Stochastic Models for the Spread of HIV in a Mobile Heterosexual Population

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Abstract

An important factor in the dynamic transmission of HIV is the mobility of the population. We formulate various stochastic models for the spread of HIV in a heterosexual mobile population, under the assumptions of constant and varying population sizes. We also derive deterministic and diffusion analogues for these models, using a convenient rescaling technique, and analyze their stability conditions and equilibrium behavior. We illustrate the dynamic behavior of the models and their approximations via a range of numerical experiments.

Keywords: HIV/AIDS, Mobility, Multiple Patches, Epidemiology, Density Dependent Markov Process, Diffusion Approximation.

1 Introduction

One of the most urgent public-health problems in developing countries is the AIDS (Acquired Immune Deficiency Syndrome) epidemic, caused by the Human Immunodeficiency Virus (HIV). Since the first cases of AIDS were identified in 1981, the number of HIV infected people and AIDS deaths per year has continued to rise rapidly. In 2004, some 40 million people were living with HIV, which has killed over 20 million since 1981 and 3 million in 2003 alone [22]. The epidemic is not homogeneous within geographical regions. Some countries are more affected than others. Even at country level there are usually wide variations in infection levels between different provinces, states or districts, and between urban and rural areas. In reality, the national picture is made up of a series of epidemics with their own characteristics and dynamics.

The dynamic transmission of HIV is quite complex and there is no other human infection which has the same epidemiological characteristics with a similar mode of transmission. For instance, the incubation period after infection with HIV is known to be extremely long and is measured in years rather than days (such as in the case of measles, for example). During this period the individuals stay healthy and can unknowingly

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transmit the disease to others. In addition, although the disease is known as a sexually-transmitted disease, it is also passed on from infected mothers to their babies, and from sharing infected syringes, which is common among injecting drug users. All these factors have made it difficult to understand how this epidemic spreads in the population. The growth of movement among populations further increases the contact between individuals in different patches and, consequently, it might trigger more epidemics. Thus, the migration of people among subgroups has many significant consequences for the outcome of epidemic spread [19]. Indonesia in particular, as one of the most populous countries in the world, with a high population mobility among its regions [8], seems to have a high risk for the spread of the epidemic [22]. The number infected has increased sharply, and the prevalence among provinces varies widely.

Mathematical models based on the underlying transmission mechanism of HIV might help the medical and scientific community understand better how the disease spreads in the community. Even though the actual data needed for the models might not be accurate or even available, such modelling is still vital in investigating how changes in the various assumptions and parameter values affect the course of the epidemic [9]. Therefore, by developing such mathematical models, we can to some extent anticipate its spread in different populations and evaluate the potential effectiveness of different approaches for bringing the epidemic under control, and thus help to devise effective strategies to minimize the destruction caused by this epidemic.

Mathematical models for the spread of the HIV/AIDS epidemic have been studied extensively since the first cases were recognized in the late 80’s; see for example [6, 16, 15, 10, 11, 20, 21]. However, this area of study is still challenging, since so many different factors affect the transmission of HIV. Most of the articles have focused on only a single population of constant size, although some studies have stressed the importance of variable population size in epidemic dynamics [7, 15, 6]. In addition, many models have only focused on a single homosexual population [20], whereas in much of the world, heterosexual contact is the predominant mode of transmission [22]. Finally, the spatial aspect of the epidemic and, related with this, the mobility of the population, is often ignored. All these assumptions might limit the application of such models in describing the complex dynamics of the epidemic.

The purpose of this paper is to develop new mathematical models for the spread of HIV that incorporate factors such as mobility, heterosexual transmission and varying population size, which are crucial for countries such as Indonesia, with its many distinct regions. The models will be stochastic in nature, as opposed to the more common deterministic models. However, we will show that the more natural stochastic approach can be approximated well with the traditional deterministic approach, which can be analyzed in more detail, in particular with respect to equilibrium behavior. In addition we derive stochastic diffusion approximations, which show that the original process around the equilibrium can be approximated well by an Ornstein-Uhlenbeck process. Both the deterministic and diffusion approximations are derived using the theory of density dependent processes [12, 17].

Our models are motivated mostly by the work of [6] and [15], both of which formulate deterministic models of HIV spread in a heterogeneous population. They consider the female and male subpopulations separately (individuals are well-mixed only in their subpopulation), and assume that HIV transmission is possible only through sexual contact between female and male. There are some differences between the two models: [6]
assumes that the rate of new recruits of susceptibles (for both males and females) is constant, whereas in [15] this rate is assumed to be proportional to the total population, which varies in time. In [6] only males choose partners from the female subpopulation. Thus, susceptible males and females become infected at a rate which is proportional to the size of the total female population. On the other hand, [15] assumes also that females choose partners from the male subpopulation. Therefore, susceptible males are infected relative to the total female population and susceptible females become infected relative to the total male population. Consequently, the models [6] and [15] have slightly different formulations for the infection rate of susceptibles. Furthermore, both study the situation under the assumption of a varying population.

The rest of the paper is organized as follows. In Section 2, we describe the various stochastic models. We start with a single, constant (i.e., a closed system) or varying (i.e., an open system) population with a female and male subpopulation, and then look at the case of a multiple-patch population, incorporating the mobility of people. In Section 3, we present various results from Kurtz [12, 13] concerning density dependent processes. In particular, we review under what conditions, and in what manner, such a stochastic process converges to its deterministic and diffusion counterpart. In Section 4 we will use the results from Section 3 to study the dynamics of our stochastic models. This approach has been used recently in the study of epidemic models; see for example [5, 4]. Numerical experiments are presented in Section 5. Finally, in Section 6, we summarize our findings and give direction for future research.

## 2 Models

In this section we formulate various stochastic models for the spread of HIV in both a single population and in multiple populations, under the assumption of either a constant or varying population size.

### 2.1 Model with a Closed Single Population

We consider first a closed (constant) single heterosexual population of size $N$ in which all individuals, both females and males, are well mixed in the population. We assume, as in [6] and [15], that a susceptible female gets infected only by an infected male (via sexual contact) and, similarly, a susceptible male gets the infection only from an infected female. A single female or male selects her/his partner (of different sex) randomly from the whole population.

Let the random variables $S_F(t), I_F(t), S_M(t), I_M(t)$ and $A(t)$ represent the number of susceptible females, infected females, susceptible males, infected males, and the number of AIDS cases at time $t$, respectively. We assume that a susceptible female (male) will be infected by an infected male (female) at a rate that is proportional to the fraction of infected males (females):

$$
\lambda_F = \beta \frac{I_M(t)}{N} \quad \left(\lambda_M = \beta \frac{I_F(t)}{N}\right),
$$

where $\lambda_F$ and $\lambda_M$ are called the forces of infection (see also Remark 2.1). We assume that all individuals, including AIDS people, die at a natural death rate $\mu$. In addition, AIDS people also die from the disease, at rate $\delta$. All deaths are replaced (balanced) by births of susceptibles, at a proportion $\alpha$ for females and $(1 - \alpha)$ for males. Thus, the birth rates
for susceptible females and males are $B_F = \alpha (\mu N + \delta A)$ and $B_M = (1 - \alpha) (\mu N + \delta A)$, respectively. The infected individuals develop AIDS at rate $\gamma$. This situation can be viewed as a stochastic Susceptible-Infected-Removed (SIR) model; see for example [1]. The scheme is illustrated in Figure 1.

Figure 1: The scheme of the model. Susceptible females (males) are infected by infected males (females) via sexual contact only, indicated by the dashed lines.

**Remark 2.1 (Force of Infection)** The parameter $\beta$ is defined in [6] as the product of the contact rate $\kappa$ per unit time and the probability $p$ that a successive number of contacts leads to infection. The constants $\kappa$ and $p$ are given as follows: $\kappa = \frac{1}{T}$ and $p = 1 - (1 - h)^cT$, where $T$ is the time interval between two encounters with new partners, $c$ is the average number of sexual contacts between partners, and $h$ is the probability that one sexual contact between a susceptible and an infected individual leads to infection.

Consider the process $(X(t), t \geq 0)$, with

$$X(t) = \left(S_F(t), I_F(t), S_M(t), I_M(t)\right),$$

which takes values in $E \subset \mathbb{N}^4$, where $\mathbb{N}$ is the set of positive integers (including zero). We model $(X(t), t \geq 0)$ as a Continuous Time Markov Chain (CTMC) (see for example [18]), where the transition rates are chosen according to the description above. Thus, we assume that given the whole history $X(s), s \leq t$, a future state of the system, $X(t + \Delta t)$, depends only on the current state $X(t)$. In the formulation of the model we can ignore $A(t)$, since the population size, $N = S_F(t) + I_F(t) + S_M(t) + I_M(t) + A(t)$, is constant for all $t$. If one is interested in the number of AIDS cases, one can find it from $A(t) = N - S_F(t) - I_F(t) - S_M(t) - I_M(t)$.

