ORIGINAL ARTICLE

Impact of Travel Between Patches for Spatial Spread of Disease

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Abstract A multipatch model is proposed to study the impact of travel on the spatial spread of disease between patches with different level of disease prevalence. The basic reproduction number for the ith patch in isolation is obtained along with the basic reproduction number of the system of patches, $\mathcal{R}_0$. Inequalities describing the relationship between these numbers are also given. For a two-patch model with one high prevalence patch and one low prevalence patch, results pertaining to the dependence of $\mathcal{R}_0$ on the travel rates between the two patches are obtained. For parameter values relevant for influenza, these results show that, while banning travel of infectives from the low to the high prevalence patch always contributes to disease control, banning travel of symptomatic travelers only from the high to the low prevalence patch could adversely affect the containment of the outbreak under certain ranges of parameter values. Moreover, banning all travel of infected individuals from the high to the low prevalence patch could result in the low prevalence patch becoming diseasefree, while the high prevalence patch becomes even more disease-prevalent, with the resulting number of infectives in this patch alone exceeding the combined number of infectives in both patches without border control. Under the set of parameter values used, our results demonstrate that if border control is properly implemented, then it could contribute to stopping the spatial spread of disease between patches.

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1. Introduction

The H5N1 avian influenza, which has been circulating in Asia since late 2003, has jumped to Africa and the Middle East and spread through Europe, affecting bird populations in these regions. By early August 2006, this virus has caused at least 235 human infections and 137 deaths around the world (WHO, 2006). Seasonal bird migration alone probably cannot explain the westward spread in Europe, so imports of poultry and pet birds must also be considered as factors that might lead to the spread of H5N1 through countries and continents (Butler, 2006). Furthermore, its initial appearance on the African continent marks a huge leap in its geographical range, and opens up a whole new front where the vast bird reservoir could potentially spark a pandemic of human-to-human infections.

The 2003 severe acute respiratory syndrome (SARS) global epidemic demonstrated the ability due to modern globalization of infectious disease spreading to countries in several continents within a matter of days. In its aftermath and with the potential threat of a flu pandemic, several models describing spatial spread of infectious diseases have been proposed. These include the use of general compartmental models incorporating multiple patches (cities, countries, etc.) to explore the dynamics of spatial spread of disease (see, for example, Arino and van den Driessche, 2003, 2006; Wang and Mulone, 2003; Wang and Zhao, 2004; Arino et al., 2005; Salmani and van den Driessche, 2006). Examples of specific human infectious diseases modeled in this way include influenza (Hyman and LaForce, 2003);(Sattenspiel and Herring, 2003)and SARS (Ruan et al., 2006)In addition, patch models for animal diseases include foot-and-mouth disease (Chowell et al., 2006)and tuberculosos in possums (Fulford et al., 2002)

In this work, we propose a multipatch model to study the spread of influenza among the patches. We add a subpopulation of partially immune individuals to account for this important feature of influenza. Although the model is intended to be used for theoretical studies of the spread of human-to-human influenza, it can also be used as a model for studying the spread of enzootic diseases such as avian flu among birds. Partial immunity might not be important for studies of infectious disease involving poultry bird populations where the birds are slaughtered for food after a fixed time. It nonetheless could be an important consideration for studies involving wild bird populations.

The paper is organized as follows. We formulate the model in Section 2, and in Section 3, we give results regarding the basic reproduction number of the model. In Section 4, some global analysis is obtained for the model with two patches. Numerical simulations, with parameter values relevant for influenza, to complement our analytical results are given in Section 5. In Section 6, we focus our discussion on the impact of travel between high contact patches (e.g., school, hospital, urban center) and low contact patches (e.g., general community, rural area) on the spatial spread of disease.

2. Model formulation

In this section, we formulate a model describing the spread of a disease in a population with n patches taking into consideration travel among patches (Arino and van

den Driessche, 2006) and also including partially immune individuals (Hyman and LaForce, 2003). The population in patch i is divided into compartments of susceptible, incubating (infected but not yet showing symptoms), infective (infected with symptoms), recovered, and partially immune individuals. Let S_i, E_i, I_i, R_i, P_i denote, respectively, the associated population size. Then, the total population size in patch i is $N_i = S_i + E_i + I_i + R_i + P_i$ for $i = 1, 2, \ldots, n$. A partially immune compartment between the recovered and the susceptible compartments is introduced in an influenza model (Hyman and LaForce, 2003) to account for people who have partial immunity to the current strain of influenza from a previous infection by an earlier strain. We include this partially immune compartment, and assume that individuals in this compartment may become infected again (but with a reduced rate). Also, the partial immunity wanes, with these individuals returning to the susceptible compartment.

For patch i, let A_i be the recruitment, α_i, γ_i, δ_i, and η_i be the progression rates of the incubating, infective, recovered, and partially immune individuals, respectively, d_i be the natural death rate, and ϵ_i be the disease-related death rate. All parameters are assumed to be positive except that $\epsilon_i, \delta_i, \eta_i$ can be zero. We assume that individuals do not change their disease state during travel, and m_{ij}^K for $K = S, E, I, R, P$ are the constant travel rates from patch j to patch i for $i \neq j$ of susceptible, incubating, infective, recovered, and partially immune individuals, respectively, with $m_{ii}^K = 0$. The rate m_{ij}^K can be thought of as the probability per day that an individual of disease state K travels from patch j to patch i. The travel rate matrices $M^K = [m_{ij}^K]$ for $K = S, E, I, R, P$ are assumed irreducible (in Section 6, the consequence of some of these being reducible is examined).

The number of new individuals infected by infectives per unit time in patch i is given by $\beta_i(N_i) S_i I_i$. The term $\beta_i(N_i) S_i$ is the product of $\beta_i(N_i) N_i$, the average number of contacts made by each individual in patch i per unit time, and $\frac{S_i}{N_i}$, the proportion of susceptibles. It is assumed that infectivity $\beta_i(N_i)$ is a continuously differentiable, nonincreasing function of N_i with $\beta_i(0)$ finite. Note that the above assumptions encompass the widely used mass action and standard incidence disease transmission terms defined for $N_i > 0$ as well as many other forms of saturating incidence. Reduced transmissibility of incubating individuals toward susceptible individuals, and reduced infectivity of infectious individuals toward partially immune individuals are given by $\sigma_i \beta_i(N_i)$ and $\nu_i \beta_i(N_i)$, respectively, where $\sigma_i, \nu_i \in [0, 1)$. It is also assumed that incubating and infective individuals can reinfect those who are partially immune. The model flow chart for patch i omitting natural death and travel is given in Fig. 1. The above assumptions lead to the following SEIRP model for $i = 1, 2, \ldots, n$:

$$\frac{dS_i}{dt} = A_i - \beta_i(N_i) S_i (I_i + \sigma_i E_i) - d_i S_i + \eta_i P_i + \sum_{j=1}^{n} m_{ij}^S S_j - \sum_{j=1}^{n} m_{ji}^S S_i,$$

$$\frac{dE_i}{dt} = \beta_i(N_i)(S_i + \nu_i P_i)(I_i + \sigma_i E_i) - (d_i + \alpha_i) E_i + \sum_{j=1}^{n} m_{ij}^E E_j - \sum_{j=1}^{n} m_{ji}^E E_i,$$
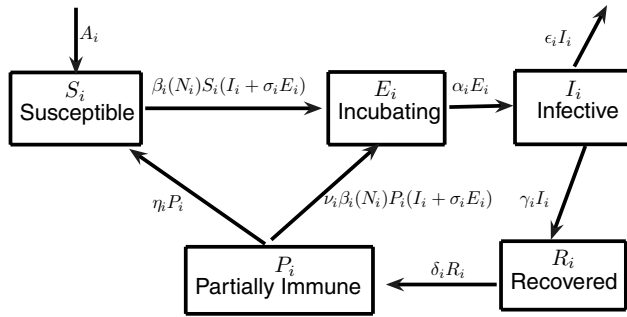
Fig. 1   Flow diagram of the SEIRP model.

