infty \quad \text{by (2.3.1)}.$$

2. If A is on the right of $1 - \frac{1}{R_0}$, i.e., $\min_{x \in A} x > 1 - \frac{1}{R_0}$,

$$\begin{aligned}
q^*(A) &= \sum_{\frac{i}{N} \in A} q_i^* \\
&\leq \sum_{\frac{i}{N} \in A} \frac{n_0^2 \rho_i + (i - n_0) n_0}{i \rho_{n_0}} \quad \text{by (2.3.3)} \\
&= \frac{n_0^2}{\rho_{n_0}} \left(\sum_{\frac{i}{N} \in A} \frac{\rho_i}{i} \right) + \left(\sum_{\frac{i}{N} \in A} \frac{i n_0 - n_0^2}{i \rho_{n_0}} \right)
\end{aligned}$$

$$= \frac{n_0^2}{\rho_{n_0}} \left(\sum_{\frac{i}{N} \in A} \frac{\rho_i}{i} \right) + \frac{n_0}{\rho_{n_0}} - \frac{n_0^2}{\rho_{n_0}} \left(\sum_{\frac{i}{N} \in A} \frac{1}{i} \right)$$

Let b_0 be the smallest value in A and $\lambda(A)$ the Lebesgue measure of A . Then

$$q^*(A) \leq \frac{n_0^2}{\rho_{n_0}} \frac{\rho_{\lfloor b_0 N \rfloor}}{\lfloor b_0 N \rfloor} N \lambda(A) + \frac{n_0}{\rho_{n_0}} - \frac{N \lambda(A)}{\lfloor b_0 N \rfloor} \frac{n_0^2}{\rho_{n_0}} \rightarrow 0 \quad \text{as } N \rightarrow \infty \quad \text{by (2.3.1).}$$

Consider now an arbitrary closed set $F \subset [0, 1]$ which does not contain $1 - \frac{1}{R_0}$. Then there exists an open neighborhood U of $1 - \frac{1}{R_0}$ such that $F \subset [0, 1] \setminus U$ and $[0, 1] \setminus U = A_1 \cup A_2$, where A_1 is a closed set on the left of $1 - \frac{1}{R_0}$ and A_2 is a closed set on the right of $1 - \frac{1}{R_0}$. Hence $q^*(F) \leq q^*(A_1) + q^*(A_2) \rightarrow 0$ as $N \rightarrow \infty$. At last, we observe that

$$\limsup_{n \rightarrow \infty} q^*(F) \leq \delta_{1 - \frac{1}{R_0}}(F) = \begin{cases} 1 & \text{,if } 1 - \frac{1}{R_0} \in F, \\ 0 & \text{,if } 1 - \frac{1}{R_0} \notin F. \end{cases}$$

From Portmanteau Theorem, we have $q^* \rightarrow \delta_{E_1}$ in distribution as $N \rightarrow \infty$. □

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