**Transition Rates**

We now have a closer look at the transition rates of the CTMC $(X(t), t \geq 0)$. In a small time interval $\Delta t$ we assume that one of the following events occurs: (1) a new susceptible female enters the group of single females, (2) a susceptible female gets infected, (3) a susceptible female dies, (4) an infected female is removed (develops AIDS or dies), (5) a new susceptible male enters the group of males, (6) a susceptible male becomes infected,
(7) a susceptible male dies, or (8) an infected male is removed (due to AIDS or natural death). The other possible events are ignored.

Suppose that the system at time $t$ is in state $k = (s_F, i_F, s_M, i_M)$, $k \in E$. The transition scheme of the process is described in Figure 2 (ignoring boundary effects).

Figure 2: The transition scheme from state $k$ to other states, where $e_i$ represents the $i$-th unit row vector in $\mathbb{N}^4$.

Thus, in any small time interval of length $\Delta t$ the process jumps from state $k$ to $k+l$ with probability $q_{k,k+l}\Delta t$, where the rates $q_{k,k+l}$ follow from the formulation above, and are given by

$$q_{k,k+l} = \begin{cases} 
\alpha (\mu N + \delta A), & l = e_1, \\
\beta \frac{1}{N} s_F, & l = -e_1 + e_2, \\
\mu s_F, & l = -e_1, \\
(\mu + \gamma) i_F, & l = -e_2, \\
(1 - \alpha) (\mu N + \delta A), & l = e_3, \\
\beta \frac{1}{N} s_M, & l = -e_3 + e_4, \\
\mu s_M, & l = -e_3, \\
(\mu + \gamma) i_M, & l = -e_4, \\
0, & \text{otherwise.}
\end{cases} \tag{2}$$

Note that the process $(X(t), t \geq 0)$ has an absorbing state 0, and once the process reaches a state where no infection is present (i.e., $I_F(t) = I_M(t) = 0$), it will remain infection free forever, and will eventually end up in 0.

### 2.2 Model with an Open Single Population

In this model, we consider a population size $N(t)$ which varies with time. We have now a slightly different interpretation for the population size. In the constant population case, we include AIDS people in the total population, which makes it possible to formulate the situation as a type of SIR model. With a varying population size, both the female and male subpopulation are simply divided into two groups of susceptibles and infectives, as in the case of the standard SI model. We no longer explicitly consider AIDS people as a part of the population, that is, $N(t) = S_F(t) + I_F(t) + S_M(t) + I_M(t)$. However, if one is interested in the number of AIDS cases at time $t$, $A(t)$, one can find it from the number of infectives who eventually develop AIDS, that is, $A(t) = \int_0^t \gamma (I_F(s) + I_M(s)) ds$. We
assume as in [6] that the number of new susceptibles of both females and males arrive into the system at a constant rate $B_F = B_M = B$ (that is, according to a Poisson process with rate $B$). Thus, the transition scheme is similar to the previous model, but the transition rates of the process are given as follows:

$$q_{k,k+1} = \begin{cases} 
B, & l = e_1, \\
\beta \frac{i_F(t)}{N(t)} s_F(t), & l = -e_1 + e_2, \\
\mu s_F(t), & l = -e_1, \\
(\mu + \gamma) i_F(t), & l = -e_2, \\
B, & l = e_3, \\
\beta \frac{i_F(t)}{N(t)} s_M(t), & l = -e_3 + e_4, \\
\mu s_M(t), & l = -e_3, \\
(\mu + \gamma) i_M(t), & l = -e_4, \\
0, & \text{otherwise},
\end{cases} \quad (3)$$

Similar to the previous case, this process has an absorbing state $0$, and once the process reaches the state with no infected individuals, it will remain infection free and will eventually go to $0$.

### 2.3 Multiple Patch Models with Varying Population Size

In order to incorporate mobility effects, we consider individuals residing in many patches or regions. The population sizes of the patches need not be equal and may vary with time. Individuals may get the infection or transmit the disease during their visit to other patches. People might visit the same patches several times and spend a varying length of time in the visited patches. Suppose $v_{rj}$ denotes the immigration rate of individuals from patch $R_r$ to $R_j$. The following diagram illustrates the mobility of people among patches.

![Diagram of mobility among patches](image)

Figure 3: The scheme for the mobility of people among patches. The size of a circle corresponding to the total population size in that patch.
We formulate two types of model, assuming that each patch (as in the previous model for a single population) contains a female and a male subpopulation. In the first type of model, we assume that individuals do not actually leave their home patches but that there is an infection force from other patches. In the second type of model, we assume that individuals do leave their home patches and spend a considerable amount of time in the visited patches before they return. They might emigrate and stay permanently in a visited patch. We call the first model the model with a force of infection and the second model the model with actual mobility. We consider both constant and varying population sizes.

In both models there are $K$ patches and each patch contains a female and male subpopulation. Let $S_F^r(t), I_F^r(t), S_M^r(t), I_M^r(t)$ represent the number of susceptible (infected) females and the number of susceptible (infected) males at time $t \geq 0$ in patch $r$, $r = 1, \ldots, K$, respectively. Define a CTMC $(X(t), t \geq 0)$ with

$$X(t) = \left( S_F^{(1)}(t), I_F^{(1)}(t), S_M^{(1)}(t), I_M^{(1)}(t), \ldots, S_F^r(t), I_F^r(t), S_M^r(t), I_M^r(t), \ldots,
S_M^{(K)}(t), I_F^{(K)}(t), S_M^{(K)}(t), I_M^{(K)}(t) \right).$$

The state of this process is a $4K$-dimensional row vector with elements in $\mathbb{N}$, that is, the state is an element of $\mathbb{N}^{4K}$.

**Model with a Force of Infection**

To formulate the first model, let $\beta_{rj}$ denote the infection rate of susceptibles in patch $r$ by infected individuals from patch $j$ and $\beta_r = \beta_{rr}$ the infection rate within patch $r$. Then, the transition rates for this situation ($r = 1, 2, \ldots, K$) are given as follows: For a constant population size

$$q_{k,k+l} = \begin{cases} 
\alpha (\mu N^{(r)} + \delta A^{(r)}), & l = e_{4r-3}, \\
\sum_{j=1}^K \beta_{rj} \frac{s_F^{(r)}}{N^{(r)}} i_M^{(j)}, & l = -e_{4r-3} + e_{4r-2}, \\
\mu s_F^{(r)}, & l = -e_{4r-3}, \\
(\mu + \gamma) i_F^{(r)}, & l = -e_{4r-2}, \\
(1 - \alpha) (\mu N^{(r)} + \delta A^{(r)}), & l = e_{4r-1}, \\
\sum_{j=1}^K \beta_{rj} \frac{s_M^{(r)}}{N^{(r)}} i_F^{(j)}, & l = -e_{4r-1} + e_{4r}, \\
\mu s_M^{(r)}, & l = -e_{4r-1}, \\
(\mu + \gamma) i_M^{(r)}, & l = -e_{4r}, \\
0, & \text{otherwise},
\end{cases}$$

with a constant $N^{(r)} = S_F^{(r)}(t) + I_F^{(r)}(t) + S_M^{(r)}(t) + I_M^{(r)}(t) + A^{(r)}(t)$, and $e_m$ the $m$-th unit vector in $\mathbb{N}^{4K}$. For the case of varying population size
\[ q_{k,k+1} = \begin{cases} 
B, & l = e_{4r-3}, \\
\sum_{j=1}^{K} \beta_{rj} \frac{s^{(r)}_{F}(s)}{N^{(r)}_{F}(t)} i^{(j)}_{M}, & l = -e_{4r-3} + e_{4r-2}, \\
\mu s^{(r)}_{F}, & l = -e_{4r-3}, \\
(\mu + \gamma) i^{(r)}_{F}, & l = -e_{4r-2}, \\
B, & l = e_{4r-1}, \\
\sum_{j=1}^{K} \beta_{rj} \frac{s^{(r)}_{M}(s)}{N^{(r)}_{M}(t)} i^{(j)}_{F}, & l = -e_{4r-1} + e_{4r}, \\
\mu s^{(r)}_{M}, & l = -e_{4r-1}, \\
(\mu + \gamma) i^{(r)}_{M}, & l = -e_{4r}, \\
0, & \text{otherwise,} 
\end{cases} \]  

with a varying size \( N^{(r)}(t) = S^{(r)}_{F}(t) + I^{(r)}_{F}(t) + S^{(r)}_{M}(t) + I^{(r)}_{M}(t) \). Note that with these notations, if there is only one patch \((r,j=1)\), the transition rates have the same form as those in the previous models for an open and closed single population.