$$\frac{\mathrm{d}I_i}{\mathrm{d}t} = \alpha_i E_i - (\gamma_i + \varepsilon_i + d_i)I_i + \sum_{j=1}^{n} m_{ij}^I I_j - \sum_{j=1}^{n} m_{ji}^I I_i,$$

$$\frac{\mathrm{d}R_i}{\mathrm{d}t} = \gamma_i I_i - (d_i + \delta_i)R_i + \sum_{j=1}^{n} m_{ij}^R R_j - \sum_{j=1}^{n} m_{ji}^R R_i,$$

$$\frac{\mathrm{d}P_i}{\mathrm{d}t} = \delta_i R_i - (d_i + \eta_i)P_i - \nu_i \beta_i(N_i)P_i(I_i + \sigma_i E_i)$$

$$+ \sum_{j=1}^{n} m_{ij}^P P_j - \sum_{j=1}^{n} m_{ji}^P P_i. \tag{1}$$

Initially, each variable is assumed to be nonnegative with $S_i(0) > 0$ and $\sum_{i=1}^{n} E_i(0) + I_i(0) > 0$. It follows that for a given set of nonnegative initial conditions, there is a unique solution to system (1). The total population size in all n patches is $N(t) = \sum_{i=1}^{n} N_i(t)$. Let $\bar{d} = \min\{d_1, d_2, \ldots, d_n\}$ and $\mathcal{A} = \sum_{i=1}^{n} A_i$. Then, the following result, which can be proved in a similar way to that of Theorem 1.1 in Salmani and van den Driessche (2006), indicates that the model is well posed and all variables remain nonnegative and bounded.

Theorem 2.1.   *Consider system (1) with nonnegative initial conditions satisfying $S_i(0) > 0$ and $\sum_{i=1}^{n} E_i(0) + I_i(0) > 0$. Then for each $i = 1, 2, \ldots, n$, $E_i(t)$, $I_i(t)$, $R_i(t)$, $P_i(t)$ remain nonnegative, $S_i(t)$ and $N_i(t)$ remain positive, and the total population $N(t)$ is in the interval $(0, \max\{\mathcal{A}/\bar{d}, N(0)\}]$.*

Notice that our patch model is an extension of those in Arino and van den Driessche (2006) and Salmani and van den Driessche (2006). It includes a new compartment, namely, partially immune individuals in each patch, and also the probability of disease transmission by incubating individuals. These additional features may be important for modeling diseases such as influenza. In Hyman and LaForce (2003), which does not include an incubating compartment in a model for the spread of influenza, travel is assumed to be independent of disease status and symmetric. Moreover, the disease does not cause death, and the

population of each patch remains constant. Notice also that our patch model keeps track of individuals present in patch i at time t, but does not keep track of where an individual resides. Models that include this are developed in Arino and van den Driessche (2003, 2006) and Sattenspiel and Herring (2003). In addition, Ruan et al. (2006) use such a model to study the effect of travel on the spread of SARS. Wang and Zhao (2006) study the spatial dispersal of disease by proposing a 2-patch SIR model with mass action incidence and a constant infectious period.

3. The basic reproduction number

In this section, we derive a formula to compute the basic reproduction number $\mathcal{R}_0$ for the general model, represented by Eq. (1), and then give a lower bound for $\mathcal{R}_0$. Both lower and upper bounds of $\mathcal{R}_0$ are given for a special case.

A diseasefree equilibrium (DFE) is a steady state solution of the system, represented by Eq. (1), with $S_i = N_i^* > 0$ and all other variables E_i, I_i, R_i, P_i equal to 0 for $i = 1, 2, \ldots, n$. Let $S^* = (N_1^*, N_2^*, \ldots, N_n^*)^{\mathrm{T}}$. Then from the first equation in Eq. (1), there is a DFE if and only if S^* satisfies $CS^* = A$ with $A = (A_1, A_2, \ldots, A_n)^{\mathrm{T}}$ and $C = D - M^S$, where $D = \mathrm{diag}(\sum_{j=1}^n m_{ji}^S + d_i)$. Note that C, which involves the travel of susceptibles, is irreducible, has positive column sums $d_1, d_2, \ldots, d_n$, and negative off-diagonal entries. Thus, C is a nonsingular M-matrix (p. 141, Berman and Plemmons (1979)), and therefore $C^{-1} > 0$. Hence $S^* = C^{-1}A > 0$ is the unique solution of $CS^* = A$. This shows that the DFE always exists and is unique. In the absence of disease, the system, represented by Eq. (1), reduces to just the first equation and S^* is stable.

Next, we consider the local stability of the DFE for the system, represented by Eq. (1). To this end, we order the infected variables by $E_1, E_2, \ldots, E_n, I_1, I_2, \ldots, I_n$ and make use of the result in van den Driessche and Watmough (2002) to obtain

$$F = \begin{bmatrix} F_{11} & F_{12} \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} \mathrm{diag}(\sigma_i \beta_i(N_i^*)N_i^*) & \mathrm{diag}(\beta_i(N_i^*)N_i^*) \\ 0 & 0 \end{bmatrix},$$

with

$$V = \begin{bmatrix} V_{11} & 0 \\ -V_{21} & V_{22} \end{bmatrix},$$

where

$$V_{11} = \mathrm{diag}\left(d_i + \alpha_i + \sum_{j=1}^n m_{ji}^E \right) - M^E,$$

$$V_{22} = \mathrm{diag}\left(\gamma_i + \epsilon_i + d_i + \sum_{j=1}^n m_{ji}^I \right) - M^I,$$

$$V_{21} = \mathrm{diag}(\alpha_i), \quad i = 1, 2, \ldots, n.$$

Note that V_{11} and V_{22} are both irreducible nonsingular $M-$matrices with positive column sums and hence

$$V_{11}^{-1} > 0, \quad V_{22}^{-1} > 0. \tag{2}$$

The basic reproduction number for the system, denoted by $\mathcal{R}_0$ is then the spectral radius of FV^{-1}, i.e., $\mathcal{R}_0 = \rho\{FV^{-1}\}$ where

$$FV^{-1} = \begin{bmatrix} F_{11} & F_{12} \\ 0 & 0 \end{bmatrix} \begin{bmatrix} V_{11}^{-1} & 0 \\ V_{22}^{-1} V_{21} V_{11}^{-1} & V_{22}^{-1} \end{bmatrix}.$$

Therefore,

$$\mathcal{R}_0 = \rho\left(F_{11} V_{11}^{-1} + F_{12} V_{22}^{-1} V_{21} V_{11}^{-1}\right). \tag{3}$$

The first term accounts for infection from incubating individuals, while the second term accounts for infection from infective individuals who survive the incubating compartment. Travel rates of infectious individuals influence the average time spent in the incubating and infective compartments. Note that $\mathcal{R}_0$ does not depend on the parameters v_i, δ_i, η_i for $i = 1, 2, \ldots, n$, nor on the travel rates of recovered and partially immune individuals.

The basic reproduction number gives an important threshold for the disease, as shown in the following result.

Theorem 3.1. *Consider the model, represented by Eq. (1). If $\mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable and if $\mathcal{R}_0 > 1$, the DFE is unstable. Moreover, if the disease transmission is standard incidence, then the DFE is globally asymptotically stable provided that $\mathcal{R}_0 < 1$.*

Proof. It follows from Theorem 2 of van den Driessche and Watmough (2002) that the DFE is locally asymptotically stable if $\mathcal{R}_0 < 1$ and is unstable if $\mathcal{R}_0 > 1$. If the disease transmission is standard incidence, then $\beta_i(N_i)N_i = \beta_i$ for $i = 1, 2, \ldots, n$. Note that $S_i + v_i P_i \leq N_i$. This gives the inequality

$$\frac{\mathrm{d}E_i}{\mathrm{d}t} \leq \beta_i(I_i + \sigma_i E_i) - (d_i + \alpha_i)E_i + \sum_{j=1}^n m_{ij}^E E_j - \sum_{j=1}^n m_{ji}^E E_i.$$

