

A TWO-PATCH EPIDEMIC MODEL WITH NONLINEAR REINFECTION

UN MODELO EPIDÉMICO DE DOS POBLACIONES CON REINFECCIÓN NO LINEAL

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Abstract

The propagation of infectious diseases and its impact on individuals play a major role in disease dynamics, and it is important to incorporate population heterogeneity into efforts to study diseases. As a simplistic but illustrative example, we examine interactions between urban and rural populations on the dynamics of disease spreading. Using a compartmental framework of susceptible–infected–susceptible (SIS) dynamics with some level of immunity, we formulate a model that allows nonlinear reinfection. We investigate the effects of population movement in a simple scenario: a case with two patches, which allows us to model population movement between urban and rural areas. To study the dynamics of the system, we compute a basic reproduction number for each population (urban and rural). We also compute steady states, determine the local stability of the disease-free steady state, and identify conditions for the existence of endemic steady states. From our analysis and computational experiments, we illustrate that population movement plays an important role in disease dynamics. In some cases, it can be rather beneficial, as it can enlarge the region of stability of a disease-free steady state.

Keywords: dynamical systems; population dynamics; mathematical modeling; biological contagions; population movement.

Resumen

La propagación de enfermedades infecciosas y su impacto en individuos juega un gran rol en la dinámica de enfermedades, y es importante incorporar heterogeneidad en la población en los esfuerzos por estudiar enfermedades. De manera simplística pero ilustrativa, se examinan interacciones entre una población urbana y una rural en la dinámica de la propagación de una enfermedad. Utilizando un sistema compartimental de dinámicas entre susceptibles–infectados–susceptibles (SIS) con cierto nivel de inmunidad, se formula un modelo que permite reinfecciones no lineales. Se investiga los efectos de movimiento de poblaciones en un escenario simple: un caso con dos poblaciones, que permite modelar movimiento entre un área urbana y otra rural. Con el fin de estudiar la dinámica del sistema, se calcula el número básico reproductivo para cada comunidad (rural y urbana). Se calculan también puntos de equilibrio, la estabilidad local del estado libre de enfermedad, y se identifican condiciones para la existencia de estados de equilibrio endémicos. Del análisis y experimentos computacionales, se ilustra que el movimiento en la población juega un rol importante en la dinámica del sistema. En algunos casos, puede ser beneficioso, pues incrementa la región de estabilidad del punto de equilibrio del estado libre de infección.

Palabras clave: sistemas dinámicos; dinámica de poblaciones; modelado matemático; contagios biológicos; movimiento de poblaciones.

Mathematics Subject Classification: 92D25, 92D30.

1 Introduction

It is relatively easy for individuals to move between towns, cities, countries, and even continents; and incorporating movement between populations has become increasingly prevalent in the modeling and analysis of disease spreading [3, 22]. It is also important to consider movement in which individuals travel to a distinct location from their place of origin and then return to their original location in a relatively short period of time. Such movement can lead to rapid spreading of infectious diseases, and examination of connected environments can give clues about the types of strategies that are needed to control disease propagation [2, 20].

In 2003, the severe acute respiratory syndrome (SARS) epidemic was a major concern among public health officials worldwide [4]. This new infectious disease spread rapidly, and scientists and researchers scrambled to try to discern how to contain its spread (e.g., by reducing the spreading rate) and to seek treatments and a vaccine. The best control measure that was found at the time was to isolate individuals who had been in contact with infected individuals. The rapid spread of the disease was associated with the movement of a doctor who was identified as “patient 0” for SARS [7, 14]. Population movement has also played an important role in subsequent events, such as the spread of ebola to the western hemisphere [5], the spread of measles in some parts of the world by travelers [6], and the resurgence of malaria through the mass migration of Nicaraguans to the northern part of Costa Rica [1].

The use of compartmental models to describe the spreading of diseases has been explored thoroughly in numerous scenarios [3, 22]. For example, when there is nonlinear reinfection, an individual who was infected previously can become infected again through contact with an infectious individual after losing immunity [30]. Several models that allow individuals to lose immunity and become infectious again also exhibit a backward bifurcation, such that a stable endemic steady state coexists with a stable disease-free steady state when the associated basic reproduction number is smaller than 1 [12, 24, 27, 28, 26]. Moreover, in some models of social contagion processes (e.g., the spread of drug use, the adoption of products, and so on), after an initial “contagion”, a backward bifurcation can arise via social inputs [27].

In the present paper, we generalize the compartmental model from Sanchez et al. [24], who studied a continuous dynamical system (in the form of coupled ordinary differential equations) that describes interactions between susceptible and infected individuals with the possibility of reinfection after loss of immunity.

In our generalization, we incorporate population movement between urban and rural environments. Taking movement into account is important for studies of disease dynamics in practice, and it changes the qualitative dynamics of disease spreading. We explore a simple case in which a population has two patches, and we obtain insights that will be useful for subsequent explorations of disease spreading in a population that includes a network of patches.

Our paper proceeds as follows. In Section 2, we describe our compartmental model of disease spreading (including nonlinear reinfection) between urban and rural environments. In Section 3, we give a formula for the model's basic reproduction number \mathcal{R}_0 , analyze the existence and local stability of the disease-free steady state, and study the existence of endemic steady states. In Section 4, we illustrate several example scenarios with numerical computations. Finally, in Section 5, we conclude and discuss biological insights of our model.

2 A two-patch compartmental model

We present a two-patch model of disease spreading in humans that incorporates nonlinear reinfection and population movement. Specifically, we generalize the model of Sanchez et al. [24] by incorporating the idea of urban versus rural environments. We use the subscript u for urban variables and parameters and the subscript r for rural variables and parameters. For $j \in \{u, r\}$, let S_j , I_j , and \tilde{S}_j denote the numbers of susceptible, infected, and post-recovery susceptible individuals, respectively. New susceptible individuals enter the system in proportion to the total population N_j , where $N_j = S_j + I_j + \tilde{S}_j$. Let μ_j denote the rate of both births and deaths. (For simplicity, we assume that they are the same.) Susceptible individuals become infected at rate β_j , infected individuals transition to a state of post-recovery susceptibility at rate γ_j , and post-recovery susceptible individuals are reinfected at rate ρ_j . Such reinfection corresponds to infectious diseases (such as tuberculosis and malaria [15, 16]) in which subsequent infections are possible after loss of immunity. Typically, in such diseases, an initial infection tends to produce stronger symptoms than subsequent reinfections [9]. We model population movement between patches using the functions $\delta_{ij}(t)$, which denotes the fraction of individuals who travel from patch $i \in \{u, r\}$ to patch $j \in \{u, r\}$ (with $i \neq j$) at time t .

Our model consists of the following coupled system of ordinary differential equations:

$$\begin{aligned}
 \frac{dS_u}{dt} &= \mu_u N_u - \beta_u \frac{I_u}{N_u} S_u - \mu_u S_u + \delta_{ru} S_r - \delta_{ur} S_u, \\
 \frac{dI_u}{dt} &= \beta_u \frac{I_u}{N_u} S_u - (\mu_u + \gamma_u) I_u + \rho_u \frac{I_u}{N_u} \tilde{S}_u + \delta_{ru} I_r - \delta_{ur} I_u, \\
 \frac{d\tilde{S}_u}{dt} &= \gamma_u I_u - \rho_u \frac{I_u}{N_u} \tilde{S}_u - \mu_u \tilde{S}_u + \delta_{ru} \tilde{S}_r - \delta_{ur} \tilde{S}_u, \\
 \frac{dS_r}{dt} &= \mu_r N_r - \beta_r \frac{I_r}{N_r} S_r - \mu_r S_r + \delta_{ur} S_u - \delta_{ru} S_r, \\
 \frac{dI_r}{dt} &= \beta_r \frac{I_r}{N_r} S_r - (\mu_r + \gamma_r) I_r + \rho_r \frac{I_r}{N_r} \tilde{S}_r + \delta_{ur} I_u - \delta_{ru} I_r, \\
 \frac{d\tilde{S}_r}{dt} &= \gamma_r I_r - \rho_r \frac{I_r}{N_r} \tilde{S}_r - \mu_r \tilde{S}_r + \delta_{ur} \tilde{S}_u - \delta_{ru} \tilde{S}_r,
 \end{aligned} \tag{1}$$

with initial conditions $S_j(0) = S_{j0}$, $I_j(0) = I_{j0}$, and $\tilde{S}_j(0) = \tilde{S}_{j0}$ (for $j \in \{u, r\}$). Additionally, $N_{j0} = S_{j0} + I_{j0} + \tilde{S}_{j0}$ for $j \in \{u, r\}$.