*Model with Actual Mobility*

In this model, we assume that people physically visit other patches. During their visit the infected individuals can transmit the disease to the susceptibles in the visited patches, and susceptibles visiting a patch might get the infection from an infected individuals in a visited patch. This situation is modelled by considering people moving from one patch to another without any forces of infection from outside of patch; however we do have a force of infection within patch. The force of infection within a patch may differ from patch to patch. We consider for this situation a varying population size only, since it is more realistic. The transition rates of the process are given by
3 Density Dependence and Diffusion Approximation

To study the dynamic behavior of the stochastic models formulated previously, we present some results developed by Kurtz [12, 13]. These results also justify to some extent the use of deterministic models, which is quite common in modelling the epidemic spread, whereas the real situation is in fact a random processes.

**Definition 3.1** A one-parameter family of CTMCs \((X^{(N)}(t), t \geq 0)\) with state space \(E \subset \mathbb{Z}^d\) and transition rates \((q_{ij})\) is called density dependent if there exists a continuous function \(f(x, l) : \mathbb{R}^d \times \mathbb{Z}^d \to \mathbb{R}\), such that

\[
q_{k,k+l} = \begin{cases} 
  B, & l = e_{4r-3}, \\
  \beta_l s^{(r)}_{N(l)} i^{(r)}_M, & l = -e_{4r-3} + e_{4r-2}, \\
  \mu s^{(r)}_M, & l = -e_{4r-3}, \\
  \rho_{rj} U^{(r)}_{N(l)} s^{(r)}_M, & l = -e_{4r-3} + e_{4j-3}, \\
  \rho_{rj} U^{(r)}_{N(l)} i^{(r)}_M, & l = -e_{4r-2} + e_{4j-2}, \\
  (\mu + \gamma) i^{(r)}_M, & l = -e_{4r-2}, \\
  B, & l = e_{4r-1}, \\
  \beta_l s^{(r)}_{N(l)} i^{(r)}_M, & l = -e_{4r-1} + e_{4r}, \\
  \mu s^{(r)}_M, & l = -e_{4r-1}, \\
  \rho_{rj} U^{(r)}_{N(l)} s^{(r)}_M, & l = -e_{4r-1} + e_{4j-1}, \\
  \rho_{rj} U^{(r)}_{N(l)} i^{(r)}_M, & l = -e_{4r} + e_{4j}, \\
  (\mu + \gamma) i^{(r)}_M, & l = -e_{4r}, \\
  0, & \text{otherwise}.
\]

Suppose \((X(t) = X^{(N)}, t \geq 0)\) is a density dependent process (from now on we drop the superscript \(N\)). By rescaling with \(N\) we obtain another a CTMC \((X_N(t), t \geq 0)\) called the density process. Thus,

\[
X_N(t) = \frac{1}{N} X(t).
\]

It turns out that under certain mild conditions \((X_N(t))\) converges to a deterministic process that is the solution of a system of first order ODEs that is governed by the following function \(F\):

\[
F(x) = \sum_{l \in \mathbb{Z}^d} l f(x, l).
\]
Theorem 3.1 (Deterministic Approximation). Suppose that there exists (1) an open set \(E \subset \mathbb{R}^d\) where the function \(f(x,l)\) is bounded for each \(l\) and (2) the function \(F\) is Lipschitz continuous on \(E\). Then, for every trajectory \((x(\tau,x_0), \tau \geq 0)\) satisfying the following system of ODEs

\[
\frac{d}{d\tau} x(\tau,x_0) = F(x(\tau,x_0)),
\]
\[
x(0,x_0) = x_0, \quad x(\tau,x_0) \in E, \quad 0 \leq \tau \leq t,
\]

\[
\lim_{N \to \infty} X_N(0) = x_0 \text{ implies for every } \delta > 0,
\]
\[
\lim_{N \to \infty} \mathbb{P} \left( \sup_{\tau \leq t} \left| X_N(\tau) - x(\tau,x_0) \right| > \delta \right) = 0, \text{ for every } t \geq 0.
\]

The proof is given in [12].

Theorem 3.1 implies that the process \((X_N(t))\) can be approximated to first order by a deterministic process, for large \(N\). If the density process \((X_N(t))\) is initially closed to \(x_0\), it will tend to stay closed to the trajectory \((x(\tau,x_0), \tau \leq t)\) in some appropriate time-interval, subject to small random oscillations about the path.

It is even possible to describe the behavior of the random fluctuations of the density process \((X_N(t),t \geq 0)\) around its deterministic approximation. This is done via a diffusion approximation, which is governed by two \(d \times d\) matrices \(G = G(x) = (g_{ij}(x))\) and \(H = H(x) = (h_{ij}(x))\) defined by

\[
g_{ij}(x) = \sum_{i=1}^{d} \sum_{j=1}^{d} l_i l_j f(x,l), \text{ where } l = (l_1, \ldots, l_d) \in \mathbb{Z}^d,
\]

and

\[
h_{jk}(x) = \frac{\partial F_j(x)}{\partial x_k}.
\]

Note that \(H(x)\) is simply the Jacobian matrix of \(F(x)\).

Theorem 3.2 (Diffusion Approximation). Suppose \(F(x)\) is bounded and Lipschitz continuous on \(E\). Suppose \(G(x)\) is also bounded and uniformly continuous on \(E\). Suppose that

\[
\lim_{N \to \infty} \sqrt{N} \left( X_N(0) - x_0 \right) = z.
\]

Then, as \(N \to \infty\), the family of processes \((Z_N(t),t \geq 0)\), defined by

\[
Z_N(t) = \sqrt{N} \left( X_N(t) - x(t,x_0) \right), \quad 0 \leq t \leq s,
\]

converges weakly in \(D[0,t]\) to a Gaussian diffusion \((Z(t),t \geq 0)\) with initial value \(Z(0) = z\) and with characteristic function \(\mathbb{E} e^{i\theta Z(t)} \equiv \psi(t,\theta)\) that satisfies

\[
\frac{\partial \psi}{\partial \tau}(t,\theta) = -\frac{1}{2} \sum_{j=1}^{d} \sum_{k=1}^{d} \theta_j \theta_k g_{jk}(x(t,x_0)) \psi(t,\theta) + \sum_{j=1}^{d} \sum_{k=1}^{d} \theta_j h_{jk}(x(t,x_0)) \frac{\partial \psi}{\partial \theta_k}(t,\theta). \quad (8)
\]
Only in special cases can one obtain an explicit expression for the characteristic function. However, using (8) one can easily determine the mean vector and covariance matrix of $Z(t)$. In particular, the mean vector of $Z(t)$ is given by

$$
\mu = \mathbb{E}Z(t) = M(t) z,
$$

where $M(t) = e^{\int_0^t H_s \, ds}$, that is, the unique solution to

$$
\frac{dM(t)}{dt} = H(t) M(t), \quad \text{with} \quad M(0) = I. \tag{10}
$$

On the other hand, the covariance matrix, $\Sigma(t)$, of $Z(t)$ is given by

$$
\Sigma(t) = M(t) \left( \int_0^t M(s)^{-1} G(x(s,x_0)) \left( M(s)^{-1} \right)^T ds \right) M(t)^T,
$$

which is the unique solution to

$$
\frac{d\Sigma(t)}{dt} = H(t) \Sigma(t) + \Sigma(t) H(t)^T + G(x(t,x_0)), \quad \text{with} \quad \Sigma_0 = \Sigma(0) = 0. \tag{11}
$$

If $X_N(0)$ and $x_0$ are chosen to be equal to an equilibrium point $x^*$ of the ODE system in Theorem 3.1, one can be far more precise in specifying the approximating diffusion. Namely, in that case $(Z(t))$ is an Ornstein-Uhlenbeck (OU) process (i.e., a stationary, Gaussian, and Markovian process), with local drift matrix $H(x^*)$ and local covariance matrix $G = G(x^*)$. In particular, $Z(t)$ has a Gaussian/normal distribution with zero mean and a covariance matrix $\Sigma$ which is given by the solution of (12) with $\frac{d\Sigma}{dt} = 0$; see [3]. It follows that $X_N(t)$ has an approximate Gaussian distribution with

$$
\text{Var}(X_N(t)) \approx \frac{1}{N} \Sigma,
$$

and the mean, obtained by setting $z = \sqrt{N}(X_N(0) - x_0)$, is given by

$$
\mathbb{E}X_N(t) \approx x^*. \tag{14}
$$

Therefore, we can approximate the equilibrium distribution of the process $(X(t), t \geq 0)$ by a multivariate normal distribution with mean vector $\mu = N X_N^*$ and covariance matrix $N\Sigma$. For more general results density dependent processes we refer the reader to [2] and [17].