Consider the linear system

$$\frac{\mathrm{d}E_i}{\mathrm{d}t} = \beta_i(I_i + \sigma_i E_i) - (d_i + \alpha_i)E_i + \sum_{j=1}^n m_{ij}^E E_j - \sum_{j=1}^n m_{ji}^E E_i,$$

$$\frac{\mathrm{d}I_i}{\mathrm{d}t} = \alpha_i E_i - (\gamma_i + \varepsilon_i + d_i)I_i + \sum_{j=1}^n m_{ij}^I I_j - \sum_{j=1}^n m_{ji}^I I_i. \tag{4}$$

The right-hand side of the above system has $F - V$ as its coefficient matrix. Again, by proof of Theorem 2 of van den Driessche and Watmough (2002), each eigenvalue of $F - V$ has negative real part if $\mathcal{R}_0 < 1$. Thus, any solution of Eq. (4) satisfies $\lim_{t \to \infty} E_i = 0$ and $\lim_{t \to \infty} I_i = 0$ for $i = 1, 2, \ldots, n$. Using a comparison

theorem (Theorem B.1, Smith and Waltman, 1995), each solution of the system, represented by Eq. (1), satisfies $\lim_{t \to \infty} E_i = 0$ and $\lim_{t \to \infty} I_i = 0$ for $i = 1, 2, \ldots, n$. Using a similar argument as in the proof of Theorem 2.2, Salmani and van den Driessche (2006), $\lim_{t \to \infty} R_i(t) = 0$, and similarly $\lim_{t \to \infty} P_i(t) = 0$. Thus the DFE is globally asymptotically stable provided that $\mathcal{R}_0 < 1$. ∎

Let $a_i = \gamma_i + \epsilon_i + d_i$ and $c_i = d_i + \alpha_i$ for $i = 1, 2, \ldots, n$. In the rest of the paper, we assume standard incidence disease transmission, namely, $\beta_i(N_i) = \frac{\beta_i}{N_i}$ giving $\beta_i(N_i)N_i = \beta_i > 0$. In the case that there is no travel between patch i and all other patches, the basic reproduction number in patch i in isolation is given by

$$\mathcal{R}_0^{(i)} = \frac{\sigma_i \beta_i}{c_i} + \frac{\beta_i \alpha_i}{a_i c_i}. \tag{5}$$

We define a modified reproduction number (modified by travel of infecteds out of patch i) in patch i,

$$\widetilde{\mathcal{R}}_0^{(i)} = \frac{\sigma_i \beta_i}{c_i + \sum_{j=1}^{n} m_{ji}^E} + \frac{\beta_i \alpha_i}{\left(c_i + \sum_{j=1}^{n} m_{ji}^E\right)\left(a_i + \sum_{j=1}^{n} m_{ji}^I\right)} < \mathcal{R}_0^{(i)}. \tag{6}$$

The following result gives bounds for the basic reproduction number for the system, represented by Eq. (1), in terms of the numbers defined in Eqs. (5) and (6) for each patch.

Theorem 3.2. *For the system, represented by Eq. (1),*

$$\mathcal{R}_0 \geq \max_{1 \leq i \leq n} \widetilde{\mathcal{R}}_0^{(i)}. \tag{7}$$

Furthermore, if $a_i = a, \alpha_i = \alpha, \sigma_i = \sigma$, and $d_i = d$ for $i = 1, 2, \ldots, n$, then

$$\max\left(\max_{1 \leq i \leq n} \widetilde{\mathcal{R}}_0^{(i)}, \min_{1 \leq i \leq n} \mathcal{R}_0^{(i)}\right) \leq \mathcal{R}_0 \leq \max_{1 \leq i \leq n} \mathcal{R}_0^{(i)}. \tag{8}$$

Proof. For $j = 1, 2$, let $V_{jj}[1']$ denote the matrix V_{jj} with row and column 1 deleted, $Y = [y_{ij}]$ and $Z = [z_{ij}]$ denote V_{11}^{-1} and V_{22}^{-1}, respectively. Let $W = [w_{ij}] = G + H$, where $G = [g_{ij}] = F_{11}Y$, $H = [h_{ij}] = F_{12}ZV_{21}Y$. It follows from (2) that $y_{ij} > 0, z_{ij} > 0$ for $i, j = 1, 2, \ldots, n$. Then, by Corollary 8.1.20 in Horn and Johnson (1985),

$$\mathcal{R}_0 = \rho(W) \geq w_{ii} = g_{ii} + h_{ii} \quad \text{for } i = 1, 2, \ldots, n.$$

Note that $g_{11} = \sigma_1 \beta_1 y_{11} = \sigma_1 \beta_1 \frac{\det V_{11}[1']}{\det V_{11}}$. By virtue of Fischer's inequality (p. 117, Horn and Johnson, 1991), it follows that

$$\det V_{11} \leq \left(c_1 + \sum_{j=1}^{n} m_{j1}^E\right) \det V_{11}[1'].$$

Therefore,

$$g_{11} \geq \frac{\sigma_1 \beta_1}{c_1 + \sum_{j=1}^{n} m_{j1}^{E}}.$$

Similarly,

$$h_{11} = \beta_1 \alpha_1 z_{11} y_{11} + \sum_{k=2}^{n} \beta_1 \alpha_k z_{1k} y_{k1}.$$

Thus,

$$h_{11} \geq \beta_1 \alpha_1 z_{11} y_{11} = \beta_1 \alpha_1 \frac{\det V_{22}[1']}{\det V_{22}} \frac{\det V_{11}[1']}{\det V_{11}}.$$

Again, by Fischer's inequality, it follows that

$$h_{11} \geq \frac{\beta_1 \alpha_1}{\left(c_1 + \sum_{j=1}^{n} m_{j1}^{E}\right) \left(a_1 + \sum_{j=1}^{n} m_{j1}^{I}\right)}.$$

Adding these shows that

$$\mathcal{R}_0 \geq \widetilde{\mathcal{R}}_0^{(1)}.$$

Similarly, it can be shown that

$$\mathcal{R}_0 \geq \widetilde{\mathcal{R}}_0^{(i)} \quad \text{for } i = 2, 3, \ldots, n$$

and this gives Eq. (7).

If $a_i = a$, $\alpha_i = \alpha$, $\sigma_i = \sigma$, and $d_i = d$ (thus $c_i = c$) for $i = 1, 2, \ldots, n$, then $w_{ij} = \sigma \beta_i y_{ij} + \alpha \beta_i \sum_{k=1}^{n} z_{ik} y_{kj}$ for $i, j = 1, 2, \ldots, n$. Without loss of generality, assume that $0 < \beta_1 \leq \beta_2 \leq \ldots \leq \beta_n$. From the fact that the matrix V_{11} has each column sum equal to $c > 0$ and the matrix V_{22} has each column sum equal to $a > 0$, it follows that $\sum_{i=1}^{n} y_{ij} = \frac{1}{c}$, $\sum_{i=1}^{n} z_{ij} = \frac{1}{a}$ for $j = 1, 2, \ldots, n$. Therefore, for the matrix W, the sum of column j is given by

$$\sum_{i=1}^{n} w_{ij} = \sum_{i=1}^{n} \sigma \beta_i y_{ij} + \sum_{i=1}^{n} \alpha \beta_i \sum_{k=1}^{n} z_{ik} y_{kj}$$

$$\leq \sigma \beta_n \sum_{i=1}^{n} y_{ij} + \alpha \beta_n \sum_{i=1}^{n} \sum_{k=1}^{n} z_{ik} y_{kj}$$

$$= \sigma \beta_n \sum_{i=1}^{n} y_{ij} + \alpha \beta_n \sum_{k=1}^{n} \left(\sum_{i=1}^{n} z_{ik}\right) y_{kj}$$

$$= \frac{\sigma \beta_n}{c} + \frac{\alpha \beta_n}{ac}$$

$$= \mathcal{R}_0^{(n)}.$$

Similarly, $\sum_{i=1}^{n} w_{ij} \geq \frac{\sigma \beta_1}{c} + \frac{\alpha \beta_1}{ac} = \mathcal{R}_0^{(1)}$. From Theorem 8.1.22 in Horn and Johnson (1985), $\rho(W)$ lies between the minimum and maximum column sums of W. Thus,

$$\min_{1 \leq i \leq n} \mathcal{R}_0^{(i)} \leq \mathcal{R}_0 = \rho(W) \leq \max_{1 \leq i \leq n} \mathcal{R}_0^{(i)}.$$

Combining with Eq. (7) immediately gives the desired Eq. (8). ∎

The analytical results give the basic reproduction numbers in isolation of the individual patches as upper and lower bounds for the basic reproduction number of the system. However, its usefulness is rather limited in practice since the range for the bounds could be too large.