By adding the first three and last three equations in (1), we see that N_u and N_r satisfy the linear dynamical system

$$\frac{d}{dt} \begin{bmatrix} N_u \\ N_r \end{bmatrix} = \begin{bmatrix} -\delta_{ur} & \delta_{ru} \\ \delta_{ur} & -\delta_{ru} \end{bmatrix} \begin{bmatrix} N_u \\ N_r \end{bmatrix}.$$

Its solution is

$$\begin{aligned}
 N_u(t) &= e^{-\int_0^t \delta(s) ds} \left[N_{u,0} + (N_{u,0} + N_{r,0}) \int_0^t \delta_{ru}(s) e^{\int_0^s \delta(h) dh} ds \right], \\
 N_r(t) &= e^{-\int_0^t \delta(s) ds} \left[N_{r,0} + (N_{u,0} + N_{r,0}) \int_0^t \delta_{ur}(s) e^{\int_0^s \delta(h) dh} ds \right],
 \end{aligned}$$

where $\delta(t) = \delta_{ur}(t) + \delta_{ru}(t)$ is the net movement of individuals at time t . The initial conditions are $N_{u,0} = N_u(0)$ and $N_{r,0} = N_r(0)$. Note that $N_u + N_r$ is constant for all t .

In our analysis, we assume at first that δ_{ru} and δ_{ur} are constant, so N_u and N_r simplify to

$$\begin{aligned}
 N_u(t) &= N_{u,0} e^{-t(\delta_{ur} + \delta_{ru})} + (N_{u,0} + N_{r,0}) \frac{\delta_{ru}}{\delta_{ru} + \delta_{ur}} \left(1 - e^{-t(\delta_{ur} + \delta_{ru})} \right), \\
 N_r(t) &= N_{r,0} e^{-t(\delta_{ur} + \delta_{ru})} + (N_{u,0} + N_{r,0}) \frac{\delta_{ur}}{\delta_{ru} + \delta_{ur}} \left(1 - e^{-t(\delta_{ur} + \delta_{ru})} \right).
 \end{aligned}$$

There are three cases:

1. There is no population movement (i.e., $\delta_{ur} = \delta_{ru} = 0$), which corresponds to the case of independent patches that was studied in [24]. In this case, each patch has a backward bifurcation, and the steady state can depend on the number of initially infected individuals.

2. Population movement occurs exclusively from one patch to the other. For example, suppose that $\delta_{ur} = 0$ and $\delta_{ru} > 0$. In this case, $\lim_{t \rightarrow \infty} N_r(t) = 0$ (i.e., eventually, the entire population is in u). There is a backward bifurcation in this case as well, but now there is a total population of $N_{u,0} + N_{r,0}$ in the urban patch. We explore this case in Example 1 in Section 4.
3. There is population movement in both directions between the two patches (i.e., $\delta_{ur} > 0$ and $\delta_{ru} > 0$). This is the primary scenario (and the principal novel contribution) of the present paper.

3 Analysis of our model

3.1 Disease-free steady state and basic reproduction number

Because the total population is constant, we can eliminate \tilde{S}_r from the dynamical system (1). We then compute the Jacobian matrix of the reduced system and evaluate it at the disease-free steady state

$$(S_u^*, I_u^*, \tilde{S}_u^*, S_r^*, I_r^*, \tilde{S}_r^*) = (S_u^*, 0, 0, S_r^*, 0, 0) \quad (2)$$

to obtain the matrix

$$\begin{bmatrix} -\delta_{ur} & \mu_u - \beta_u & & \mu_u & \delta_{ru} & 0 \\ 0 & \eta_{ur} & & 0 & 0 & \delta_{ru} \\ -\delta_{ru} & \gamma_u - \delta_{ru} & -\delta_{ru} - \delta_{ur} - \mu_u & -\delta_{ru} & -\delta_{ru} & -\beta_r \\ \delta_{ur} - \mu_r & -\mu_r & & -\mu_r & -\mu_r - \delta_{ru} & -\beta_r \\ 0 & \delta_{ur} & & 0 & 0 & \eta_{ru} \end{bmatrix}, \quad (3)$$

where $\eta_{ur} = \beta_u - \delta_{ur} - \gamma_u - \mu_u$ and $\eta_{ru} = \beta_r - \delta_{ru} - \gamma_r - \mu_r$. For the dynamical system (1), steady states with $I_u = I_r = 0$ necessarily also satisfy $\tilde{S}_u = \tilde{S}_r = 0$.

The five eigenvalues of the matrix (3) are

$$\begin{aligned} \lambda_1 &= -(\delta_{ru} + \delta_{ur}), \\ \lambda_{2\pm} &= \frac{1}{2} \left[-(\delta_{ru} + \delta_{ur} + \mu_r + \mu_u) \pm \sqrt{(\delta_{ru} - \delta_{ur} + \mu_r - \mu_u)^2 + 4\delta_{ru}\delta_{ur}} \right], \\ \lambda_{3\pm} &= \frac{1}{2} \left[\eta_{ur} + \eta_{ru} \pm \sqrt{(\eta_{ur} - \eta_{ru})^2 + 4\delta_{ru}\delta_{ur}} \right]. \end{aligned}$$

All eigenvalues are real, and λ_1 and $\lambda_{2\pm}$ are negative. The two remaining eigenvalues $\lambda_{3\pm}$ are negative as long as

$$\delta_{ru}\delta_{ur} < \eta_{ur}\eta_{ru}, \quad \eta_{ur} + \eta_{ru} < 0. \quad (4)$$

When there is only one population (i.e., one patch), the basic reproduction number is $\mathcal{R}_0 = \frac{\beta}{\mu + \gamma}$. For our multiple-patch case, we define a “local basic reproduction number” for each patch:

$$\mathcal{R}_{0u} = \frac{\beta_u}{\gamma_u + \mu_u}, \quad \mathcal{R}_{0r} = \frac{\beta_r}{\gamma_r + \mu_r}.$$

We can then express the conditions in (4) as

$$\mathcal{R}_{0u} < 1 + \frac{\delta_{ur}}{\mu_u + \gamma_u}, \quad (5a)$$

$$\mathcal{R}_{0r} < 1 + \frac{\delta_{ru}}{\mu_r + \gamma_r}, \quad (5b)$$

$$\frac{\delta_{ur}}{\mu_u + \gamma_u} \frac{\delta_{ru}}{\mu_r + \gamma_r} < \left(\mathcal{R}_{0u} - 1 - \frac{\delta_{ur}}{\mu_u + \gamma_u} \right) \left(\mathcal{R}_{0r} - 1 - \frac{\delta_{ru}}{\mu_r + \gamma_r} \right). \quad (5c)$$

See Figure 1 for an illustration of a typical region in which all eigenvalues are negative. For progressively smaller δ_{ur} and δ_{ru} , the shaded region approaches the unit square.

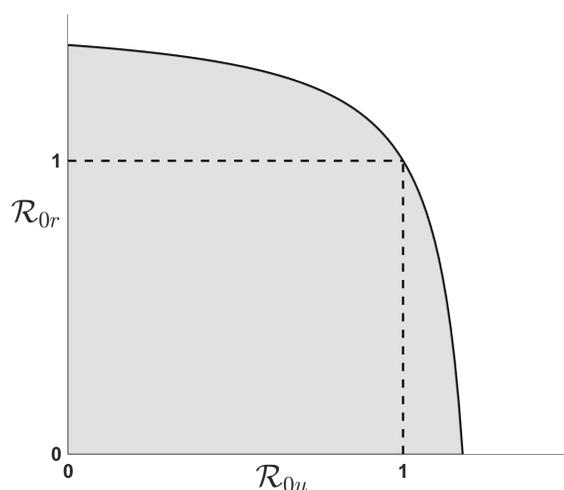


Figure 1: A typical region of local asymptotic stability of the disease-free steady state (2) of (1) that satisfies the conditions in (5) as a function of the local basic reproduction numbers \mathcal{R}_{0u} and \mathcal{R}_{0r} .