4 Analysis

In this section we analyze the stochastic models formulated in Section 2 by using the results in Section 3, and predict their dynamic behavior via their deterministic and diffusion counterparts.
4.1 Closed Single Population

To study the behavior of \((X(t), t \geq 0)\) with the transition rates \(q_{k,k+l}\) as given in (2), we show that it is a density-dependent Markov process, parameterized by the population size \(N\). By scaling with \(N\), we obtain a scaled Markov process \((X_N(t), t \geq 0)\) with \(X_N(t) = \frac{1}{N} X(t) = \frac{1}{N} (S_F(t), I_F(t), S_M(t), I_M(t))\). Define the function \(f\) as follows

\[
f(x, l) = \begin{cases} 
\alpha (\mu + \delta z), & \text{if } l = e_1, \\
\beta y_2 x_1, & \text{if } l = -e_1 + e_2, \\
\mu x_1, & \text{if } l = -e_1, \\
(\mu + \gamma) x_2, & \text{if } l = -e_2, \\
(1 - \alpha) (\mu + \delta z), & \text{if } l = e_3, \\
\beta x_2 y_1, & \text{if } l = -e_3 + e_4, \\
\mu y_1, & \text{if } l = -e_3, \\
(\mu + \gamma) y_2, & \text{if } l = -e_4, \\
0, & \text{otherwise},
\end{cases}
\]

with \(x = \frac{k}{N} = (x_1, x_2, y_1, y_2)\) and \(z = 1 - (x_1 + x_2 + y_1 + y_2)\). Then, one can check that \(q_{k,k+l} = N f(x, l)\). Therefore, \((X(t), t \geq 0)\) is, by Definition 3.1, a density dependent process. The corresponding function \(F\) is derived from (15) and (7):

\[
F(x) = \begin{pmatrix} 
\alpha (\mu + \delta z) - \beta y_2 x_1 - \mu x_1 \\
\beta y_2 x_1 - (\mu + \gamma) x_2 \\
(1 - \alpha) (\mu + \delta z) - \beta x_2 y_1 - \mu y_1 \\
\beta x_2 y_1 - (\mu + \gamma) y_2
\end{pmatrix}.
\]

The function \(F\) is Lipschitz continuous. So, the dynamic behavior of the process \((X_N(t), t \geq 0)\), see Theorem 3.1, can be approximated by a system of first order ODEs

\[
x'(t) = F(x),
\]

as \(N \to \infty\).

**Equilibria and Their Stability**

From now on we assume for simplicity that \(\alpha = \frac{1}{2}\) (i.e., females and males enter the population in equal proportion). Solving \(F(X) = 0\) in (16) gives three equilibrium points, two of which fall in the positive quadrant: the disease-free equilibrium and the positive endemic equilibrium. Let \(X^* = (x_1^*, x_2^*, y_1^*, y_2^*)\) denote a generic equilibrium of the system (17).

**Disease-free Equilibrium**

The disease-free equilibrium is given by

\[
X_1^* = (x_1^* = \frac{1}{2}, x_2^* = 0, y_1^* = \frac{1}{2}, y_2^* = 0).
\]

In the absence of the disease \((x_2 = y_2 = 0)\), the fraction of susceptibles of both females and males will reach a constant number: \(x_1 = x_1^* = \frac{1}{2}\) and \(y_1 = y_1^* = \frac{1}{2}\), respectively. We are interested in whether in the early epidemic spread (after a few infected people are
present) the number of infectives will grow or die out. The following result sheds some light onto this. Here, the basic quantity $R_0$ serves the same role as the basic reproduction rate in epidemiology.

**Theorem 4.1** Let $R_0 = \frac{\beta}{2(\mu + \gamma)}$. The disease-free equilibrium $X_1^*$ in (18) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

**Proof.** The Jacobian matrix of (16) is given by

$$
H(x) = \begin{pmatrix}
-\frac{\delta}{2} - \beta y_2 - \mu & -\frac{\delta}{2} & -\frac{\delta}{2} & -\frac{\delta}{2} - \beta x_1 \\
\beta y_2 & -(\mu + \gamma) & 0 & 0 \\
-\frac{\delta}{2} & -\frac{\delta}{2} - \beta y_1 & -\frac{\delta}{2} - \beta x_2 - \mu & -\frac{\delta}{2} \\
0 & \beta y_1 & \beta x_2 & -(\mu + \gamma)
\end{pmatrix}.
$$

(19)

Evaluating (19) at $X_1^*$ yields

$$
H(X_1^*) = \begin{pmatrix}
-\frac{\delta}{2} - \mu & -\frac{\delta}{2} & -\frac{\delta}{2} & -\frac{\delta}{2} \\
0 & -(\mu + \gamma) & 0 & 0 \\
-\frac{\delta}{2} & -\frac{\delta}{2} - \beta y_1 & -\frac{\delta}{2} - \mu & -\frac{\delta}{2} \\
0 & \beta y_1 & \beta x_2 & -(\mu + \gamma)
\end{pmatrix}.
$$

(20)

If the real parts of all the eigenvalues of this matrix are negative, then the disease-free steady-state is locally asymptotically stable. The matrix (20) has four eigenvalues

$$
r_1 = -\mu, \quad r_2 = -(\mu + \delta), \quad r_3 = -(\mu + \gamma) - \frac{\beta}{2}, \quad r_4 = -(\mu + \gamma) + \frac{\beta}{2}.
$$

(21)

Therefore, the stability of this equilibrium is determined by the last eigenvalue $r_4$, since the other eigenvalues are always negative for the non-negative parameters $\beta, \gamma, \mu, \delta$. Thus, the disease-free equilibrium is stable if and only if $r_4 = -(\mu + \gamma) + \frac{\beta}{2} < 0$ ($R_0 < 1$) and it is unstable if and only if $r_4 = -(\mu + \gamma) + \frac{\beta}{2} > 0$ ($R_0 > 1$).

**Positive Endemic Equilibrium**

The endemic equilibrium is given by

$$
X_2^* = (x_1^* = \rho, x_2^* = \eta, y_1^* = \rho, y_2^* = \eta),
$$

(22)

where $\eta = (1 - 2\rho)\Delta = (1 - \frac{1}{R_0})\Delta$, with $\rho = \frac{\mu + \gamma}{\beta}$ and $\Delta = \frac{\mu + \delta}{2\mu + \gamma + \delta}$. It is clear from (22) that the system (17) has a positive-endemic equilibrium if and only if $(1 - 2\rho) > 0$ (or equivalently $R_0 > 1$). The Jacobian matrix for the positive-endemic equilibrium is

$$
H(X_2^*) = \begin{pmatrix}
-\frac{\delta}{2} - \beta \eta - \mu & -\beta \eta & -\frac{\delta}{2} & 0 \\
-\frac{\delta}{2} & -\beta \rho & 0 & 0 \\
-\frac{\delta}{2} - \beta \eta - \mu & -\beta \eta & \frac{\beta}{2} & 0 \\
0 & \frac{\beta}{2} & 0 & -\beta \rho
\end{pmatrix}.
$$