Remark 3.1. If mass action incidence, rather than standard incidence is assumed (i.e., $\beta_i(N_i) = \beta_i$, rather than $\beta_i(N_i) = \frac{\beta_i}{N_i}$), then $R_0^{(i)}$ defined in Eq. (5) depends on the travel rates of susceptibles. Mass action incidence is assumed by Wang and Zhao (2004), and they show that for their two-patch SIS model, it is possible for the basic reproduction number of the system to be greater than the reproduction number of each individual patch in isolation.

In the next section, we consider the case of only two patches, and obtain more explicit results giving insight about the impact of travel on the spatial spread of disease between patches.

4. The model with two patches

From now on, we consider the special case of Eq. (1) with only two patches and assume standard incidence. Thus, we consider the system

$$\frac{dS_1}{dt} = A_1 - \frac{\beta_1}{N_1} S_1(I_1 + \sigma_1 E_1) - d_1 S_1 + \eta_1 P_1 + m_{12}^S S_2 - m_{21}^S S_1,$$

$$\frac{dE_1}{dt} = \frac{\beta_1}{N_1}(S_1 + \nu_1 P_1)(I_1 + \sigma_1 E_1) - (d_1 + \alpha_1) E_1 + m_{12}^E E_2 - m_{21}^E E_1,$$

$$\frac{dI_1}{dt} = \alpha_1 E_1 - (\gamma_1 + \varepsilon_1 + d_1) I_1 + m_{12}^I I_2 - m_{21}^I I_1,$$

$$\frac{dR_1}{dt} = \gamma_1 I_1 - (d_1 + \delta_1) R_1 + m_{12}^R R_2 - m_{21}^R R_1,$$

$$\frac{dP_1}{dt} = \delta_1 R_1 - (d_1 + \eta_1) P_1 - \nu_1 \frac{\beta_1}{N_1} P_1(I_1 + \sigma_1 E_1) + m_{12}^P P_2 - m_{21}^P P_1,$$

$$\frac{dS_2}{dt} = A_2 - \frac{\beta_2}{N_2} S_2(I_2 + \sigma_2 E_2) - d_2 S_2 + \eta_2 P_2 + m_{21}^S S_1 - m_{12}^S S_2,$$

$$\frac{dE_2}{dt} = \frac{\beta_2}{N_2}(S_2 + \nu_2 P_2)(I_2 + \sigma_2 E_2) - (d_2 + \alpha_2) E_2 + m_{21}^E E_1 - m_{12}^E E_2,$$

$$\frac{\mathrm{d}I_2}{\mathrm{d}t} = \alpha_2 E_2 - (\gamma_2 + \varepsilon_2 + d_2)I_2 + m_{21}^I I_1 - m_{12}^I I_2,$$

$$\frac{\mathrm{d}R_2}{\mathrm{d}t} = \gamma_2 I_2 - (d_2 + \delta_2)R_2 + m_{21}^R R_1 - m_{12}^R R_2,$$

$$\frac{\mathrm{d}P_2}{\mathrm{d}t} = \delta_2 R_2 - (d_2 + \eta_2)P_2 - \nu_2 \frac{\beta_2}{N_2} P_2(I_2 + \sigma_2 E_2) + m_{21}^P P_1 - m_{12}^P P_2.$$

The DFE of Eq. (9) is given by

$$S^* = \begin{bmatrix} N_1^* \\ N_2^* \end{bmatrix} = \begin{bmatrix} d_1 + m_{21}^S & -m_{12}^S \\ -m_{21}^S & d_2 + m_{12}^S \end{bmatrix}^{-1} \begin{bmatrix} A_1 \\ A_2 \end{bmatrix}.$$

Also,

$$F_{11} = \mathrm{diag}(\sigma_1\beta_1, \sigma_2\beta_2), \ \ F_{12} = \mathrm{diag}(\beta_1, \beta_2), \ \ V_{21} = \mathrm{diag}(\alpha_1, \alpha_2),$$

and, recalling that $a_i = \gamma_i + \epsilon_i + d_i$ and $c_i = d_i + \alpha_i$ for $i = 1, 2$,

$$V_{11} = \begin{bmatrix} c_1 + m_{21}^E & -m_{12}^E \\ -m_{21}^E & c_2 + m_{12}^E \end{bmatrix}, \ \ V_{22} = \begin{bmatrix} a_1 + m_{21}^I & -m_{12}^I \\ -m_{21}^I & a_2 + m_{12}^I \end{bmatrix}.$$

Hence, $\mathcal{R}_0 = \rho(W)$, where

$$W = F_{11}V_{11}^{-1} + F_{12}V_{22}^{-1}V_{21}V_{11}^{-1} = \begin{bmatrix} w_{11} & w_{12} \\ w_{21} & w_{22} \end{bmatrix} \tag{9}$$

with

$$w_{11} = \frac{\sigma_1\beta_1(c_2 + m_{12}^E)}{c_1c_2 + c_1m_{12}^E + c_2m_{21}^E} + \frac{\beta_1\alpha_1(c_2 + m_{12}^E)(a_2 + m_{12}^I) + \beta_1\alpha_2 m_{21}^E m_{12}^I}{(c_1c_2 + c_1m_{12}^E + c_2m_{21}^E)(a_1a_2 + a_1m_{12}^I + a_2m_{21}^I)},$$

$$w_{12} = \frac{\sigma_1\beta_1 m_{12}^E}{c_1c_2 + c_1m_{12}^E + c_2m_{21}^E} + \frac{\beta_1\alpha_1 m_{12}^E(a_2 + m_{12}^I) + \beta_1\alpha_2(c_1 + m_{21}^E)m_{12}^I}{(c_1c_2 + c_1m_{12}^E + c_2m_{21}^E)(a_1a_2 + a_1m_{12}^I + a_2m_{21}^I)},$$

$$w_{21} = \frac{\sigma_2\beta_2 m_{21}^E}{c_1c_2 + c_1m_{12}^E + c_2m_{21}^E} + \frac{\beta_2\alpha_1 m_{21}^I(c_2 + m_{12}^E) + \beta_2\alpha_2 m_{21}^E(a_1 + m_{21}^I)}{(c_1c_2 + c_1m_{12}^E + c_2m_{21}^E)(a_1a_2 + a_1m_{12}^I + a_2m_{21}^I)},$$

$$w_{22} = \frac{\sigma_2\beta_2(c_1 + m_{21}^E)}{c_1c_2 + c_1m_{12}^E + c_2m_{21}^E} + \frac{\beta_2\alpha_1 m_{12}^E m_{21}^I + \beta_2\alpha_2(c_1 + m_{21}^E)(a_1 + m_{21}^I)}{(c_1c_2 + c_1m_{12}^E + c_2m_{21}^E)(a_1a_2 + a_1m_{12}^I + a_2m_{21}^I)}.$$

It follows from Eq. (9) that

$$\mathcal{R}_0 = \frac{1}{2}\left(w_{11} + w_{22} + \sqrt{(w_{11} - w_{22})^2 + 4w_{12}w_{21}}\right). \tag{10}$$

From Theorem 3.1, we have the following result.

Theorem 4.1. *For the two-patch model, assume that the disease transmission is standard incidence. Then, the DFE is globally asymptotically stable if $\mathcal{R}_0 < 1$ and is unstable if $\mathcal{R}_0 > 1$, where $\mathcal{R}_0$ is given by Eq. (10).*

As expected, an increase in σ_i or β_i increases $\mathcal{R}_0$. The dependence of $\mathcal{R}_0$ on α_i is more complicated, since α_i is contained in c_i, which appears in both the denominator and numerator of entries of W. To investigate how $\mathcal{R}_0$ changes with the other parameters, we first assume that all travel rates for incubating and infective individuals are equal, namely, $m_{ij}^E = m_{ij}^I = m$ for $i, j = 1, 2$. The proof of the following result is given in the Appendix.