We have thus established the following lemma.

Lemma 1 *Assume that the inequalities (5) hold. It then follows that the disease-free steady state (2) of the dynamical system (1) is locally asymptotically stable.*

Remark 1 The conditions in (5) are satisfied when $\mathcal{R}_{0u} < 1$ and $\mathcal{R}_{0r} < 1$. We then have local stability in the rural and urban patches if we treat them as independent. Additionally, from Lemma 1, we see that it is possible to obtain local asymptotic stability for the disease-free steady state (2) even when one or both local basic reproduction numbers are larger than 1. In such a scenario, population movement is beneficial, as it leads to local asymptotic stability of the disease-free steady state in situations in which this is not the case for independent patches. We illustrate such a scenario in Example 2 in Section 4.

3.2 Technical tool: the Poincaré–Miranda theorem

As preparation for analyzing the existence of steady states in our model, we briefly recall some classical results by Poincaré and others. See [13, 17, 29, 31] for detailed accounts of the relevant theory. In 1817, Bolzano proved the following well-known theorem.

Theorem 1 *Suppose that $f : [a, b] \rightarrow \mathbb{R}$ is a continuous function such that $f(a) \cdot f(b) < 0$. There then exists $c \in (a, b)$ such that $f(c) = 0$.*

Definition 1 *Let $I^n = [0, 1]^n$, and let ∂I^n denote its boundary. For each $i \in \{1, \dots, n\}$, let*

$$I_i^- = \{x \in I^n \mid x_i = 0\}, \quad I_i^+ = \{x \in I^n \mid x_i = 1\}$$

be the opposite i -th faces of the boundary ∂I^n .

In 1883–1884, Poincaré announced a generalization of Bolzano’s theorem without providing a proof.

Theorem 2 (Poincaré) *Let $F : I^n \rightarrow \mathbb{R}^n$, with $F = (F_1, \dots, F_n)$, be a continuous map such that*

$$F_i(I_i^-) \subseteq (-\infty, 0]$$

and

$$F_i(I_i^+) \subseteq [0, +\infty)$$

for every $i \in \{1, \dots, n\}$. It then follows that there exists $c \in I^n$ such that $F(c) = 0$.

In the 1940s, Miranda rediscovered Poincaré’s theorem and showed that it is logically equivalent to Brouwer’s fixed-point theorem. Since then, this result has often been called the Poincaré–Miranda theorem. We require a modified version of the Poincaré–Miranda theorem in two dimensions.

Proposition 1 *Let $F : [0, 1]^2 \rightarrow \mathbb{R}^2$ such that $F(x, y) = (F_1(x, y), F_2(x, y))^T$ is continuous and $F(0, 0) = 0$. Assume that*

$$\begin{aligned} F_1(x, 0) > 0 & \text{ for all } x \in (0, 1], & F_1(x, 1) < 0 & \text{ for all } x \in [0, 1], \\ F_2(0, y) > 0 & \text{ for all } y \in (0, 1], & F_2(1, y) < 0 & \text{ for all } y \in [0, 1]. \end{aligned}$$

Assume additionally that $\partial F_1/\partial y$ and $\partial F_2/\partial x$ are both continuous from the right at $(0, 0)$, with $\frac{\partial F_1}{\partial y}(0, 0) > 0$ and $\frac{\partial F_2}{\partial x}(0, 0) > 0$. It then follows that there exists $(x_0, y_0) \in (0, 1)^2$ such that $F(x_0, y_0) = (0, 0)^T$.

Proof. Because F is continuous, both F_1 and F_2 are also continuous. Using the facts that $F_1(x, 0) > 0$ for all $x \in (0, 1]$ and that $\partial F_1/\partial x$ is continuous from the right, it follows that there exists $\epsilon_0 > 0$ such that $\frac{\partial F_1}{\partial x}(x, 0) > 0$ for all $x \in (0, \epsilon_0)$. By the implicit function theorem, for $x \in (0, \epsilon_0)$, one can write $y = g_1(x)$, where the function g_1 is differentiable. Therefore,

$$g_1'(0) = -\frac{\frac{\partial F_1}{\partial x}(0, 0)}{\frac{\partial F_1}{\partial y}(0, 0)}. \tag{6}$$

By the continuity of F_1 in the compact set $[0, 1]^2$ and using Equation (6), it follows that there exists $\epsilon_1 > 0$ such that $F_1(x, \epsilon_1) > 0$ for all $x \in [0, 1]$. By the same argument, there also exists $\epsilon_2 \in (0, 1)$ such that $F_2(\epsilon_2, y) > 0$ for all $y \in [0, 1]$. By the Poincaré–Miranda theorem, there must exist $(x_0, y_0) \in [\epsilon_1, 1] \times [\epsilon_2, 1]$ such that $F(x_0, y_0) = (0, 0)$. ■

3.3 Existence of multiple-population endemic steady states

We now examine endemic steady states, in which there are infected individuals at steady state in both the urban and the rural patches.

We start by proving the following lemma.

Lemma 2 *Suppose that $\mathcal{R}_{0u} > 1 + \frac{\delta_{ur}}{\mu_u + \gamma_u}$ and $\mathcal{R}_{0r} > 1 + \frac{\delta_{ru}}{\mu_r + \gamma_r}$. It then follows that there exists at least one endemic steady state, for which both $I_u^* > 0$ and $I_r^* > 0$. In other words, there are infected individuals at steady state in both the urban and the rural patches.*

Proof. We deduce the existence of a solution of the following nonlinear system of algebraic equations:

$$\begin{aligned}
0 &= \mu_u N_u - \beta_u \frac{I_u}{N_u} S_u - \mu_u S_u + \delta_{ru} S_r - \delta_{ur} S_u, \\
0 &= \beta_u \frac{I_u}{N_u} S_u - (\mu_u + \gamma_u) I_u + \rho_u \frac{I_u}{N_u} \tilde{S}_u + \delta_{ru} I_r - \delta_{ur} I_u, \\
0 &= \gamma_u I_u - \rho_u \frac{I_u}{N_u} \tilde{S}_u - \mu_u \tilde{S}_u + \delta_{ru} \tilde{S}_r - \delta_{ur} \tilde{S}_u, \\
0 &= \mu_r N_r - \beta_r \frac{I_r}{N_r} S_r - \mu_r S_r + \delta_{ur} S_u - \delta_{ru} S_r, \\
0 &= \beta_r \frac{I_r}{N_r} S_r - (\mu_r + \gamma_r) I_r + \rho_r \frac{I_r}{N_r} \tilde{S}_r + \delta_{ur} I_u - \delta_{ru} I_r, \\
0 &= \gamma_r I_r - \rho_r \frac{I_r}{N_r} \tilde{S}_r - \mu_r \tilde{S}_r + \delta_{ur} \tilde{S}_u - \delta_{ru} \tilde{S}_r.
\end{aligned} \tag{7}$$

We introduce a pair of parameters, $(b_u, b_r) \in [0, 1]^2$, and we consider the auxiliary linear system

$$\begin{aligned}
0 &= \mu_u N_u - \beta_u b_u S_u - \mu_u S_u + \delta_{ru} S_r - \delta_{ur} S_u, \\
0 &= \beta_u b_u S_u - (\mu_u + \gamma_u) I_u + \rho_u b_u \tilde{S}_u + \delta_{ru} I_r - \delta_{ur} I_u, \\
0 &= \gamma_u I_u - \rho_u b_u \tilde{S}_u - \mu_u \tilde{S}_u + \delta_{ru} \tilde{S}_r - \delta_{ur} \tilde{S}_u, \\
0 &= \mu_r N_r - \beta_r b_r S_r - \mu_r S_r + \delta_{ur} S_u - \delta_{ru} S_r, \\
0 &= \beta_r b_r S_r - (\mu_r + \gamma_r) I_r + \rho_r b_r \tilde{S}_r + \delta_{ur} I_u - \delta_{ru} I_r, \\
0 &= \gamma_r I_r - \rho_r b_r \tilde{S}_r - \mu_r \tilde{S}_r + \delta_{ur} \tilde{S}_u - \delta_{ru} \tilde{S}_r.
\end{aligned} \tag{8}$$