(23)
This matrix has four eigenvalues

\[
\begin{align*}
    r_1 &= \frac{1}{2}(B_1 + \sqrt{\Theta_1}), \\
    r_2 &= \frac{1}{2}(B_1 - \sqrt{\Theta_1}), \\
    r_3 &= \frac{1}{2}(B_2 + \sqrt{\Theta_2}), \\
    r_4 &= \frac{1}{2}(B_2 - \sqrt{\Theta_2}),
\end{align*}
\]

where

\[
\begin{align*}
    B_1 &= -\beta \eta - \mu - 2\beta \rho, \\
    B_2 &= -\beta \eta - \mu - \delta, \\
    \Theta_1 &= 4\beta^2 \Delta^2 \rho^2 - 4\beta^2 \Delta^2 \rho - 4\beta \Delta \rho \mu + \beta^2 \Delta^2 + 2\beta \Delta \mu + \mu^2 - 4\mu \beta \rho + 4\beta^2 \rho^2, \\
    \Theta_2 &= 4\beta^2 \Delta^2 \rho^2 - 4\beta \Delta \rho \mu - 4\beta^2 \Delta^2 \rho + 4\delta \beta \Delta \rho + \mu^2 + 2\beta \Delta \mu + 2\delta \mu + \beta^2 \Delta^2 \\
    &\quad - 2\delta \beta \Delta + \delta^2 - 4\beta^2 \Delta \rho + 8\beta^2 \Delta \rho^2.
\end{align*}
\]

If \( R_0 > 1 \) (or \( 2\rho < 1 \)), it follows that \( B_1, B_2 < 0 \). Therefore, \( \text{Re}(r_2) \) and \( \text{Re}(r_4) \) are always negative. We need to show that for some \( \beta, \mu, \gamma, \delta > 0 \), \( \text{Re}(r_1) \) and \( \text{Re}(r_3) \) are also negative. If \( \Theta_1 \leq 0 \) and \( \Theta_2 \leq 0 \), \( \text{Re}(r_1) = B_1 < 0 \) and \( \text{Re}(r_3) = B_2 < 0 \). Now, suppose that \( \Theta_1 > 0 \) and \( \Theta_2 > 0 \). Let \( C_1 = -B_1 > 0 \) and let \( C_2 = -B_2 \). Then, we obtain

\[
\Theta_1 - C_1^2 = -8\mu \beta \rho + 4\beta^2 \Delta \rho (2\rho - 1) < 0.
\]

and

\[
\Theta_2 - C_2^2 = 4\delta \beta \Delta (2\rho - 1) + 4\beta^2 \Delta \rho (2\rho - 1) < 0.
\]

From (24), we have \( \Theta_1 - C_1^2 < 0 \iff 0 < \Theta_1 < C_1^2 \iff 0 < \sqrt{\Theta_1} < C_1 \). Thus, \( -C_1 + \sqrt{\Theta_1} = B_1 + \sqrt{\Theta_1} < 0 \), which implies \( \text{Re}(r_1) < 0 \). From (25), we have \( \Theta_2 - C_2^2 < 0 \iff 0 < \Theta_2 < C_2^2 \iff 0 < \sqrt{\Theta_2} < C_2 \). Thus, \( -C_2 + \sqrt{\Theta_2} = B_2 + \sqrt{\Theta_2} < 0 \), which implies \( \text{Re}(r_3) < 0 \). We summarize these findings in the following theorem.

**Theorem 4.2** The endemic equilibrium \( X_2^* \) exists iff \( R_0 > 1 \), and it is locally asymptotically stable.

**Diffusion Approximation**

The approximating OU process \( (Z(t), t \geq 0) \) around the equilibrium point \( X_2^* \) has local drift matrix \( H(X_2^*) \) in (23), and local covariance matrix \( G(X_2^*) \), defined in Theorem 3.2, as follows

\[
G(X_2^*) = \begin{pmatrix}
g_{11} & g_{12} & 0 & 0 \\
g_{21} & g_{22} & 0 & 0 \\
0 & 0 & g_{33} & g_{34} \\
0 & 0 & g_{43} & g_{44}
\end{pmatrix},
\]

where

\[
\begin{align*}
g_{11} &= \frac{1}{2}(\mu + \delta A) + \beta x_1^* y_2^* + \mu x_1^*, \\
g_{12} &= g_{21} = \beta x_1^* y_2^*, \\
g_{22} &= \beta x_1^* y_2^* + (\mu + \gamma) x_2^*, \\
g_{33} &= \frac{1}{2}(\mu + \delta A) + \beta x_2^* y_1^* + \mu y_1^*, \\
g_{34} &= g_{43} = \beta x_2^* y_1^*, \\
g_{44} &= \beta x_2^* y_1^* + (\mu + \gamma) y_2^*.
\end{align*}
\]
Therefore, we can approximate the equilibrium distribution of the process \((X(t), t \geq 0)\) by a multivariate normal distribution, see (14) and (13), with mean \(\mu = NX_2^*\) and covariance matrix \(N\Sigma\).

### 4.2 Open Single Population

To derive a deterministic analogue, as in the previous model, we show that the process \((X(t), t \geq 0)\) with the transition rates \(q_{k,k+\ell}\) as given in (3) is a density-dependent Markov process parameterized by \(V = \frac{x}{\mu}\). We will see shortly that this constant corresponds to the total population size in the disease-free equilibrium. Define \(x = \frac{X}{X^*} = (x_1(t), x_2(t), y_1(t), y_2(t))\). Then, we can write

\[
q_{k,k+\ell} = V f(x, l),
\]

where \(f(x, l)\) is given by

\[
f(x, l) = \begin{cases} 
\frac{\mu}{2}, & l = e_1, \\
\beta \frac{v}{v_0} x_1, & l = -e_1 + e_2, \\
\mu x_1, & l = -e_1, \\
(\mu + \gamma) x_2, & l = -e_2, \\
\frac{\mu}{2}, & l = e_3, \\
\beta \frac{v}{v_0} y_1, & l = -e_3 + e_4, \\
\mu y_1, & l = -e_3, \\
(\mu + \gamma) y_2, & l = -e_4, \\
0, & \text{otherwise},
\end{cases}
\]

with \(v = x_1 + x_2 + y_1 + y_2\). Therefore, the process \((X(t), t \geq 0)\) is a density dependent Markov process. As the parameter \(V \rightarrow \infty\), by Theorem 3.1, the dynamic behavior of the scaled Markov process \((X_V(t), t \geq 0)\) can be approximated by a system of first order ODEs \(x' = F(x)\), with \(F(x)\) defined as follows:

\[
F(x) = \begin{pmatrix}
\frac{\mu}{2} - \beta \frac{v}{v_0} x_1 - \mu x_1 \\
\beta \frac{v}{v_0} x_1 - (\mu + \gamma) x_2 \\
\frac{\mu}{2} - \beta \frac{v}{v_0} y_1 - \mu y_1 \\
\beta \frac{v}{v_0} y_1 - (\mu + \gamma) y_2
\end{pmatrix}.
\]

Again, we examine the dynamic behavior of the deterministic model around its equilibrium points.

### Equilibrium Points and Analysis

This system also has two equilibrium points: the disease-free and the endemic equilibrium. As in the previous model, the disease-free equilibrium is

\[
X_1^* = \left( x_1^* = \frac{1}{2}, x_2^* = 0, y_1^* = \frac{1}{2}, y_2^* = 0 \right).
\]

The Jacobian matrix of (28) is in the form

\[
H(X_1^*) = \begin{pmatrix}
\Lambda - \mu & \Lambda - \Theta & \Lambda & \Psi + \Lambda \\
-\Lambda & -\Lambda + \Theta - \mu - \gamma & \Psi - \Lambda & -\Lambda \\
\Lambda & \Lambda - \Theta & -\Psi + \Lambda - \mu & \Lambda \\
-\Lambda & -\Lambda + \Theta & \Psi - \Lambda & -\Lambda - \mu - \gamma
\end{pmatrix}.
\]
with \( \Lambda = \frac{\beta y}{\mu} \), \( \Theta = \frac{\beta y}{\mu} \) and \( \Psi = \frac{\beta y}{\mu} \). Evaluated at the disease-free equilibrium (29), we obtain

\[
H(X_1^*) = \begin{pmatrix}
-\mu & -\frac{\beta}{2} & 0 & 0 \\
0 & \frac{\beta}{2} - \mu - \gamma & 0 & 0 \\
0 & -\frac{\beta}{2} & -\mu & 0 \\
0 & \frac{\beta}{2} & 0 & -\mu - \gamma
\end{pmatrix}.
\] (31)

This matrix (31) has four eigenvalues (two of which are equal)

\[
r_1 = r_2 = -\mu, \quad r_3 = \frac{1}{2} \beta - \mu - \gamma, \quad \text{and} \quad r_4 = -\mu - \gamma.
\] (32)

Thus, the stability of this equilibrium is determined by \( r_3 \), since the other eigenvalues are always negative for the non-negative parameters \( \beta, \gamma, \mu, \delta \). Hence, the disease-free equilibrium is stable if and only if \( \frac{1}{2} \beta - \mu - \gamma < 0 \) \( (R_0 = \frac{\beta}{2(\mu + \gamma)} < 1) \) and it is unstable if and only if \( r_3 = \frac{1}{2} \beta - \mu - \gamma > 0 \) \( (R_0 > 1) \).

