Global stability of a two-patch cholera model with fast and slow transmissions

Samuel Bowong[a,2] Jean M.-S. Lubuma[b,1] Berge Tsanou[b,c,2]

[a]*Department of Mathematics and Computer Science, University of Douala, P.O. Box 24157 Douala, Cameroon*
[b]*Department of Mathematics and Applied Mathematics, University of Pretoria, Pretoria 0002, South Africa*
[c]*Department of Mathematics and Computer Science, University of Dschang, P.O. Box 67 Dschang, Cameroon.*

Abstract

A two-patch model for a waterborne disease, such as cholera, is considered, with the aim of investigating the impact of human population movements between two cities (patches). We derive the reproduction number $\mathcal{R}_0$, which depends on human movement rates. It is shown that the disease-free equilibrium is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$. Three types of equilibria are explored: boundary endemic equilibria (patch-1 disease-free equilibrium and patch-2 disease-free equilibrium); interior endemic equilibrium (both patches endemic). They depend on four threshold parameters. The global asymptotic stability of equilibria is established using Lyapunov functions that combine quadratic, Volterra-type and linear functions. The theory is supported by numerical simulations, which further suggest that the human movement can increase or reduce the spread of the disease in one patch.

Keywords: Metapopulation, Waterborne disease, Cholera, Lyapunov function, Global stability, Numerical simulations.
Mathematical Subject Classifications: 92A15, 34D20, 37B25.

1. Introduction

Cholera is a waterborne diarrheal disease that continues to impoverish countries in the third world and poses a massive threat to their development. Without prompt treatment, an infected individual may die of dehydration in a matter of hours in severe cases [9]. After several years of steady increase, from 2007 the number of cholera cases reported to the World Health Organization (WHO), as well as the number of countries which reported cholera cases, showed a considerable decrease [37]. Yet the disease is still a threat to many countries. For instance in 2012 alone, a cumulative total of 245 393 cases, including 3034 deaths with a case-fatality rate of 1.2%, were reported to WHO from all continents. This involves 48 countries among which, 27 from Africa, 12 from Asia, 6 from Americas and 3 from Europe and Oceania. Furthermore, the recent cholera outbreaks in the following countries led to a large number of infectious and deaths [37]: Angola (2012), Cameroon (2010-2012), Congo (2008, 2012), Haiti (2010-2011), India (2007), Iraq (2008, 2012), Kenya (2010), Nigeria (2010), Philippines (2012), UK (2012), Vietnam (2009) and Zimbabwe(2008-2009).

Cholera is an acute intestinal infection. There are two etiological agents/serogroups (*vibrio cholerae* O1 and *vibrio cholerae* O139) each of which can colonize the small intestine and produce an enterotoxin responsible for a watery diarrhea. The cholera pathogen can survive in some aquatic environments from three months to two years, in association with zoo-plankton, phytoplankton and other aquatic organisms [9, 25]. Moreover, as reported in [25], free-living *vibrio cholerae* were

[1]Corresponding author: J.M.-S. Lubuma, Department of Mathematics and Applied Mathematics, University of Pretoria, Pretoria 0002, South Africa, E-mail: jean.lubuma@up.ac.za, Tel: +27(0)12 420 2222, Fax: +27(0)12 420 3893.
[2]E-mail addresses: sbowong@gmail.com (S. Bowong), berge.tsanou@up.ac.za (B.Tsanou).
Samuel Bowong and Berge Tsanou are also members of LIRIMA-GRIMCAPE Team Project, Cameroon.

able to reach concentrations which are three times higher than the known minimum infectious dose. This highlights the important role the growth of free-living *vibrio cholerae* can play in the propagation of cholera during outbreaks.

Individuals become infected by consuming water or food from reservoirs contaminated by virulent strains of the bacterium *vibrio cholerae*. This is referred to as indirect/slow transmission [4, 5, 7, 9]. Furthermore, transmission can happen through direct/fast contact with an infected individual [13, 17, 23, 26]. Although there is no permanent immunity to cholera, it was shown in [16] that immunity is serogroup specific. In particular, substantial immunity to *vibrio cholerae* O1 preexisted in the population of Bangladesh [13], which can explain the absence of transfer from recovered to susceptible individuals in most mathematical models [9, 12, 26, 32, 38].

The dynamics of cholera is complex due to the multiple interactions between the human host and the pathogen in the water environment [27], which contributes to both direct and indirect transmission pathways. A deep understanding of the disease dynamics would have a significant impact on the effective prevention and control strategies [10, 26]. Mathematical modeling and numerical simulations have the potential, and offer a promising way, to achieve this. Many efforts have been and are still being devoted to the modeling of this disease. For a chronological history of the modeling of cholera, we refer the reader to the work [35] which mentions the first mathematical model developed in [7]. We also refer the reader to the overview paper [31] and the references therein for single-patch models.