Suppose that $(S_u, I_u, \tilde{S}_u, S_r, I_r, \tilde{S}_r)$ is a solution of the system (8), which is linear in its variables S_i, I_i , and \tilde{S}_i (with $i \in \{u, r\}$). This solution also satisfies the nonlinear system (7) if $I_u/N_u = b_u$ and $I_r/N_r = b_r$. By adding all of the equations in (8), we see that $\delta_{ur} N_u = \delta_{ru} N_r$. We then rescale variables in (8) by substituting

$$\begin{aligned}
s_u &= \frac{S_u}{N_u}, & s_r &= \frac{S_r}{N_r}, \\
i_u &= \frac{I_u}{N_u}, & i_r &= \frac{I_r}{N_r}, \\
\tilde{s}_u &= \frac{\tilde{S}_u}{N_u}, & \tilde{s}_r &= \frac{\tilde{S}_r}{N_r}
\end{aligned}$$

to obtain a linear system of algebraic equations with parameters b_u and b_r . This system is

$$\mu_u - (\beta_u b_u + \mu_u + \delta_{ur}) s_u + \delta_{ur} s_r = 0, \tag{9a}$$

$$\beta_u b_u s_u - (\mu_u + \gamma_u + \delta_{ur}) i_u + \rho_u b_u \tilde{s}_u + \delta_{ur} i_r = 0, \tag{9b}$$

$$\gamma_u i_u - \rho_u b_u \tilde{s}_u - (\mu_u + \delta_{ur}) \tilde{s}_u + \delta_{ur} \tilde{s}_r = 0, \tag{9c}$$

$$\mu_r - (\beta_r b_r + \mu_r + \delta_{ru}) s_r + \delta_{ru} s_u = 0, \tag{9d}$$

$$\beta_r b_r s_r - (\mu_r + \gamma_r + \delta_{ru}) i_r + \rho_r b_r \tilde{s}_r + \delta_{ru} i_u = 0, \tag{9e}$$

$$\gamma_r i_r - \rho_r b_r \tilde{s}_r - (\mu_r + \delta_{ru}) \tilde{s}_r + \delta_{ru} \tilde{s}_u = 0. \tag{9f}$$

We now solve Equations (9a) and (9d) to obtain

$$s_u(b_u, b_r) = \frac{\beta_r \mu_u b_r + \delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_r \mu_u}{(\beta_u b_u + \mu_u + \delta_{ur})(\beta_r b_r + \mu_r + \delta_{ru}) - \delta_{ru} \delta_{ur}},$$

$$s_r(b_u, b_r) = \frac{\beta_u \mu_r b_u + \delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_r \mu_u}{(\beta_u b_u + \mu_u + \delta_{ur})(\beta_r b_r + \mu_r + \delta_{ru}) - \delta_{ru} \delta_{ur}}.$$

Using Equations (9b), (9c), (9e), and (9f), we solve for i_u and i_r to obtain

$$i_u(b_u, b_r) = \frac{1}{\Delta} \left(s_r \beta_r \delta_{ur} b_r \Delta_{i_u}^{(1)} + s_u \beta_u b_u \Delta_{i_u}^{(2)} \right),$$

$$i_r(b_u, b_r) = \frac{1}{\Delta} \left(s_u \beta_u \delta_{ru} b_u \Delta_{i_r}^{(1)} + s_r \beta_r b_r \Delta_{i_r}^{(2)} \right),$$

where

$$\Delta_{i_u}^{(1)} = \delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_u \mu_r + \rho_r (\mu_u + \delta_{ur}) b_r + \rho_u (\gamma_r + \mu_r + \delta_{ru}) b_u + \rho_u \rho_r b_u b_r,$$

$$\Delta_{i_u}^{(2)} = (\delta_{ru} + \gamma_r + \mu_r) (\delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_r \mu_u) + (\delta_{ru} + \mu_r) (\delta_{ur} + \mu_u) \rho_r b_r + (\delta_{ru} + \mu_r) (\delta_{ru} + \gamma_r + \mu_r) \rho_u b_u + (\delta_{ru} + \mu_r) \rho_u \rho_r b_u b_r,$$

$$\Delta_{i_r}^{(1)} = \delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_u \mu_r + \rho_u (\mu_r + \delta_{ru}) b_u + \rho_r (\gamma_u + \mu_u + \delta_{ur}) b_r + \rho_u \rho_r b_u b_r,$$

$$\Delta_{i_r}^{(2)} = (\delta_{ur} + \gamma_u + \mu_u) (\delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_r \mu_u) + (\delta_{ur} + \mu_u) (\delta_{ru} + \mu_r) \rho_u b_u + (\delta_{ur} + \mu_u) (\delta_{ur} + \gamma_u + \mu_u) \rho_r b_r + (\delta_{ur} + \mu_u) \rho_u \rho_r b_u b_r,$$

$$\Delta = (\delta_{ur} \mu_r + \delta_{ru} \mu_u + \mu_r \mu_u) [(\delta_{ru} + \gamma_r + \mu_r + b_r \rho_r) \times (\delta_{ur} + \gamma_u + \mu_u + b_u \rho_u) - \delta_{ur} \delta_{ru}].$$

One can write similar expressions for $\tilde{s}_u(b_u, b_r)$ and $\tilde{s}_r(b_u, b_r)$. The solution $(s_u, i_u, \tilde{s}_u, s_r, i_r, \tilde{s}_r)$ of (9) satisfies the nonlinear algebraic system (7) if and only if $i_u(b_u, b_r) = b_u$ and $i_r(b_u, b_r) = b_r$. We then define

$$\begin{aligned} G_1(b_u, b_r) &= i_u(b_u, b_r) - b_u, \\ G_2(b_u, b_r) &= i_r(b_u, b_r) - b_r. \end{aligned}$$

We will show that the system

$$G_1(b_u, b_r) = G_2(b_u, b_r) = 0 \tag{10}$$

has at least one solution $(b_u, b_r) \in (0, 1)^2$. This implies that there exists a solution of the nonlinear algebraic system (7) with $i_u > 0$ and $i_r > 0$. This solution corresponds to a steady state with a nonzero infected population in both the urban and the rural patches.

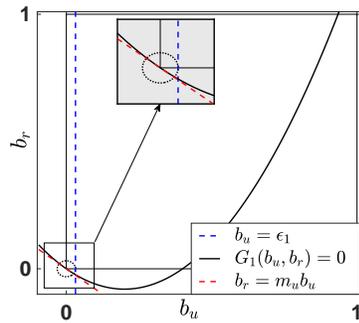
Consider the surface $z_1 = G_1(b_u, b_r)$. We have that $G_1(0, b_r) = i_u(0, b_r) \geq 0$ for $b_r \in [0, 1]$, with equality when $b_r = 0$. We seek a positive solution of Equation (10). A straightforward calculation yields

$$\begin{aligned} \frac{\partial G_1}{\partial b_u}(0, 0) &= \frac{-\delta_{ur}(\gamma_r + \mu_r) + (\beta_u - \gamma_u - \mu_u)(\delta_{ru} + \gamma_r + \mu_r)}{\delta_{ur}(\gamma_r + \mu_r) + (\delta_{ru} + \gamma_r + \mu_r)(\gamma_u + \mu_u)} \\ &> \frac{\delta_{ur}\delta_{ru}}{\delta_{ur}(\gamma_r + \mu_r) + (\delta_{ru} + \gamma_r + \mu_r)(\gamma_u + \mu_u)} > 0, \end{aligned}$$

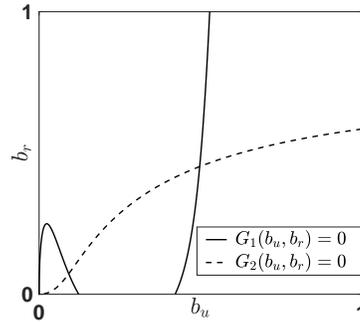
because $\beta_u > \gamma_u + \mu_u + \delta_{ur}$ (by hypothesis). Analogously, we compute that

$$\frac{\partial G_2}{\partial b_r}(0, 0) > 0. \tag{11}$$

We also compute that $G_1(1, b_r) = i_u(1, b_r) - 1 < 0$ for $b_r \in [0, 1]$ and that $G_2(b_u, 1) < 0$ for $b_u \in [0, 1]$. By Proposition 1, we conclude that there exists $(b_u, b_r) \in (\epsilon_1, 1) \times (\epsilon_2, 1)$ such that $G_1(b_u, b_r) = G_2(b_u, b_r) = 0$. Therefore, the nonlinear algebraic system (7) has a solution that corresponds to a steady state with positive values for both I_u^* and I_r^* . ■



(a) The curve $G_1(b_u, b_r) = 0$ has a tangent with slope $m_u < 0$ at the origin.