Next, we analyze the endemic equilibrium. The endemic equilibrium is of the form

\[
X_2^* = \left( x_1^* = \xi_1, x_2^* = \xi_2, y_1^* = \xi_1, y_2^* = \xi_2 \right),
\] (33)

where \( \xi_1 = \frac{\mu}{\beta - 2 \gamma} \), \( \xi_2 = \frac{\mu \beta (1 - 2 \rho)}{2 \rho \beta (\beta - 2 \gamma)} \) and \( \rho = \frac{\mu + \gamma}{\beta} \). So, a positive endemic equilibrium occurs if \( (1 - 2 \rho) > 0 \), that is, \( R_0 > 1 \). The Jacobian matrix evaluated around this positive endemic equilibrium \( X_2^* \) has four eigenvalues:

\[
r_1 = -\mu, \quad r_2 = -\mu - \gamma, \quad r_3 = \frac{1}{4 \beta} \left( B + \sqrt{\Theta} \right), \quad r_4 = \frac{1}{4 \beta} \left( B - \sqrt{\Theta} \right),
\] (34)

with

\[
B = \beta (2 \gamma - \beta), \\
\Theta = 36 \gamma^2 \beta^2 - 12 \beta^3 \gamma + \beta^4 - 64 \mu \gamma^2 \beta - 32 \mu^2 \gamma \beta + 48 \mu \gamma \beta^2 - 32 \gamma^3 \beta + 16 \mu^2 \beta^2 - 8 \mu \beta^3.
\]

Since \( R_0 > 1 \) \( \iff \beta > 2 (\mu + \gamma) > 2 \gamma \), we have \( B < 0 \). Let \( C = -B > 0 \), then

\[
\Theta - C^2 = 32 \gamma^2 \beta^2 - 8 \beta^3 \gamma - 64 \mu \gamma^2 \beta - 32 \mu^2 \gamma \beta + 48 \mu \gamma \beta^2 + 48 \mu \gamma \beta^2 - 32 \gamma^3 \beta + 16 \mu^2 \beta^2 - 8 \mu \beta^3
\]

\[
= 8 \mu \beta^2 (2 \gamma + 2 \mu - \beta) - 8 \gamma \beta (2 \gamma + 2 \mu - \beta)^2.
\] (35)

Since \( R_0 > 1 \), that is, \( 2(\mu + \gamma) - \beta < 0 \) (for a positive-endemic equilibrium), where \( \Theta - C^2 < 0 \). Therefore, \( -C + \sqrt{\Theta} = B + \sqrt{\Theta} < 0 \), which implies \( \text{Re}(r_3) < 0 \). We summarize these results in the following theorem.

**Theorem 4.3** The disease-free equilibrium \( X_1^* \) (29) is locally asymptotically stable if \( R_0 < 1 \) and unstable if \( R_0 > 1 \). A stable positive endemic equilibrium \( X_2^* \) (5) exists iff \( R_0 > 1 \).

Thus both the open and closed population models, under the assumption of both constant and variable population size, have the same stability conditions: the disease-free equilibrium is stable if \( R_0 < 1 \), otherwise, it is unstable, and the endemic equilibrium occurs when \( R_0 > 1 \) and it is stable. The differences are only in the size of the endemic equilibrium and the eigenvalues of the corresponding Jacobian matrix.

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4.3 Multiple Patch Models

To study the dynamic behaviour of the multiple patch models presented in Section 2, we also apply the deterministic and diffusion approach as in the case of a single population. We construct a density Markov process by scaling with a certain parameter, and derive a deterministic model to approximate the scaled process. The deterministic analogues of those two multiple patch models are given next.

Model with a Force of Infection

For the multiple patch model with constant population size; if all patches have equal size $N$, we can use this parameter as a scale factor for all random variables in the process. However, for the case where the patches have unequal size, all random variables are scaled by the total population size $N = \sum_{r=1}^{R} N^{(r)}$ and we define an extra constant $c^{(r)} = \frac{N^{(r)}}{N}$ for each $r$. Thus, one can obtain $q_{k,k+1} = N f(x,l), \quad r = 1, \ldots, K$ where $f$ is given as follows

$$f(x,l) = \begin{cases} 
\alpha \left( \frac{\mu}{c^{(r)}} + \delta z^{(r)} \right), & l = e_{4r-3}, \\
\sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ x_1^{(r)} \ y_2^{(j)}, & l = -e_{4r-3} + e_{4r-2}, \\
\mu x_1^{(r)}, & l = -e_{4r-3}, \\
(\mu + \gamma) z_2^{(r)}, & l = -e_{4r-2}, \\
(1 - \alpha) \left( \frac{\mu}{c^{(r)}} + \delta z^{(r)} \right), & l = e_{4r-1}, \\
\sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ y_1^{(r)} \ x_2^{(j)}, & l = -e_{4r-1} + e_{4r}, \\
\mu z_1^{(r)}, & l = -e_{4r-1}, \\
(\mu + \gamma) y_2^{(r)}, & l = -e_{4r}, \\
0, & \text{otherwise}, 
\end{cases} \quad (36)$$

with $z^{(r)} = 1 - \left( x_1^{(r)} + x_2^{(r)} + y_1^{(r)} + y_2^{(r)} \right)$.

As $N \rightarrow \infty$, we can apply again the results of Kurtz and derive the following deterministic analogue, for the process with transition rates (4):

$$\frac{dx_1^{(r)}}{dt} = \alpha \left( \frac{\mu}{c^{(r)}} + \delta z^{(r)} \right) - \sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ x_1^{(r)} \ y_2^{(j)} - \mu x_1^{(r)},$$

$$\frac{dx_2^{(r)}}{dt} = \sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ x_1^{(r)} \ y_2^{(j)} - (\mu + \gamma) x_2^{(r)},$$

$$\frac{dy_1^{(r)}}{dt} = (1 - \alpha) \left( \frac{\mu}{c^{(r)}} + \delta z^{(r)} \right) - \sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ y_1^{(r)} \ x_2^{(j)} - \mu y_1^{(r)},$$

$$\frac{dy_2^{(r)}}{dt} = \sum_{j=1}^{K} \beta_{rj} \ c^{(r)} \ y_1^{(r)} \ x_2^{(j)} - (\mu + \gamma) y_2^{(r)},$$

with $z^{(r)} = \frac{1}{c^{(r)}} - \left( x_1^{(r)} + x_2^{(r)} + y_1^{(r)} + y_2^{(r)} \right)$.
For the case of varying population case, the ODEs version of the stochastic model is derived by parameterizing each random variables of the process \((X(t), t \geq 0)\), with the transition rates \((5)\), with a parameter \(V = \frac{2B}{\mu}\) (as in the single varying population model). The deterministic system is given by the following equations:

\[
\begin{align*}
\frac{dx_1^{(r)}}{dt} &= \frac{\mu}{2} - \sum_{j=1}^{K} \beta_{rj} \frac{x_1^{(r)}}{n^{(r)}} y_2^{(j)} - \mu x_1^{(r)}, \\
\frac{dx_2^{(r)}}{dt} &= \sum_{j=1}^{K} \beta_{rj} \frac{x_1^{(r)}}{n^{(r)}} y_2^{(j)} - (\mu + \gamma) x_2^{(r)}, \\
\frac{dy_1^{(r)}}{dt} &= \frac{\mu}{2} - \sum_{j=1}^{K} \beta_{rj} \frac{y_1^{(r)}}{n^{(r)}} x_2^{(j)} - \mu y_1^{(r)}, \\
\frac{dy_2^{(r)}}{dt} &= \sum_{j=1}^{K} \beta_{rj} \frac{y_1^{(r)}}{n^{(r)}} x_2^{(j)} - (\mu + \gamma) y_2^{(r)},
\end{align*}
\]

with \(n^{(r)} = x_1^{(r)} + x_2^{(r)} + y_1^{(r)} + y_2^{(r)}\).