Theorem 4.2. *If $m_{ij}^E = m_{ij}^I = m$ for $i, j = 1, 2$ and $\sigma_1 = \sigma_2 = \sigma, \alpha_1 = \alpha_2 = \alpha, a_1 = a_2 = a, c_1 = c_2 = c, \beta_1 \neq \beta_2$, then an increase in a or m decreases $\mathcal{R}_0$.*

In the case that infectives of both patches are too sick to travel ($m_{ij}^I = 0$ for $i, j = 1, 2$) with other conditions as in Theorem 4.2, a similar technique shows that an increase in travel of incubating individuals (m_{ij}^E) decreases $\mathcal{R}_0$.

It is analytically interesting to note that, with the conditions of Theorem 4.2, as the travel rate becomes large, the basic reproduction number $\mathcal{R}_0$ in Eq. (10) approaches the mean value of $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$, i.e., $\mathcal{R}_0 \to \frac{1}{2}(\mathcal{R}_0^{(1)} + \mathcal{R}_0^{(2)})$ as $m \to \infty$. This can be seen from the form of W in the proof of Theorem 4.2. Thus if $\mathcal{R}_0^{(i)} > 2$, then $\mathcal{R}_0 > 1$. In this limit case, the two patches merge into one, and even large travel rates do not control the disease.

A referee pointed out that the result of Theorem 4.2 is in accord with previous work in ecological modeling (e.g., Hastings, 1983; McPeek and Holt, 1992; and Cantrell and Cosner, 2003). These authors demonstrate that for ecological models with spatial heterogeneity but with dispersal rates that do not depend on location, increasing the rate of dispersal is often detrimental to a population.

5. Numerical simulations

Assuming standard incidence disease transmission, we present some numerical simulations for two patches to illustrate how $\mathcal{R}_0$ changes with travel rates, with a choice of parameters relevant for human influenza (Ferguson et al., 2005; Hyman and LaForce, 2003). In the next section, we present simulations for restricted travel.

The model parameters with time unit as 1 day are taken as: $\alpha_1 = \alpha_2 = 0.5$, $\gamma_1 = \gamma_2 = 0.25$ (the average incubating time is 2 days and the average infective time is 4 days), $\epsilon_1 = \epsilon_2 = 2.0 \times 10^{-5}$, $d_1 = d_2 = \frac{1}{60 \times 365} \approx 4.57 \times 10^{-5}$, $\beta_1 = 0.35$, $\beta_2 = 0.1$, $\sigma_1 = \sigma_2 = 0.01$, $\delta_1 = \delta_2 = 2.74 \times 10^{-3}$, $\eta_1 = \eta_2 = 1.37 \times 10^{-3}$, $\nu_1 = \nu_2 = 0.01$ and $A_1 = A_2 = 1$. Note that the two patches are assumed to differ only in infectivity, modeling high and low contact patches for the same disease outbreak. These parameters yield the respective basic reproduction numbers in isolation of
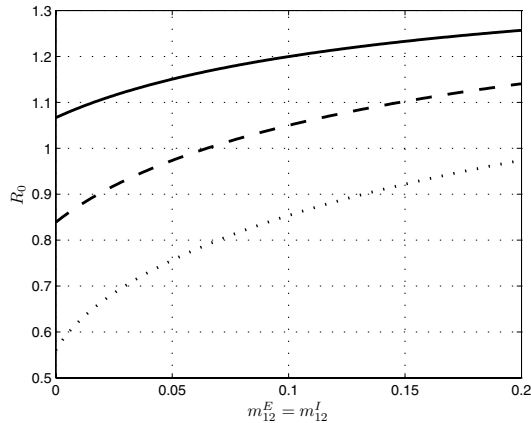
Fig. 2 $\mathcal{R}_0$ vs $m_{12}^E = m_{12}^I$ for fixed $m_{21}^E = m_{21}^I$. Parameters as in text. The three curves from top to bottom correspond to : $m_{21}^E = m_{21}^I = 0.05, 0.1, 0.2$, respectively.

$\mathcal{R}_0^{(1)} \approx 1.41 > 1$ and $\mathcal{R}_0^{(2)} \approx 0.40 < 1$. Hence, we consider the hypothetical scenario of disease spread between a high prevalence endemic region (patch 1) and a low prevalence region where a minor outbreak could be eradicated (patch 2). We first keep $m_{21}^E = m_{21}^I$ fixed with values at 0.05, 0.1, and 0.2 and let $m_{12}^E = m_{12}^I$ vary from 0 to 0.2. The curves of $\mathcal{R}_0$ are given in Fig. 2.

Figure 2 shows that by keeping the same travel rate from patch 1 to patch 2, an increase in the travel rate from patch 2 (the patch with lower disease transmission rate) to patch 1 (the patch with higher disease transmission rate) results in an increase in $\mathcal{R}_0$. Consequently, we can conclude that travel between the two patches may cause the disease to become endemic in both patches if the travel rate from patch 2 to patch 1 is sufficiently large and that from patch 1 to patch 2 is sufficiently small. The numerical simulation in Fig. 2 also shows that for the chosen parameters and keeping $m_{12}^E = m_{12}^I$ fixed, an increase in $m_{21}^E = m_{21}^I$ leads to a decrease in $\mathcal{R}_0$. In particular, $\mathcal{R}_0$ could conceivably decrease to a value less than 1 if the travel rate from the high prevalence patch to the low prevalence patch, namely $m_{21}^E = m_{21}^I$, is high enough.

If all travel rates from one patch to the other are the same, i.e., $m_{12}^E = m_{12}^I = m_{21}^E = m_{21}^I = m$, then an increase in m leads to a decrease in $\mathcal{R}_0$ (Fig. 3), as predicted by Theorem 4.2. Note that, for these parameter values, $\mathcal{R}_0 < 1$ if $m > 0.16$.

Taking $m = 0.18$ and subsequently $\mathcal{R}_0 < 1$, the disease dies out eventually since the DFE is globally asymptotically stable by Theorem 4.1. To investigate how the infective population sizes in the two patches change over time and die out eventually, we numerically simulate the system, represented by Eq. (9), using the parameter values given at the beginning of this section, and in Fig. 4 plot I_1 and I_2 against time. The infective population sizes in both patches eventually decrease to zero although there is an initial increase of infectives in patch 2.

Next, we use the same parameter values except that $m = 0.02$, and subsequently $\mathcal{R}_0 > 1$ (see Fig. 3). For a time period of 6000 days, the numerical simulation of
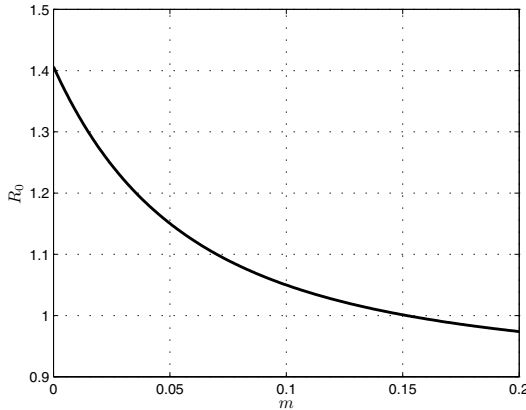
Fig. 3 $\mathcal{R}_0$ vs m, where $m = m_{12}^E = m_{12}^I = m_{21}^E = m_{21}^I$.

the system, represented by Eq. (9), in this case given in Fig. 5 shows that in both patches there is an initial shape increase in the number of infectives followed by a decrease. There are damped transient oscillations about an endemic equilibrium; whereas Hyman and LaForce (2003) observe sustained oscillations when β_i is periodic.