(b) The curves $G_1(b_u, b_r) = 0$ and $G_2(b_u, b_r) = 0$ intersect at two points with positive coordinates.

Figure 2: Endemic steady states in urban (vertical axis) and rural (horizontal axis) environments. In these steady states, an infected population persists in both the rural and the urban patches.

Remark 2 There are at most 9 steady states, because Equation (10) has at most 9 solutions. (It is equivalent to a polynomial equation of degree 9.) Using numerical computations, we observe the existence of two or more distinct endemic steady states. However, we need to explore them further to characterize them; see Figure 2b and Examples 3 and 7 in Section 4.

4 Examples

We now present some numerical simulations of the dynamical system (1) for a variety of parameter values. Using these examples, we illustrate that population movement strongly influences how a disease can propagate. For our simulations, we use MATLAB and its ordinary differential equation solver ODE45 (see the appendix).

Example 1 We first explore the behavior of our model (1) when $\delta_{ur} = 0$ and $\delta_{ru} \neq 0$, which describes population movement in one direction (specifically, from the rural patch to the urban one). In some countries, it is common for individuals in rural areas to travel to urban areas for work [8]. This is a type of short-term mobility. We consider the following parameter values:

$$\begin{aligned} \mu_u &= 1/(365 \cdot 80), & \rho_u &= 0.08, & \gamma_u &= 0.01, & \beta_u &= 0.03, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 0.04, & \gamma_r &= 0.01, & \beta_r &= 0.02, \end{aligned}$$

with initial conditions

$$\begin{aligned} S_{u0} &= 999, & I_{u0} &= 1, & \tilde{S}_{u0} &= 0, \\ S_{r0} &= 300, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0. \end{aligned}$$

In this case,

$$\mathcal{R}_{0u} > 1 \quad \text{and} \quad \mathcal{R}_{0r} \approx 2.$$

In Figure 3, we show $I_u(t)$ for different values of δ_{ru} . We show the solutions for both the urban and the rural patches when $\delta_{ru} = 0$ (i.e., when there is no population movement) and $\delta_{ru} = 0.01$ in Figure 4. We observe that population movement in one direction increases the number of infected individuals and that increasing the value of δ_{ru} affects only the speed of approach to a steady state.

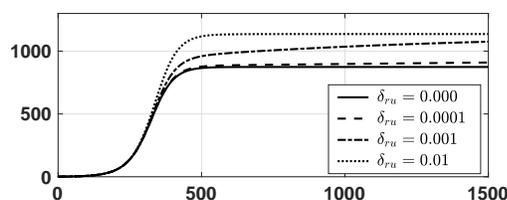


Figure 3: The number I_u of infected individuals in the urban patch as a function of time (in days) for $\delta_{ur} = 0$ and different values of δ_{ru} ; see Example 1. In this example, there is movement only from the rural patch to the urban one.

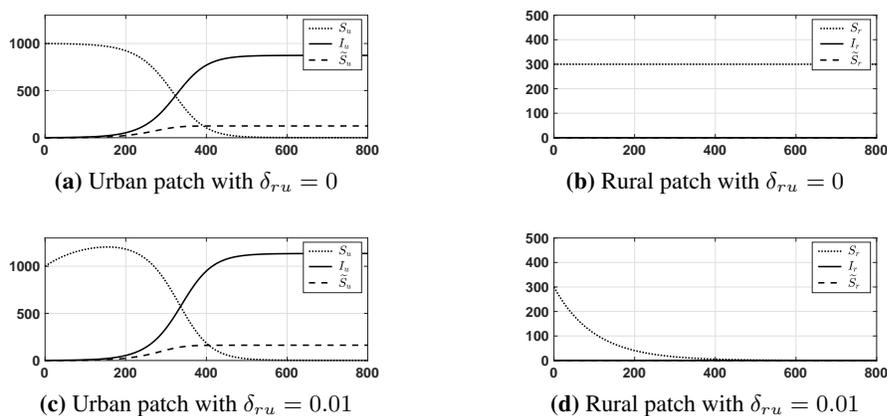


Figure 4: Effect of population movement in just one direction. In this scenario, $\delta_{ru} \neq 0$ and $\delta_{ur} = 0$, so there is movement only from the rural patch to the urban one; see Example 1. In these plots, we show the number of individuals in each state as a function of time (in days).

Example 2 We now compare the effects of conditions (5a) and (5b) to the standard condition $\mathcal{R}_0 < 1$ for local asymptotic stability of the disease-free steady state (2). We use the parameter values

$$\begin{aligned}\mu_u &= 1/(365 \cdot 80), & \rho_u &= 0.08, & \gamma_u &= 0.01, & \beta_u &= 3 \cdot 10^{-2}, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 0.40, & \gamma_r &= 0.10, & \beta_r &= 2 \cdot 10^{-5}\end{aligned}$$

and initial conditions

$$\begin{aligned}S_{u0} &= 999, & I_{u0} &= 1, & \tilde{S}_{u0} &= 0, \\ S_{r0} &= 300, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0.\end{aligned}$$

We calculate that $\mathcal{R}_{0u} \approx 2.9$ and $\mathcal{R}_{0r} \approx 2 \cdot 10^{-4}$. Therefore, in the absence of population movement, disease persists in the urban patch but dies out in the rural patch; see Figures 5a and 5b. For $\delta_{ur} = \delta_{ru} = 0.05$, we calculate that $\frac{\delta_{ur}}{\gamma_u + \mu} \approx 5.98$, so the conditions in (5) are satisfied. Therefore, the disease-free steady state is locally asymptotically stable; see Figures 5c and 5d.

In this example, there exists one endemic steady state, for which $\left(\frac{I_u^*}{N_u^*}, \frac{I_r^*}{N_r^*}\right) \approx (0.82, 0.76)$. We study two variations:

- (1) When the number of initially infected individuals is sufficiently large, we reach the endemic steady state. See Figure 6a for an illustration with initial conditions $S_{u0} = 900$ and $I_{u0} = 100$.
- (2) When we increase β_u slightly to $\beta_u = 5.3 \cdot 10^{-2}$, condition (5c) is no longer satisfied, and the system reaches an endemic steady state when we start with only a single infected individual in the urban patch; see Figure 6b.

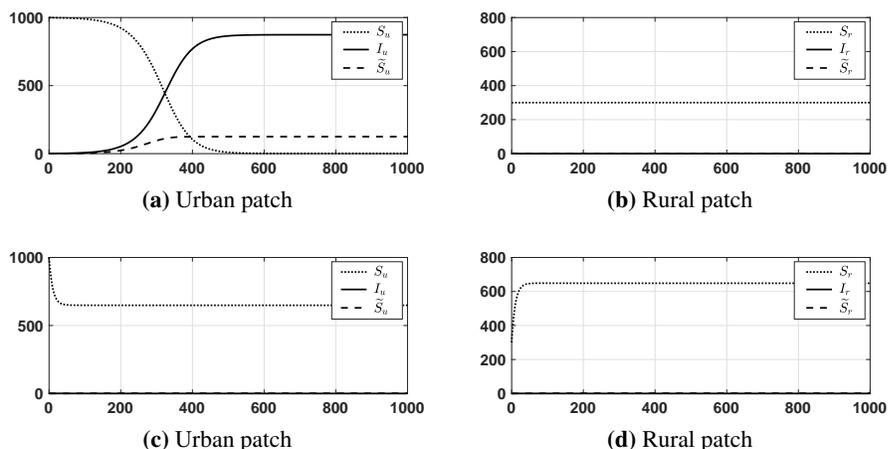


Figure 5: Illustration of the influence of population movement on disease dynamics in the urban and rural patches. (Top) In the absence of population movement (i.e., $\delta_{ur} = \delta_{ru} = 0$), the urban patch reaches an endemic state. (Bottom) For $\delta_{ur} = \delta_{ru} = 0.05$, both populations reach a disease-free steady state. In this sense, population movement allows the disease to die out; see Example 2. In these plots, we show the number of individuals in each state as a function of time (in days).