For the past few years, metapopulation models have extensively been studied in order to understand the dynamics of infectious diseases in general [2, 6, 12, 38] and of the cholera in particular [4, 6, 12, 38]. The model for cholera investigated in [12] includes both direct and indirect transmissions as well as water and human movements between patches. The authors considered the water movement as a migration, which is not realistic. A patch model without human movement is considered in [4].

More recently, a two patch cholera model has been considered in [28] with incorporation of the displacement of susceptible and infected individuals, excluding migration of recovered individuals and bacteria cells. However, these assumptions are not realistic and the results obtained are not correct. They proved the existence of two boundary endemic equilibrium and one interior endemic equilibrium. They also showed that the boundary endemic equilibria are locally asymptotically stable if the corresponding disease threshold quantities are greater than the unity. Usually, due to severe diarrhea and vomiting, infected individuals cannot migrate. Also, it is realistic that recovered individuals migrate. Assuming the contrary of this results in not having boundary endemic equilibria.

On the other hand, global stability of epidemic patch models is always mathematically challenging [11, 15, 18, 34]. None of the works mentioned above has considered the global stability of the interior endemic equilibrium point, and of the different boundary endemic equilibria whenever they exist.

This paper builds on the existing works mentioned above and fills some of the gaps observed there, apart from fixing some inconsistencies in [28]. In view of the usefulness and the current investigation on the spread of cholera on heterogeneous populations and taking into account human movements, we link two patches that could be cities, towns, regions or countries. Population movements between patches may be justified by the migration or travel within patches on the understanding that infected individuals cannot move due to severe diarrhea and vomiting.

For each patch, we consider a classical S-I-R (Susceptible-Infected-Recovered) epidemic model with a pathogen compartment denoted by B. We compute the disease-free equilibrium and the reproduction number $\mathcal{R}_0 = \max\{\mathcal{R}_0^{(1)}, \mathcal{R}_0^{(2)}\}$ where $\mathcal{R}_0^{(i)}$ is the threshold quantity of patch i when the migration of humans takes place. We do an in-depth analysis of the global asymptotic stability of the disease-free equilibrium and endemic equilibria. In this regard, another feature of this work is the construction of new Lyapunov functions of gradual complexity. Numerical simulations are presented to support the theory and to get insight on the role of the human movement on the dynamics of the disease.

This work is an extension and full paper of the presentation made at the Biomath 2014 conference, Sofia, Bulgaria, 22 – 27 June 2014. The rest of the paper is organized as follows. After

the formulation of the model in Section 2, we present its quantitative and qualitative analysis in Section 3. Numerical simulations are provided in Section 4. The last Section is devoted to concluding remarks on how our findings fit in the literature and on possible extensions.

2. The model formulation

The setting of this work is a two patchy metapopulation S-I-R epidemic model with a pathogen compartment. This is a relevant extension of the original model in [32] in two respects. Firstly, we take into account the disease related death rate since cholera is a fatal disease with death occurring in few hours in severe cases if no treatment is undertaken [9]. Secondly, we consider a constant recruitment in the susceptible class. With these two additional assumptions, the total human population is no longer constant as it is the case in [32]. At time t, we denote by $S_i(t), I_i(t), R_i(t), B_i(t)$ susceptible humans, infected humans, recovered human and pathogen concentration in water in patch i ($i = 1, 2$), respectively.

Following [9, 32, 35, 38], we assume that there is a constant renewal A_i of susceptible individuals in the S_i class. This inflow may occur by birth, immigration or lost of temporary acquired immunity (since cholera does not confer life-long immunity [16]).

Susceptible individuals in patch i become infected following two possible routes of transmission: either by direct contact with infected individuals (also called fast-transmission), or indirectly through contact with contaminated water (referred to as slow-transmission) where *vibrio cholerae* are present. Thus in each patch i, an infected individual generates secondary infections in two ways: through direct contact with susceptible individuals in the same patch i at rate β_i per unit time, and by first shedding pathogens into the water compartment, with which susceptible individuals eventually come into contact at rate $\lambda_{b,i}$ per unit time. Infected individuals I_i shed pathogens into the water compartment B_i at rate α_i.

Pathogens are assumed to decay more rapidly than they grow in the environment. This results in the pathogen net decay rate ε_i which is actually the difference between the growth and death rates. For more general descriptions of the growth of the cholera pathogen in nature, we refer the reader to [25]. Infected individuals recover at rate γ_i. Susceptible, infected and recovered human individuals have the same natural death rate μ_i. Infected individuals die because of disease at rate δ_i.