Some interesting observations can be made from our results regarding the role that travel plays in the spatial spread of a disease. Figure 2 demonstrates the possibility that, for a low prevalence patch with a minor disease outbreak (basic reproduction numbers in isolation $\mathcal{R}_0^{(2)}$ less than 1), open travel with a high prevalence patch could lead to the disease becoming endemic. However, for a high prevalence patch with endemic disease in isolation (basic reproduction numbers
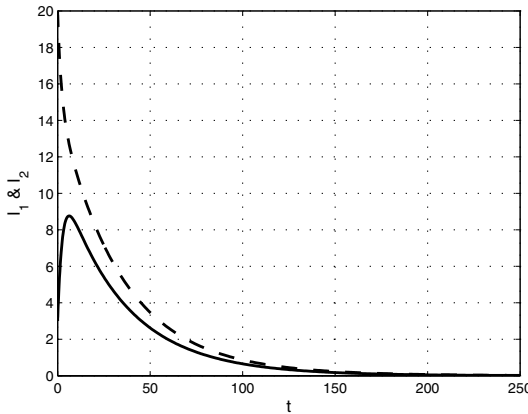
Fig. 4 Numerical solution of the system, represented by Eq. (9), with parameters as in the text and $m = 0.1$ showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs. time t. Initial conditions are: $S_1(0) = 17000$, $E_1(0) = 10$, $I_1(0) = 20$, $R_1(0) = 0$, $P_1(0) = 3000$; $S_2(0) = 17200$, $E_2(0) = 1$, $I_2(0) = 3$, $R_2(0) = 0$, $P_2(0) = 3000$.
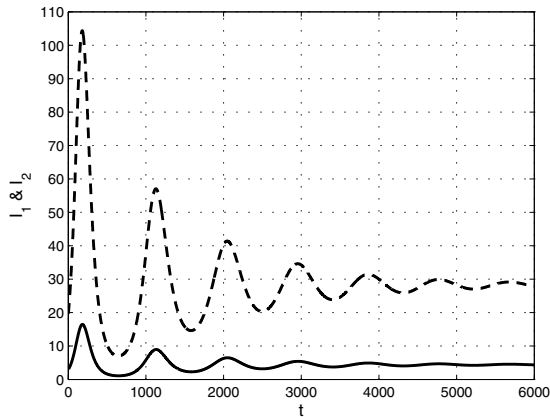
Fig. 5 Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs. time t. Parameter values and initial conditions are the same as in Fig. 4 except that $m = 0.02$.

in isolation $\mathcal{R}_0^{(1)}$ greater than 1), open travel with a low prevalence patch could eradicate the disease. Essentially, under appropriate parameter ranges, travel between patches dilutes the overall prevalence to the point that it could either lessen the severity of an endemic patch or worsen a minor outbreak region. Further evidence can be found in Figs. 3 and 4 in which assuming all travel rates are equal, the disease can be eventually eradicated if the travel rates are sufficiently large.

The value $\mathcal{R}_0^{(1)} \approx 1.41$ taken is near the lower bound of the range 1.4–2 of pandemic influenza $\mathcal{R}_0$ values examined recently by Ferguson et al. (2006) and is slightly lower than the range 1.6–2.4 considered by Germann et al. (2006). From our discussion under Theorem 4.2, if $\mathcal{R}_0^{(1)} > 2$, then the disease cannot be controlled by equal travel rates.

6. Discussion of travel restrictions

To consider hypothetical intervention scenarios, we set $m_{21}^I = 0$ and keep all other parameters the same as for Fig. 2. This models a situation in which the authority bans all travel of symptomatic travelers from patch 1 (the high prevalence patch), to patch 2 (the low prevalence patch). In comparison with Fig. 2, Fig. 6 shows this gives an overall increase in the value of the basic reproduction number $\mathcal{R}_0$. More specifically, for $m_{21}^E = 0.2$, stopping all travel of symptomatic travelers from patch 1 to patch 2 adversely impacts the epidemic by driving the basic reproduction number above 1, thus prolonging the epidemic that otherwise would be eradicated.

Conversely, Fig. 7 shows that stopping all travel of symptomatic travelers from patch 2 to patch 1 (setting $m_{12}^I = 0$) could alleviate the epidemic, lowering the basic reproduction number to below 1, thus successfully preventing further spread of the outbreak.
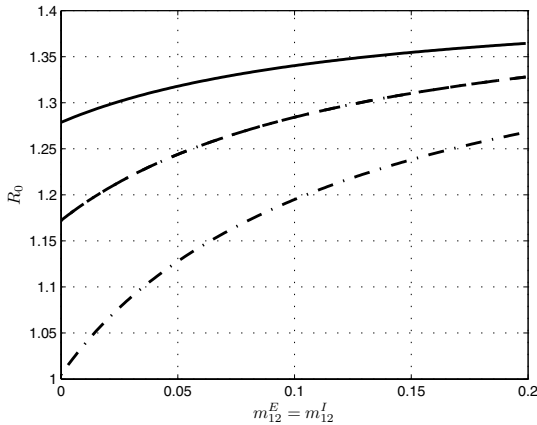
Fig. 6 $\mathcal{R}_0$ vs $m_{12}^E = m_{12}^I$ for fixed $m_{21}^I = 0$. The three curves from top to bottom correspond to : $m_{21}^E = 0.05, 0.1, 0.2$, respectively.

Therefore, the policy of border control to ban travel of symptomatic travelers only from the high to the low prevalence patch could affect the containment of the outbreak adversely (Figs. 2 and 6). However, banning travel of symptomatic travelers only from the low to the high prevalence patch always has a positive impact (Figs. 2 and 7).

We now set $m_{21}^I = 0$ and keep all other parameters the same as in Fig. 5. Figure 8 shows that the disease is still endemic in both patches, but with a larger number of infectives in the high prevalence patch and a smaller number of infectives in the low prevalence patch. Thus, once again, banning all travel of symptomatic travelers from the high to the low prevalence patch may be detrimental to the intervention
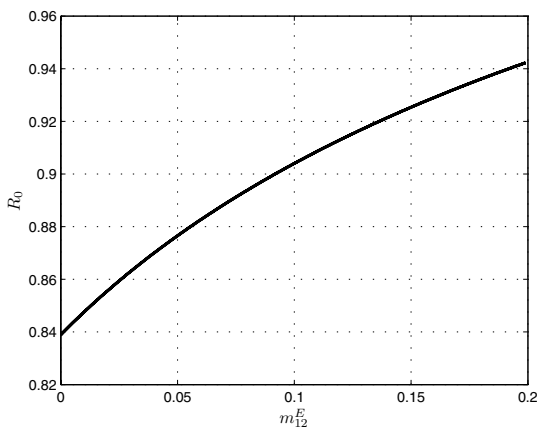

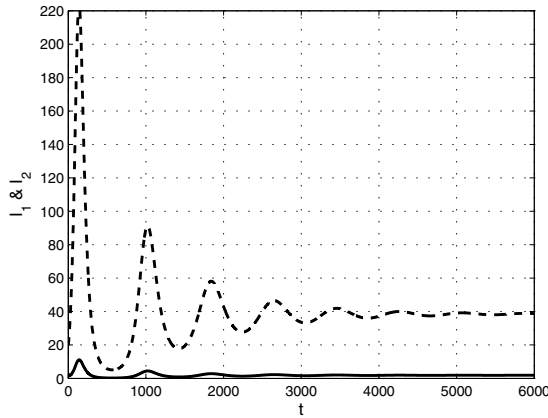**Fig. 7** $\mathcal{R}_0$ vs m_{12}^E with $m_{12}^I = 0$ for fixed $m_{21}^E = m_{21}^I = 0.1$.

Fig. 8 Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs time t. Parameters as in Fig. 5 except that $m_{21}^I = 0$.

and control of the outbreak in patch 1, and the total number of infecteds may increase.

Now, when we set $m_{12}^I = 0$ and keep all other parameters the same as in Fig. 5, i.e., banning travel of symptomatic travelers from the low to the high prevalence patch only, the disease persists in both patches but with (slightly) smaller numbers of infectives in the high prevalence patch (Fig. 10). This indicates the importance of border control out of a low prevalence patch and into a high prevalence patch.