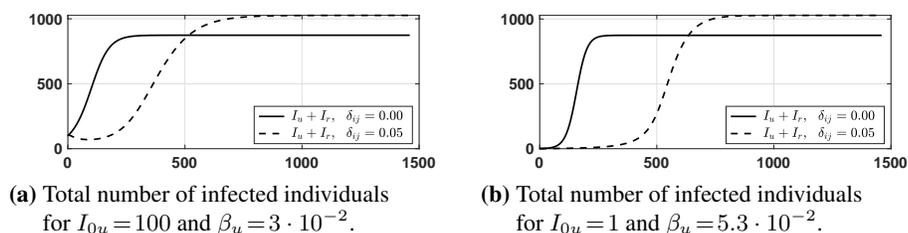


Figure 6: Effect of the conditions in (5) on infected classes of individuals; see Example 2. In these plots, the horizontal axis gives the time (in days).

Example 3 We now give an example with two endemic steady states. We use the parameter values

$$\mu_u = 1/(365 \cdot 70), \quad \rho_u = 0.80, \quad \gamma_u = 0.15, \quad \beta_u = 3 \cdot 10^{-4}, \quad \delta_{ur} = 0.04, \\ \mu_r = 1/(365 \cdot 70), \quad \rho_r = 0.40, \quad \gamma_r = 0.10, \quad \beta_r = 2 \cdot 10^{-5}, \quad \delta_{ru} = 0.05.$$

We fix the initial conditions

$$\begin{aligned} N_{u0} &= 1000, & \tilde{S}_{u0} &= 0, \\ N_{r0} &= 300, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0 \end{aligned}$$

and vary the initial number of infected individuals in the urban patch from 0 to N_u . In this case, there are two endemic steady states, with $(I_u^*/N_u^*, I_r^*/N_r^*) \approx (0.09, 0.07)$ and $(I_u^*/N_u^*, I_r^*/N_r^*) \approx (0.49, 0.45)$, which we illustrate in Figure 2b. We show I_u^* and I_r^* as a function of I_{0u} in Figure 7. The steady state $(I_u^*/N_u^*, I_r^*/N_r^*) \approx (0.09, 0.07)$ is unstable.

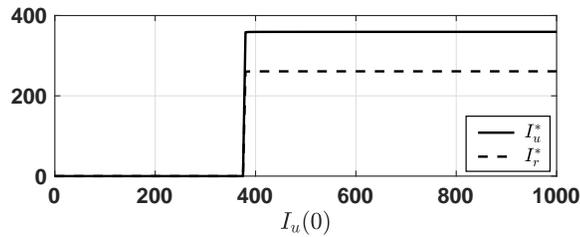


Figure 7: The number of infected individuals in the urban and rural patches at an endemic steady state as a function of the initial condition $I_u(0)$; see Example 3.

Example 4 In this example, we explore the dependence on \mathcal{R}_{0u} and \mathcal{R}_{0r} in our model to illustrate the region of local asymptotic stability from (5). We consider the parameter values

$$\begin{aligned} \mu_u &= 1/(365 \cdot 70), & \rho_u &= 0.80, & \gamma_u &= 0.01, & \delta_{ur} &= 0.005, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 0.40, & \gamma_r &= 0.05, & \delta_{ru} &= 0.010. \end{aligned}$$

We fix the initial conditions

$$\begin{aligned} N_{u0} &= 999, & I_{u0} &= 1, & \tilde{S}_{u0} &= 0, \\ N_{r0} &= 300, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0 \end{aligned}$$

and vary β_u and β_r ; see our results in Figure 8. We observe that the conditions in (5) precisely describe the disease-free region (in gray). Therefore, \mathcal{R}_{0u} or \mathcal{R}_{0r} can be slightly larger than 1 in situations with a disease-free steady state. This is not the case when we consider just one patch, so population movement can be beneficial.

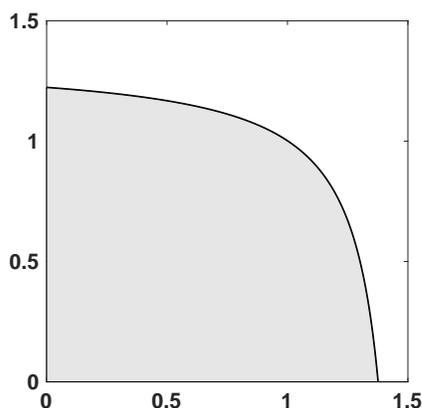


Figure 8: Population as a function of the local basic reproduction numbers in the urban \mathcal{R}_{0u} (horizontal axis) and rural \mathcal{R}_{0r} (vertical axis) environments; see Example 4. The gray area represents the region of local asymptotic stability of both (urban and rural) populations from Lemma 1.

Example 5 In this example, we study how a disease spreads through the two populations as we vary the movement parameters δ_{ur} and δ_{ru} when we start with a single infected individual in one patch and no infected individuals in the other patch. We consider the parameter values

$$\begin{aligned} \mu_u &= 1/(365 \cdot 70), & \rho_u &= 0.80, & \gamma_u &= 0.15, & \beta_u &= 3 \cdot 10^{-1}, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 0.40, & \gamma_r &= 0.10, & \beta_r &= 2 \cdot 10^{-3}. \end{aligned}$$

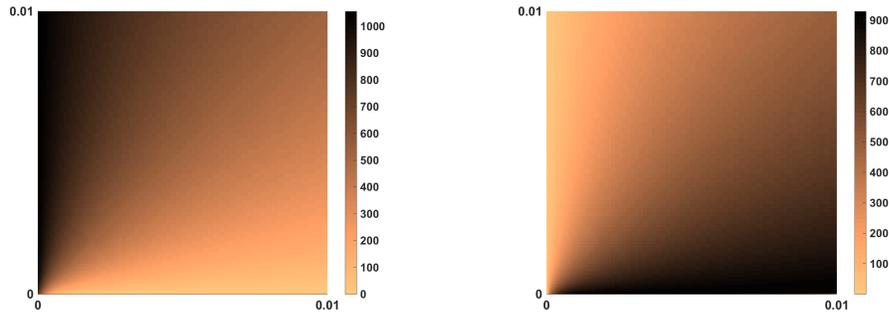
We fix the initial conditions

$$\begin{aligned} N_{u0} &= 99999, & I_{u0} &= 1, & \tilde{S}_{u0} &= 0, \\ N_{r0} &= 30000, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0 \end{aligned}$$

and vary δ_{ur} and δ_{ru} . We show our results in Figure 9.

Example 6 To model different population movement between patches on weekdays and weekends, we now take δ_{ur} and δ_{ru} to be piecewise-constant and periodic. Specifically, we use the functions $\delta_{ur}(t)$ and $\delta_{ru}(t)$ that we show in Figure 10. In Figure 11, we show the results of our numerical computations using the parameter values

$$\begin{aligned} \mu_u &= 1/(365 \cdot 70), & \rho_u &= 0.80, & \gamma_u &= 0.15, & \beta_u &= 3 \cdot 10^{-4}, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 0.40, & \gamma_r &= 0.10, & \beta_r &= 2 \cdot 10^{-5} \end{aligned}$$



(a) Steady-state fraction (I_u^*) of infected individuals in the urban patch.

(b) Steady-state fraction (I_r^*) of infected individuals in the rural patch.

Figure 9: The effect of a single infected individual in the urban patch as a function of the movement parameters δ_{ur} (horizontal axis) and δ_{ru} (vertical axis); see Example 5.

and initial conditions

$$\begin{aligned}
 N_{u0} &= 999, & I_{u0} &= 1, & \tilde{S}_{u0} &= 0, \\
 N_{r0} &= 300, & I_{r0} &= 0, & \tilde{S}_{r0} &= 0.
 \end{aligned}$$

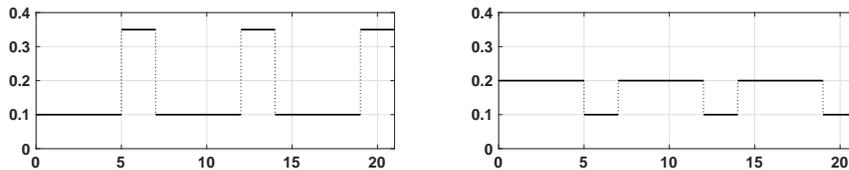


Figure 10: Periodic, piecewise-constant values of the movement parameters (left) δ_{ur} and (right) δ_{ru} as a function of time (in days). We use these functions in Example 6.