Model with Actual Mobility

As explained previously that for the model with actual mobility we only consider the case under a varying population size. The ODE analogue of this model is given, after scaling the process \((X(t), t \geq 0)\) (with transition rates in \((6)\)) with \(V = \frac{2B}{\mu}\), by the following system:

\[
\begin{align*}
\frac{dx_1^{(r)}}{dt} &= \frac{\mu}{2} - \beta_r \frac{x_1^{(r)}}{n^{(r)}} y_2^{(r)} - \mu x_1^{(r)} + \sum_{j=1}^{K} \rho_{rj} \frac{u^{(j)}}{n^{(j)}} x_1^{(j)} - \frac{u^{(r)}}{n^{(r)}} x_1^{(r)}, \\
\frac{dx_2^{(r)}}{dt} &= \beta_r \frac{x_1^{(r)}}{n^{(r)}} y_2^{(r)} - (\mu + \gamma) x_2^{(r)} + \sum_{j=1}^{K} \rho_{rj} \frac{u^{(j)}}{n^{(j)}} x_2^{(j)} - \frac{u^{(r)}}{n^{(r)}} x_2^{(r)}, \\
\frac{dy_1^{(r)}}{dt} &= \frac{\mu}{2} - \beta_r \frac{y_1^{(r)}}{n^{(r)}} x_2^{(r)} - \mu y_1^{(r)} + \sum_{j=1}^{K} \rho_{rj} \frac{u^{(j)}}{n^{(j)}} y_1^{(j)} - \frac{u^{(r)}}{n^{(r)}} y_1^{(r)}, \\
\frac{dy_2^{(r)}}{dt} &= \beta_r \frac{y_1^{(r)}}{n^{(r)}} x_2^{(r)} - (\mu + \gamma) y_2^{(r)} + \sum_{j=1}^{K} \rho_{rj} \frac{u^{(j)}}{n^{(j)}} y_2^{(j)} - \frac{u^{(r)}}{n^{(r)}} y_2^{(r)},
\end{align*}
\]

where \(n^{(r)} = x_1^{(r)} + x_2^{(r)} + y_1^{(r)} + y_2^{(r)}\).

Here, we have not proved analytically the existence and the stability of their equilibria points. However, we consider the endemic equilibria numerically and use them to derive the diffusion counterparts.

5 Numerical Experiments and Discussion

In this section we illustrate the behavior of the various population models and their deterministic and diffusion approximations via a number of numerical experiments. The
following parameters are the same in each experiment: The natural death rate is $\mu = 0.02$ (which corresponds to the life expectancy 50 years), the death rate due to AIDS is $\delta = 0.05$ (which means a life expectancy for AIDS people of only 20 years), and the removal rate is $\gamma = 0.08$ (which corresponds to a 12 year infectious period of HIV before AIDS sets in). We always assume $\alpha = \frac{1}{2}$, which implies a 50 : 50 ratio of females and males in the recruitment of new susceptibles. The other parameter settings are explained in each individual experiment.

5.1 Models for a Single Population

In these experiments the important parameter is $\beta$, since it determines the stability of the disease-free equilibrium (see Section 4 for the threshold condition assuming the parameters $\mu$ and $\gamma$ are fixed). The numerical results in Figure 4, for the deterministic model with a constant single population, illustrate how crucial the parameter $\beta$ is.

![Bifurcation diagram](image1.png)

(a) Bifurcation diagram. The solid and dashed lines denote stable and unstable equilibria, respectively.

![Dynamics of infected females](image2.png)

(b) The dynamics of the number of infected females.

![Dynamics of infected males](image3.png)

(c) The dynamics of the number of infected males.

Figure 4: (a). The stability of the disease-free equilibrium, and the birth of the endemic equilibrium as the parameter $\beta$ varies. (b) and (c) illustrate how the disease-free equilibrium of the deterministic model behaves for three different values of $\beta$, ($0.5(R_0 > 1); 0.2(R_0 = 1); 0.1(R_0 < 1)$).

It can be seen from the two logarithmic plots in Figure 4(b) and 4(c) that when $R_0$ is below the threshold ($R_0 < 1$) the proportion of infectives of both females and males, after a few infectives are introduced in the population, returns to no infection, but it grows away from the disease-free equilibrium if $R_0$ is above the threshold ($R_0 > 1$).

The value of the parameter $\beta$ can be set by using the formula in Remark 2.1. For the purpose of our numerical study, we choose the parameter $\beta = 0.5$ so that $R_0 > 1$ which results in a positive endemic equilibrium. We then look at how the stochastic processes converge to their deterministic and diffusion approximation around the equilibrium.

Model with a Closed Single Population

For the numerical experiments, we apply the parameter settings above and use the following initial values: 50,000 susceptible females and 50,000 susceptible males, 100 infected males, no infected females, and no AIDS cases. So, the total population size, $N = 100100$. 
Figure 5 describes the dynamic behaviour in the male subpopulation (similar results hold for the female subpopulation).

(a) The number of male infectives versus time.
(b) The dynamic behavior in the male subpopulation.
(c) The graph of (b) around the endemic equilibrium.

Figure 5: Stochastic and Deterministic Model for Male Subpopulation.

We can see that the stochastic process remains close to the trajectory of its deterministic analogue during a finite time interval. We should note that the process will eventually leave the trajectory and be absorbed in the disease-free equilibrium.

The following histograms describe the empirical distribution of the number of infectives based on a simulation of the CTMC with transition rates (2) around the equilibrium point of the deterministic process.

(a) The distribution of the number of the infected females.
(b) The distribution of the number of the infected males.

Figure 6: Equilibrium distributions around the endemic equilibrium.

These numerical results illustrate that the “stationary” distribution of the process can be approximated by a normal distribution. The empirical means and standard deviations for the number of infected females (males) are 14010 and 127.1 (14031 and 132), respectively. From the diffusion approximation, the exact form of the mean $\mu = N X^*_2$ and covariance matrix $N \Sigma$ of $X(t)$ can be calculated from Equations (9) and (11), which numerically can be found to be

\[
\mu = (20020, 14014, 20020, 14014),
\]

and

\[
N \Sigma = N \begin{pmatrix}
0.2933721451 & -0.08025078370 & 0.04948499776 & -0.1197492163 \\
-0.08025078370 & 0.1685788924 & -0.1197492163 & 0.08475444096 \\
0.04948499776 & -0.1197492163 & 0.2933721451 & -0.08025078370 \\
-0.1197492163 & 0.08475444096 & -0.08025078370 & 0.1685788924
\end{pmatrix}.
\]
The means and standard deviations obtained from the diffusion approximation for the number of infected females (males), which are 14014 and 129.9 for both females and males, are close to the experiment results.

To illustrate the accuracy of this diffusion approximation, we plot the dynamic behavior of the male subpopulation around the equilibrium point, together with its diffusion analogue, see Figure 7.

Figure 7: The stochastic model and its deterministic and diffusion analogues for a constant population size for male subpopulation.

We see that the equilibrium distribution of infectives around the endemic equilibrium is closely approximated by a two-dimensional Gaussian distribution derived from the diffusion process.

Model with an Open Single Population

In these experiments we use the same parameters as in the model with a single closed (constant) population. In addition, we set $B = 1000$. The following figure illustrates that the stochastic process for an open single population converges to its deterministic counterpart.

Figure 8: Stochastic and Deterministic Model for the Female Subpopulation.

From the diffusion approximation, the mean and covariance of the process $(X(t), t \geq 0)$ can be approximated by using Equations (14) and (13). The Gaussian distribution
derived from the diffusion process (with \( V = 100,000 \)) has the mean vector
\[
\mu = V X^*_2 = (5882, 8823, 5882, 8823),
\]
and the covariance matrix \( V \Sigma \), with
\[
\Sigma = \begin{pmatrix}
0.08565685893 & -0.001747475767 & 0.01428207858 & -0.02308460238 \\
-0.001747475767 & 0.08496559914 & -0.02308460237 & 0.02484510713 \\
0.01428207858 & -0.02308460237 & 0.08565685893 & -0.001747475777 \\
-0.02308460238 & 0.02484510713 & -0.001747475777 & 0.08496559913
\end{pmatrix}.
\]

The following figures illustrate the accuracy of the diffusion approach in approximating the distribution of susceptibles and infectives around the equilibrium point.

(a) The p.d.f of female population corresponding to the diffusion approximation.

(b) The stochastic process with its deterministic limit, and the contour lines corresponding to the p.d.f in (a).

Figure 9: The stochastic model and its deterministic and diffusion analogue for varying population size for the female subpopulation.

5.2 Multiple Patch Models

In these numerical experiments, we carry out the simulations with \( M = 10 \) patches, in all multiple patch models. We set the initial values to 50,000 susceptibles females and 50,000 susceptibles males for each patch. The infected people — set to be 100 infected males — are assumed to be initially concentrated only in patch 1. Thus, initially no infected individuals are present in other patches. All parameters (except \( \beta \)) have the same values as specified previously.