Travel restrictions previously considered maintain the matrix W given by Eq. (9) irreducible. In the event that there is no travel of infecteds from patch i to patch j, then M^E and M^I become reducible and hence W becomes reducible.
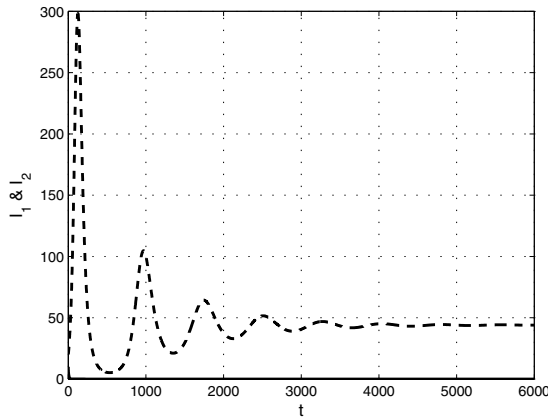

Fig. 9 Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs time t. Parameters are the same as in Fig. 5 except that $m_{21}^E = m_{21}^I = 0$.
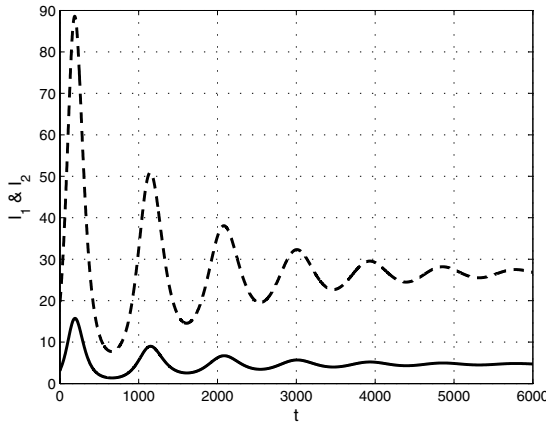
Fig. 10   Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs time t. Parameters as in Fig. 5 except that $m_{12}^I = 0$.

Setting $m_{21}^E = m_{21}^I = 0$, i.e., banning all travel of infecteds from the high to the low prevalence patch, the infected equations for patch 2 uncouple. If $E_2(0) = I_2(0) = 0$, then $E_2(t) = I_2(t) = 0$ for all $t \geq 0$, i.e., patch 2 remains diseasefree. If $E_1(0) + I_1(0) > 0$, then disease persists in patch 1 provided $\mathcal{R}_0^{(1)} > 1$, but it dies out if $\mathcal{R}_0^{(1)} < 1$. If $E_i(0) + I_i(0) > 0$ for $i = 1, 2$, then the dynamics in patch 1 is governed by $\mathcal{R}_0^{(1)}$ and the dynamics in patch 2 is governed by $\widetilde{\mathcal{R}}_0^{(2)}$.

Taking the same parameters as in Fig. 5 except that $m_{21}^E = m_{21}^I = 0$, then $\mathcal{R}_0^{(1)} \approx 1.41 > 1$ and $\widetilde{\mathcal{R}}_0^{(2)} \approx 0.36 < 1$. Thus, the disease in patch 1 becomes endemic and the disease in patch 2 dies out very rapidly (see Fig. 10).
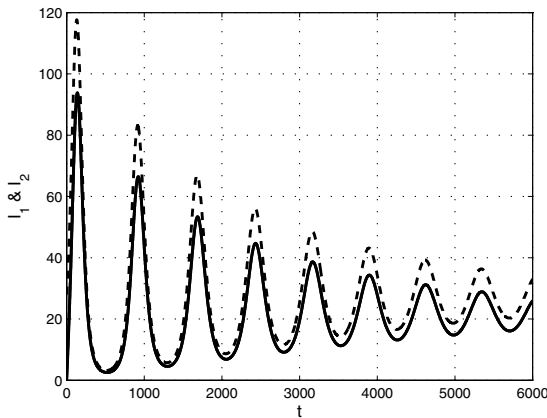

Fig. 11   Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs time t. Parameters and initial conditions as in text. $m_{12}^E = m_{12}^I = 0, m_{21}^E = m_{21}^I = 0.02$.
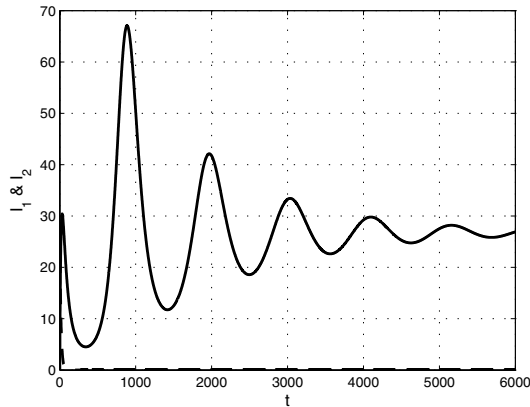
Fig. 12 Numerical solution of the system, represented by Eq. (9), showing I_1 (*dashed curve*) and I_2 (*solid curve*) vs time t. Parameters and initial conditions as in text. $m_{12}^E = m_{12}^I = 0, m_{21}^E = m_{21}^I = 0.10$.

Similarly, setting $m_{12}^E = m_{12}^I = 0$ (i.e., banning all infected travelers from patch 2 to patch 1), the dynamics of patches 1 and 2 are governed by $\widetilde{\mathcal{R}}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$, respectively. For $\mathcal{R}_0^{(1)} > 1$ and $\mathcal{R}_0^{(2)} > 1$, disease becomes endemic in patch 2, but patch 1 may become diseasefree if travel rates give $\widetilde{\mathcal{R}}_0^{(1)} < 1$, even if $E_2(0) = I_2(0) = 0$ and $E_1(0) + I_1(0) > 0$ (i.e., patch 2 is initially diseasefree and patch 1 is not). As demonstrated in Fig. 11, the disease persists in both patches; whereas in Fig. 12, patch 1 becomes diseasefree very rapidly and disease persists in patch 2. In both Figs. 11 and 12, all parameter values are the same as stated at the beginning of Section 5 except that $\beta_1 = 0.4$, $\beta_2 = 0.3$. Thus $\mathcal{R}_0^{(1)} \approx 1.61 > 1$ and $\mathcal{R}_0^{(2)} \approx 1.21 > 1$. We set $m_{ij}^K = 0.02$ for $K = S, R, P$ and $i, j = 1, 2$. In Fig. 11, we set $m_{12}^E = m_{12}^I = 0$, $m_{21}^E = m_{21}^I = 0.02$, which yields $\widetilde{\mathcal{R}}_0^{(1)} \approx 1.43 > 1$. In Fig. 12, we set $m_{12}^E = m_{12}^I = 0$, $m_{21}^E = m_{21}^I = 0.10$, which yields $\widetilde{\mathcal{R}}_0^{(1)} \approx 0.96 < 1$. Initial conditions are: $S_1(0) = 16,000$, $E_1(0) = 15$, $I_1(0) = 28$, $R_1(0) = 0$, $P_1(0) = 5,000$; $S_2(0) = 16,000$, $E_2(0) = 0$, $I_2(0) = 0$, $R_2(0) = 0$, $P_2(0) = 5,000$.

During the 2003 SARS outbreak, travel warnings to all affected areas were issued by WHO (2003) to prevent travelers from entering and becoming infected. Dozens of countries also issued border control either banning travelers from entering or placing them under quarantine. See Ruan et al. (2006) for a study of a patch model for the spread of SARS. For our influenza model, from a public health point of view, it is imperative for the low prevalence patch to stop travel of sick (both incubating and infective) individuals from the high prevalence patch. Our results show that, for the parameter values considered, border control does not necessarily always have a positive impact on the overall spread of disease and it is more important to ban travel of infected individuals from a low prevalence patch to a high prevalence patch. Moreover, an increase of travel rates in the opposite direction (from a high to a low prevalence patch), while theoretically alleviating the spatial spread of the disease, may not be an implementable policy.

The conclusions drawn in this work are valid for the set of parameters used, most of which were taken from recent literature. In the event of a new highly pathogenic influenza strain, which might result in vastly different disease parameter values, our analytic results would hold, but numerical simulations would need to be redone.

As a final remark, we note again that while the model is proposed for the spread of human influenza, it can also be used, with some appropriate modifications and parameter changes, as the basis of a theoretical model to study the spread of enzootic diseases such as avian flu among birds.