Example 7 We now revisit Remark 2, where we stated that we observe the existence of several distinct endemic steady states in our numerical computations. Equation (10) is equivalent to a polynomial equation (in (b_u, b_r)) of degree 9, for which there can exist at most 9 real solutions for (i_u^*, i_r^*) . For the parameter values

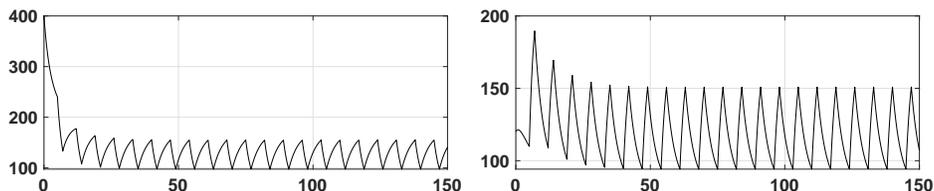


Figure 11: The number of infected individuals in the (left) urban (i.e., $I_u(t)$) and (right) rural (i.e., $I_r(t)$) populations as a function of time (in days) for the periodic, piecewise-constant movements δ_{ur} and δ_{ru} from Figure 10; see Example 6.

$$\begin{aligned} \mu_u &= 1/(365 \cdot 70), & \rho_u &= 1, & \gamma_u &= 0.15, & \beta_u &= 3 \cdot 10^{-4}, & \delta_{ur} &= 4 \cdot 10^{-6}, \\ \mu_r &= 1/(365 \cdot 70), & \rho_r &= 2, & \gamma_r &= 1.00, & \beta_r &= 2 \cdot 10^{-3}, & \delta_{ru} &= 5 \cdot 10^{-5}, \end{aligned}$$

we see that all 9 solutions are in $[0, 1]^2$. They correspond to feasible steady states (i_u^*, i_r^*) ; see Figure 12. We see numerically that 4 of these points are locally stable.

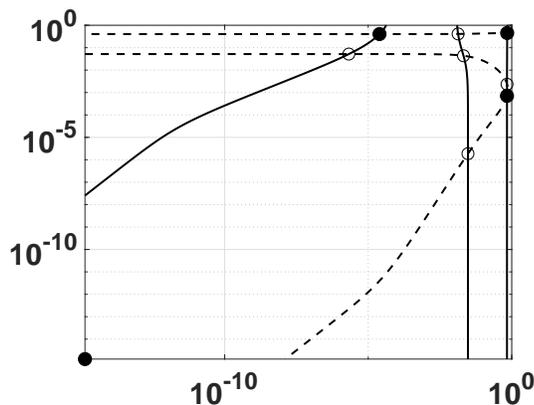


Figure 12: We illustrate the existence of multiple stable and unstable steady states of (1) that we obtain by solving (9). We plot the curves $G_1(i_u, i_r) = 0$ (solid curves) and $G_2(i_u, i_r) = 0$ (dashed curves). We observe numerically that there are 4 locally asymptotically stable steady states, illustrating that population movement between patches can introduce multiple steady states. We show the locally stable steady states with solid disks and the other steady states with open disks.

5 Conclusions and discussion

The dynamics of spreading diseases are influenced significantly by spatial heterogeneity and population movement. In this paper, we illustrated the importance of incorporating movement into models of disease dynamics using a simple but biologically meaningful model. Specifically, we constructed a two-patch compartmental model that incorporates (1) population movement between urban and rural patches and (2) the possibility of reinfection after recovery.

When there is sufficient movement, there are regions of local asymptotic stability of the disease-free steady-state even when the basic reproduction number $\mathcal{R}_{0j} > 1$ for $j \in \{u, r\}$. This arises predominantly from the numerous individuals who move between patches.

The exploration of interacting populations plays an important role in the understanding of disease dynamics. Many models of disease spreading focus on a single population [3], but populations do not exist in isolation. Using our two-patch model with urban and rural environments, we illustrated several examples of plausible real-world scenarios in which incorporating population movement yields insightful information about disease spreading and epidemics. We expect that such dynamics will be relevant for studies of disease spreading on networks, such as when many people commute daily between their homes in rural areas and work in urban centers (as is the case in many countries in South and Central America).

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A MATLAB Code for Example 4.1

```
1 % final time
2 T = 4*365;
3 % ODE initial conditions
4 Su0 = 999; Iu0 = 1; Ru0 = 0;
5 Sr0 = 300; Ir0 = 0; Rr0 = 0;
```

```

6  init_cond = [Su0;Iu0;Ru0;Sr0;Ir0;Rr0];
7  % ODE coefficients
8  dur = @(t) 0.05;
9  dru = @(t) 0.05;
10 mu = @(t) 1/(365*80);
11 mr = @(t) 1/(365*70);
12 pu = @(t) .08;
13 pr = @(t) .04;
14 gu = @(t) .01;
15 gr = @(t) .01;
16 bu = @(t) 0.03;
17 br = @(t) 0.02;
18
19 % define ODE
20 f1 = @(t,x) mu(t).*(x(1)+x(2)+x(3))-bu(t).*x(1).*x(2)
      ./ (x(1)+x(2)+x(3))-mu(t).*x(1)+dru(t).*x(4)-dur(t)
      .*x(1);
21 f2 = @(t,x) bu(t).*x(1).*x(2)./(x(1)+x(2)+x(3))-(mu(t)
      )+gu(t)).*x(2) + pu(t).*x(2).*x(3)./(x(1)+x(2)+x
      (3))+dru(t).*x(5)-dur(t).*x(2);
22 f3 = @(t,x) gu(t).*x(2)-pu(t).*x(2).*x(3)./(x(1)+x(2)
      +x(3))-mu(t).*x(3)+dru(t).*x(6)-dur(t).*x(3);
23 f4 = @(t,x) mr(t).*(x(4)+x(5)+x(6))-br(t).*x(4).*x(5)
      ./ (x(4)+x(5)+x(6))-mr(t).*x(4)+dur(t).*x(1)-dru(t)
      .*x(4);
24 f5 = @(t,x) br(t).*x(4).*x(5)./(x(4)+x(5)+x(6))-(mr(t)
      )+gr(t)).*x(5) + pr(t).*x(5).*x(6)./(x(4)+x(5)+x
      (6))+dur(t).*x(2)-dru(t).*x(5);
25 f6 = @(t,x) gr(t).*x(5)-pr(t).*x(5).*x(6)./(x(4)+x(5)
      +x(6))-mr(t).*x(6)+dur(t).*x(3)-dru(t).*x(6);
26 ff = @(t,x) [f1(t,x);f2(t,x);f3(t,x);f4(t,x);f5(t,x);
      f6(t,x)];
27 % options for ode solver
28 options = odeset('RelTol',1e-10,'Stats','off','AbsTol
      ',1e-10);
29 % solve ODE
30 [tout,xout] = ode45(ff,[0,T],init_cond,options);
31
32 figure

```

```

33 % plot solution for urban patch
34 subplot(3,1,1)
35 plot(tout,xout(:,1),'k'), hold on
36 plot(tout,xout(:,2),'-k')
37 plot(tout,xout(:,3),'-k')
38 legend({'$S_u$', '$I_u$', '$\widetilde{S}_u$'},
        'Interpreter','Latex')
39 title('Urban')
40 axis([0 T 0 1000])
41 grid on
42 % plot solution for rural patch
43 subplot(3,1,2)
44 plot(tout,xout(:,4),'k'), hold on
45 plot(tout,xout(:,5),'-k')
46 plot(tout,xout(:,6),'-k')
47 legend({'$S_r$', '$I_r$', '$\widetilde{S}_r$'},
        'Interpreter','Latex')
48 title('Rural')
49 axis([0 T 0 1000])
50 grid on