Models with Force of Infection

In this model, we assumed that within-patch mixing is stronger (and often considerably stronger) than between-patch mixing, and hence that the between-patch transmission parameters \( \beta_{rj} \) (for \( r \neq j \)) are small compared to the within-patch transmission parameters \( \beta_r \) (or \( \beta_{rr} \)); see [14]. In addition, the force of infection from the patch where the infection is initially concentrated to the other patches is assumed to be stronger than the forces among other patches. We might consider this patch, for example, as
a big city where people from other small cities come visit more often. With these assumptions, we set the values of \( \beta \) as follows: \( \beta_r = 0.5, \beta_{1j} = 0.5, j = 1, \ldots, 10, \) and \( \beta_{rj} = 0.01, r = 2, \ldots, 10, j = 1, \ldots, 10. \)

The following numerical results (see Figure 10) describe the dynamic behavior of the process and its deterministic analogue in patch 1 for the female subpopulation. This behaviour is similar to that in other patches, for each subpopulation.

![Figure 10: Stochastic and Deterministic Model.](image)

(a) The number of female infectives versus time. (b) The dynamic behavior of in the female subpopulation. (c) The graph of (b) around the endemic equilibrium.

We conclude that the stochastic process in the multiple patch model, at least from the numerical evidence, converges to its deterministic version.

To obtain the diffusion approximation, we evaluate the equilibrium points by solving the deterministic counterparts numerically. Then, we determine numerically the mean vectors and the covariance matrices around these equilibrium for their multivariate Gaussian distribution. These results can be seen in Table 1 and Table 2 for the case of constant population sizes and varying population sizes, respectively.

Table 1: Means and standard deviations of the Diffusion approximation; for the closed population model.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \mu )</td>
<td>( \sigma )</td>
</tr>
<tr>
<td>1</td>
<td>15666</td>
<td>126</td>
</tr>
<tr>
<td>2-10</td>
<td>18667</td>
<td>129</td>
</tr>
</tbody>
</table>

Table 2: Means and standard deviations of the diffusion approximation; for the open population model.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \mu )</td>
<td>( \sigma )</td>
</tr>
<tr>
<td>1</td>
<td>9080</td>
<td>91.0</td>
</tr>
<tr>
<td>2-10</td>
<td>9550</td>
<td>93.4</td>
</tr>
</tbody>
</table>

These calculation are in close agreement with the empirical means and standard deviations obtained by simulating the stochastic process and collecting data after equilibrium has been reached. We summarize in Table 3 and Table 4 the sample means and sam-
ple standard deviations obtained from a Monte Carlo simulation for a closed and open multiple population, respectively, with the force of infection.

Table 3: Sample means and standard deviations for the model of a constant population size.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\bar{\mu}$</td>
<td>$\bar{\sigma}$</td>
</tr>
<tr>
<td>1</td>
<td>15665</td>
<td>126</td>
</tr>
<tr>
<td>2</td>
<td>18675</td>
<td>129</td>
</tr>
<tr>
<td>3</td>
<td>18668</td>
<td>126</td>
</tr>
<tr>
<td>4</td>
<td>18669</td>
<td>126</td>
</tr>
<tr>
<td>5</td>
<td>18670</td>
<td>131</td>
</tr>
<tr>
<td>6</td>
<td>18658</td>
<td>128</td>
</tr>
<tr>
<td>7</td>
<td>18661</td>
<td>122</td>
</tr>
<tr>
<td>8</td>
<td>18672</td>
<td>131</td>
</tr>
<tr>
<td>9</td>
<td>18673</td>
<td>125</td>
</tr>
<tr>
<td>10</td>
<td>18668</td>
<td>134</td>
</tr>
</tbody>
</table>

Table 4: Sample means and standard deviations for the model of a varying population size.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\bar{\mu}$</td>
<td>$\bar{\sigma}$</td>
</tr>
<tr>
<td>1</td>
<td>9085.1</td>
<td>91.2</td>
</tr>
<tr>
<td>2</td>
<td>9559.7</td>
<td>90.7</td>
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<td>3</td>
<td>9554.1</td>
<td>96.2</td>
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<tr>
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<td>9552.2</td>
<td>91.7</td>
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<td>9552.6</td>
<td>90.1</td>
</tr>
<tr>
<td>6</td>
<td>9561.1</td>
<td>91.1</td>
</tr>
<tr>
<td>7</td>
<td>9554.3</td>
<td>92.2</td>
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<tr>
<td>8</td>
<td>9551.6</td>
<td>89.4</td>
</tr>
<tr>
<td>9</td>
<td>9546.1</td>
<td>94.8</td>
</tr>
<tr>
<td>10</td>
<td>9553.1</td>
<td>93.2</td>
</tr>
</tbody>
</table>

Model with Actual Mobility

For the model with actual mobility, we assume that the forces of infection within a patch are the same for all patches, which is set at $\beta_i = 0.5$. The initial numbers of susceptibles and infective in each patch are as in the model with force of infection. Here, we assume that the number of people leaving their home patches is equal for all patches ($u_r = 10$) and they will visit other patches with the same probability.

The mean vector and standard deviation of the multivariate Gaussian distribution corresponding to the diffusion approximation are obtained in the same way as before and the corresponding mean vector and standard deviation of the stochastic models are presented in Table 5 and Table 6, respectively. Again there is close agreement with the sample means and variances obtained by Monte Carlo simulation.
Table 5: Means and standard deviations of Multivariate Gaussian distribution.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \mu )</td>
<td>( \sigma )</td>
</tr>
<tr>
<td>1-10</td>
<td>8824</td>
<td>92.19</td>
</tr>
</tbody>
</table>

Table 6: Sample means and sample standard deviations from numerical experiments.

<table>
<thead>
<tr>
<th>Patches</th>
<th>Infected Females</th>
<th>Infected Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \hat{\mu} )</td>
<td>( \hat{\sigma} )</td>
</tr>
<tr>
<td>1</td>
<td>8809.4</td>
<td>93.34</td>
</tr>
<tr>
<td>2</td>
<td>8823.6</td>
<td>95.84</td>
</tr>
<tr>
<td>3</td>
<td>8813.5</td>
<td>93.62</td>
</tr>
<tr>
<td>4</td>
<td>8817.0</td>
<td>96.04</td>
</tr>
<tr>
<td>5</td>
<td>8835.8</td>
<td>95.63</td>
</tr>
<tr>
<td>6</td>
<td>8824.5</td>
<td>93.92</td>
</tr>
<tr>
<td>7</td>
<td>8811.5</td>
<td>89.68</td>
</tr>
<tr>
<td>8</td>
<td>8830.8</td>
<td>98.32</td>
</tr>
<tr>
<td>9</td>
<td>8824.7</td>
<td>96.90</td>
</tr>
<tr>
<td>10</td>
<td>8838.4</td>
<td>86.97</td>
</tr>
</tbody>
</table>

Thus, the deterministic and diffusion approach can be applied to study the dynamic behavior of the stochastic multiple patch model with the actual mobility.

6 Conclusion and Future Research

The dynamic behavior of the stochastic models for the spread of HIV presented in this paper are well approximated by their deterministic and diffusion counterparts. We find the same threshold conditions \( R_0 = 1 \) for a disease-free equilibrium in the case of both an open and closed single population. As \( R_0 > 1 \) (above threshold), this equilibrium loses its stability and a stable endemic state occurs. The numerical results also indicate that there exists a positive-stable endemic equilibrium in the multiple patch models, although we have not proved this analytically. Although the stochastic models presented in this paper are perhaps too simple to describe the actual spread of HIV, they provide some clues how e.g., more realistic models can be formulated. Moreover, for future research, it should be feasible to use the deterministic and diffusion approaches to study more complex stochastic models of HIV/AIDS spread; for example, stochastic models in a mobile heterogeneous population, classified according to age and sexual behavior, or (since the disease is primarily a sexually transmitted disease) models that include partnership pattern formation. Another possible direction for future research is to consider how control strategies may be devised. For example, to find a strategy that provides the greatest reduction in the endemic level of the disease for a given cost, or to find the cheapest strategy that guarantees a upper level of prevalence of HIV in all patches. Finally, taking into account the available statistical data and control strategies into the models will further improve our understanding how the disease spread into the heterogeneous population. However, as many factors of consideration are included in the models,
the complexity of the models increases.

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References