Appendix: Proof of Theorem 4.2

Proof. It is clear that an increase in a decreases each entry in the matrix W, and so decreases the basic reproduction number $\mathcal{R}_0$. Under the parameter assumptions,

$$W = \begin{bmatrix} \beta_1 u & \beta_1 v \\ \beta_2 v & \beta_2 u \end{bmatrix},$$

where

$$u = \frac{\sigma(c+m)}{c(c+2m)} + \frac{\alpha(2m^2 + (a+c)m + ac)}{ac(c+2m)(a+2m)},$$

$$v = \frac{\sigma m}{c(c+2m)} + \frac{\alpha m(a+c+2m)}{ac(c+2m)(a+2m)}.$$

By Eq. (10), $\mathcal{R}_0$ is the larger root of the quadratic equation

$$\lambda^2 - (\beta_1 + \beta_2)u\lambda + \beta_1\beta_2(u^2 - v^2) = 0. \tag{A.1}$$

It follows from the above expressions that

$$u + v = \frac{\alpha + \sigma a}{ac}, \quad u - v = \frac{\alpha + \sigma(a+2m)}{(c+2m)(a+2m)},$$

giving

$$u^2 - v^2 = \frac{\alpha + \sigma a}{ac} \frac{\alpha + \sigma(a+2m)}{(c+2m)(a+2m)}.$$

It follows from $u + v = \frac{\alpha + \sigma a}{ac}$ that $\frac{\partial u}{\partial m} = -\frac{\partial v}{\partial m}$. Taking partial derivatives with respect to m for Eq. (A.1) gives

$$(2\lambda - (\beta_1 + \beta_2)u)\frac{\partial \lambda}{\partial m} = \lambda(\beta_1 + \beta_2)\frac{\partial u}{\partial m} - \beta_1\beta_2\frac{\partial(u^2 - v^2)}{\partial m}$$

$$= \left(\lambda(\beta_1 + \beta_2) - 2\beta_1\beta_2\frac{\alpha + \sigma a}{ac}\right)\frac{\partial u}{\partial m}.$$

From the definition of u,

$$\frac{\partial u}{\partial m} = -\frac{\alpha(4m + a + c) + \sigma(4m^2 + 4am + a^2)}{[(c + 2m)(a + 2m)]^2} < 0.$$

Note that $2\lambda|_{\lambda=\mathcal{R}_0} > (\beta_1 + \beta_2)u$. Therefore, to show that $\frac{\partial \mathcal{R}_0}{\partial m} < 0$, i.e., to show $\frac{\partial \lambda}{\partial m}|_{\lambda=\mathcal{R}_0} < 0$, it suffices to show that for $\lambda = \mathcal{R}_0$,

$$(\beta_1 + \beta_2)\lambda - 2\beta_1\beta_2\frac{\alpha + \sigma a}{ac} > 0.$$

We first claim that $\lambda > \frac{1}{2}(\beta_1 + \beta_2)(u + v)$. Since

$$\lambda = \frac{1}{2}\left[(\beta_1 + \beta_2)u + \sqrt{(\beta_1 + \beta_2)^2 u^2 - 4\beta_1\beta_2(u^2 - v^2)}\right],$$

it is equivalent to show that

$$(\beta_1 + \beta_2)^2 u^2 - 4\beta_1\beta_2(u^2 - v^2) > (\beta_1 + \beta_2)^2 v^2,$$

or

$$(\beta_1 - \beta_2)^2(u^2 - v^2) > 0.$$

This is automatically true since $u > v > 0$. It follows from $\lambda > \frac{1}{2}(\beta_1 + \beta_2)(u + v)$ that

$$(\beta_1 + \beta_2)\lambda > \frac{1}{2}(\beta_1 + \beta_2)^2(u + v) = \frac{1}{2}\frac{\alpha + \sigma a}{ac}(\beta_1 + \beta_2)^2.$$

Thus, as required,

$$(\beta_1 + \beta_2)\lambda - 2\beta_1\beta_2\frac{\alpha + \sigma a}{ac} > \frac{1}{2}\frac{\alpha + \sigma a}{ac}(\beta_1 - \beta_2)^2 > 0.$$

Acknowledgments

References

Arino, J., Jordan, R., van den Driessche, P., 2005. Quarantine in a multi-species epidemic model with spatial dynamics. Math. Biosci.

Arino, J., van den Driessche, P., 2003. A multi-city epidemic model. Math. Popul. Stud. 10, 175–193.

Arino, J., van den Driessche, P., 2006. Disease spread in metapopulations. In: Nonlinear Dynamics and Evolution Equations. Vol. 48. Fields Institute Communications.

Berman, A., Plemmons, R. J., 1979. Non-negative Matrices in the Mathematical Sciences. Academic, New York.

Butler, D., 2006. Doubts hang over source of bird flu spread, Nature 439, 772.

Cantrell, R.S., Cosner, C., 2003. Spatial Ecology via Reaction-Diffusion Equations. Wiley, New York.

Chowell, G., Rivas, A.L., Hengartner, N.W., Hyman, J.M., Castillo-Chavez, C., 2006. The role of spatial mixing in the spread of foot-and-mouth disease. Prev. Vet. Med. 73, 297–314.

Ferguson, N.M., Cummings, D.A.T., Cauchemez, S., Fraser, C., Riley, S., Meeyai, A., Iamsirithaworn, S., Burke, D. S., 2005. Strategies for containing an emerging influenza pandemic in southeast Asia. Nature 437, 209–214.

Ferguson, N.M., Cummings, D.A.T., Fraser, C., Cajka, J.C., Cooley, P.C., Burke, D.S., 2006. Strategies for mitigating an influenza pandemic. Nature 442, 448–452.

Fulford, G.R., Roberts, M.G., Heesterbeek, J.A.P., 2002. The metapopulation dynamics of an infectious disease: Tuberculosis in possums. Theor. Popul. Biol. 61, 15–29.

Germann, T.C., Kadau, K., Longini, I.M. Jr., Macken, C.A., 2006. Mitigation strategies for pandemic influenza in the United States. PNAS 103, 5935–5940.

Hastings, A., 1983. Can spatial variation alone lead to selection for dispersal? Theor. Popul. Biol. 24, 244–251.

Horn, R.A., Johnson, C.R., 1985. Matrix Analysis. Cambridge University Press, New York.

Horn, R.A., Johnson, C.R., 1991. Topics in Matrix Analysis. Cambridge University Press, New York.

Hyman, J.M., LaForce, T., 2003. Modeling the spread of influenza among cities. In: Banks, H.T., Castillo-Chavez, C. (Eds.), Bioterrorism. SIAM, New York, pp. 211–236.

McPeek, M.A., Holt, R.D., 1992. The evolution of dispersal in spatially and temporally varying environments. Am. Nat. 140, 1010–1027.

Ruan, S., Wang, W., Levin, S.A., 2006. The effect of global travel on the spread of SARS. Math. Bios. Eng. 3, 205–218.

Salmani, M., van den Driessche, P., 2006. A model for disease transmission in a patchy environment. Disc. Cont. Dyna. Syst. Ser. B 6, 185–202.

Sattenspiel, L., Herring, D.A., 2003. Simulating the effect of quarantine on the spread of the 1918–1919 flu in central Canada. Bull. Math. Biol. 65, 1–26.

Smith, H.L., Waltman, P., 1995. The Theory of the Chemostat. Cambridge University Press, New York.

van den Driessche, P., Watmough, J., 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Math. Biosci. 180, 29–48.

Wang, W., Mulone, G., 2003. Threshold of disease transmission in a patchy environment. J. Math. Anal. Appl. 285, 321–335.

Wang, W., Zhao, X.-Q., 2004. An epidemic model in a patchy environment. Math. Biosci. 190, 97–112.

Wang, W., Zhao, X.-Q., 2006. An epidemic model with population dispersal and infection period. SIAM J. Appl. Math.

World Health Organization (WHO), 2003. Summary of WHO measures related to international travel. Available at: http:// www. who. int/csr/sars/ travelupdate/en/. Accessed August 8, 2006.

World Health Organization (WHO), 2006. Cumulative number of confirmed human cases of Avian influenza A/(H5N1) reported to WHO. Available at: http://www. who. int/csr/disease/avian_influenza/country/cases _table_2006_08_08/en/index.html. Accessed August 8.