```

References

- [1] L. Alvarado, *Costa Rica once again under malaria alert*, The Costa Rica Star, 2018. Available at <https://news.co.cr/costa-rica-once-again-under-malaria-alert/73681>, accessed 25/04/2019.
- [2] D. Bichara, C. Castillo-Chavez, *Vector-borne diseases models with residence times — A Lagrangian perspective*, Math. Biosci. **281**(2016), 128–138. doi: 10.1016/j.mbs.2016.09.006
- [3] F. Brauer, C. Castillo-Chavez, *Mathematical Models in Population Biology and Epidemiology*, 2nd edition, Springer-Verlag, Providence RI, USA, 2012.
- [4] Center for Disease Control and Prevention, *Severe acute respiratory system (SARS)*, 2019. Available at <https://www.cdc.gov/sars/index.html>

- [5] Center for Disease Control and Prevention, *Ebola (Ebola virus disease)*, 2019. Available at <https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html>
- [6] Center for Disease Control and Prevention, *Measles (Rubeola)*, 2019. Available at <https://www.cdc.gov/measles/index.html>
- [7] G. Chowell, P.W. Fenimore, M.A. Castillo-Garsow C. Castillo-Chavez, *SARS outbreaks in Ontario, Hong Kong and Singapore: The role of diagnosis and isolation as a control mechanism*, *J. Theor. Biol.* **224**(2003), no. 1, 1–8. doi: 10.1016/S0022-5193(03)00228-5
- [8] M.P. Coffee, G.P. Garnett, M. Mlilo, H.A.C.M. Voeten, S. Chandiwana, S. Gregson, *Patterns of movement and risk of HIV Infection in rural Zimbabwe*, *J. Infect. Dis.* **191**(2005), no. 1, S159–S167. doi: 10.1086/425270
- [9] J.M. Crutcher, S.L. Hoffman, *Malaria*, in: S. Baron (Ed.) *Medical Microbiology*, 4th edition, University of Texas Medical Branch at Galveston, Galveston TX, 1996, ch. 83. Available in: <https://www.ncbi.nlm.nih.gov/books/NBK8584/>
- [10] R. DeVore, A. Ron, *Approximation of functions*, *Proc. Sympos. Appl. Math.* **36**(1986), 34–56.
- [11] Z. Feng, J. X. Velasco-Hernández, *Competitive exclusion in a vector–host model for the dengue fever*, *J. Math. Biol.* **35**(1997), no. 5, 523–544. doi: 10.1007/s002850050064
- [12] Z. Feng, C. Castillo-Chavez, A. F. Capurro, *A model for tuberculosis with exogenous reinfection*, *Theor. Popul. Biol.* **57**(2000), no. 3, 235–247. doi: 10.1006/tpbi.2000.1451
- [13] H. Frankowska, *The Poincaré–Miranda theorem and viability condition*, *J. Math. Anal. Appl.* **463**(2018), no. 2, 832–837. doi: 10.1016/j.jmaa.2018.03.047
- [14] J. Gjorgjieva, K. Smith, G. Chowell, F. Sanchez, J. Snyder, C. Castillo-Chavez, *The role of vaccination in the control of SARS*, *Math. Biosci. Eng.* **2**(2005), no. 4, 753–769. doi: 10.1006/tpbi.2000.1451

- [15] J.R. Glynn, J. Murray, A. Bester, G. Nelson, S. Shearer, P. Sonnenberg, *Effects of duration of HIV infection and secondary tuberculosis transmission on tuberculosis incidence in the South African gold mines*, *AIDS* **22**(2008), no. 14, 1859–1867. doi: 10.1097/QAD.0b013e3283097cfa
- [16] J.L. Grun, W.P. Weidanz, *Antibody-independent immunity to reinfection malaria in B-cell-deficient mice*, *Infect. and Immun.* **41**(1983), no. 3, 1197–1204.
- [17] W. Kulpa, *The Poincaré–Miranda theorem*, *Amer. Math. Month.* **104**(1997), no. 6, 545–550. doi: 10.2307/2975081
- [18] S. Lee, C. Castillo-Chavez, *The role of residence times in two-patch dengue transmission dynamics and optimal strategies*, *J. Theor. Biol.* **374**(2015), no. 7, 152–164. doi: 10.1016/j.jtbi.2015.03.005
- [19] C.A. Manore, K.S. Hickmann, S. Xu, H.J. Wearing, J.M. Hyman, *Comparing dengue and chikungunya emergence and endemic transmission in A. aegypti and A. albopictus*, *J. Theor. Biol.* **356**(2014), 174–191. doi: 10.1016/j.jtbi.2014.04.033
- [20] P. Martens, L. Hall, *Malaria on the move: Human population movement and malaria transmission*, *Emerg. Infect. Diseas.* **6**(2000), no. 2, 103–109. doi: 10.3201/eid0602.000202
- [21] D. Murillo, S. Holechek, A. Murillo, F. Sanchez, C. Castillo-Chavez, *Vertical transmission in a two-strain model of dengue fever*, *Lett. Biomath.* **1**(2014), no. 2, 249–271. doi: 10.1080/23737867.2014.11414484
- [22] R. Pastor-Satorras, C. Castellano, P. van Mieghem, A. Vespignani, *Epidemic processes in complex networks*, *Rev. Mod. Phys.* **87**(2015), no. 3, 925–979.
- [23] F. Sanchez, M. Engman, L.C. Harrington, C. Castillo-Chavez, *Models for dengue transmission and control*, in: A.B. Gumel, C. Castillo-Chavez, R.E. Mickens & D.P. Clemence (Eds.) *Mathematical Studies on Human Disease Dynamics. Emerging Paradigms and Challenges*, *Contemp. Math.* **410**, Amer. Math. Soc., Providence RI, USA, 2006, pp. 311–326. doi: 10.1090/conm/410/07734

- [24] F. Sanchez, X. Wang, C. Castillo-Chavez, D. Gorman, P.J. Gruenewald, *Drinking as an epidemic — A simple mathematical model with recovery and relapse*, in: K.A. Witkiewitz & G.A. Marlatt (Eds.) *Therapist's Guide to Evidence-Based Relapse Prevention*, Academic Press, Cambridge, MA, USA, 2007, pp. 353–368. doi: 10.1016/B978-012369429-4/50046-X
- [25] F. Sanchez, D. Murillo, C. Castillo-Chavez, *Change in host behavior and its impact on the transmission dynamics of dengue*, in: R.P. Mondaini (Ed.) *International Symposium on Mathematical and Computational Biology, BIOMAT 2011 (Santiago, Chile), 2012*, pp. 191–203. doi: https://doi.org/10.1142/9789814397711_0013
- [26] F. Sanchez, J. G. Calvo, E. Segura, Z. Feng, *A partial differential equation model with age-structure and nonlinear recidivism: Conditions for a backward bifurcation and a general numerical implementation*, *Computers and Mathematics with Applications* 78(2018), no. 12, 3916–3930. doi: 10.1016/j.camwa.2019.06.021
- [27] B. Song, M. Castillo-Garsow, K.R. Rios-Soto, M. Mejran, L. Henso, C. Castillo-Chavez, *Raves, clubs and ecstasy: The impact of peer pressure*, *Math. Biosci. Eng.* 3(2006), no. 1, 249–266. doi: 10.3934/mbe.2006.3.249
- [28] B. Song, W. Du, J. Lou, *Different types of backward bifurcations due to density-dependent treatments*, *Math. Biosci. Eng.* 10(2013), no. 5–6, 1651–1668. doi: 10.3934/mbe.2013.10.1651
- [29] K. Szymańska-Dębowska, *On a generalization of the Miranda Theorem and its application to boundary value problems*, *J. Diff. Equ.* 258(2015), no. 8, 2686–2700. doi: 10.1016/j.jde.2014.12.022
- [30] A.J. Treno, P.J. Gruenewald, L.G. Remer, F. Johnson, E.A. LaScala, *Examining multi-level relationships between bars, hostility and aggression: Social selection and social influence*, *Addiction* 103(2007), no. 1, 66–77. doi: 10.1111/j.1360-0443.2007.02039.x
- [31] M. Turzánski, *The Bolzano–Poincaré–Miranda theorem — Discrete version*, *Topol. Appl.* 159(2012), no. 13, 3130–3135. doi: 10.1016/j.topol.2012.05.026