Since cholera is a very severe disease, with a high rate of dehydration, we assume in the metapopulation setting that only susceptible and recovered individuals can move. As usual [6, 12, 18, 28], we assume that the outgoing flows of susceptible and recovered individuals from patch i are constants denoted by a_i and b_i , respectively.

From the flow chart in Fig. 1, the transmission model is described by the following system of nonlinear ordinary differential equations:

$$\begin{cases} S_1^{'} &= A_1 - \lambda_{b,1} S_1 B_1 - \beta_1 S_1 I_1 - (\mu_1 + a_1) S_1 + a_2 S_2, \\ I_1^{'} &= \lambda_{b,1} S_1 B_1 + \beta_1 S_1 I_1 - (\mu_1 + \delta_1 + \gamma_1) I_1 \\ R_1^{'} &= \gamma_1 I_1 - \mu_1 R_1 + b_2 R_2 - b_1 R_1, \\ B_1^{'} &= \alpha_1 I_1 - \varepsilon_1 B_1, \\ S_2^{'} &= A_2 - \lambda_{b,2} S_2 B_2 - \beta_2 S_2 I_2 - (\mu_2 + a_2) S_2 + a_1 S_1, \\ I_2^{'} &= \lambda_{b,2} S_2 B_2 + \beta_2 S_2 I_2 - (\mu_2 + \delta_2 + \gamma_2) I_2, \\ R_2^{'} &= \gamma_2 I_2 - \mu_2 R_2 + b_1 R_1 - b_2 R_2, \\ B_2^{'} &= \alpha_2 I_2 - \varepsilon_2 B_2. \end{cases} \tag{1}$$

Although the system (1) can be used to describe general waterborne diarrheal diseases [32], we refer to it as a model for cholera because this disease is well documented and in fact, as mentioned earlier, our model builds on a couple of existing works on cholera [9, 12, 26, 28, 32].

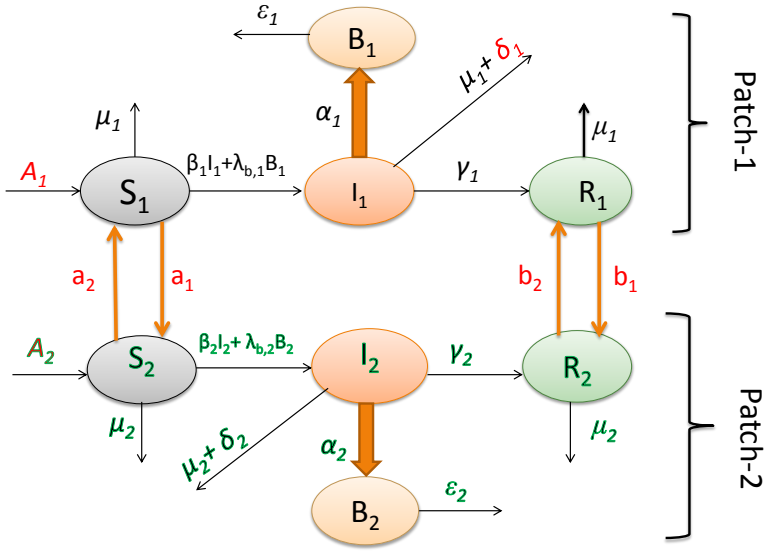

Figure 1: Flow chart of the transmission dynamics of a two-patch cholera model.

Now, let $\lambda_i = \dfrac{\alpha_i \lambda_{b,i}}{\varepsilon_i}$, and $W_i = \dfrac{\varepsilon_i}{\alpha_i} B_i$, $(i = 1, 2)$, then, the system (1) becomes

$$\begin{cases} S_1^{'} &= A_1 - \lambda_1 S_1 W_1 - \beta_1 S_1 I_1 - (\mu_1 + a_1) S_1 + a_2 S_2, \\ I_1^{'} &= \lambda_1 S_1 W_1 + \beta_1 S_1 I_1 - (\mu_1 + \delta_1 + \gamma_1) I_1, \\ R_1^{'} &= \gamma_1 I_1 - \mu_1 R_1 + b_2 R_2 - b_1 R_1, \\ W_1^{'} &= \varepsilon_1 (I_1 - W_1), \\ S_2^{'} &= A_2 - \lambda_2 S_2 W_2 - \beta_2 S_2 I_2 - (\mu_2 + a_2) S_2 + a_1 S_1, \\ I_2^{'} &= \lambda_2 S_2 W_2 + \beta_2 S_2 I_2 - (\mu_2 + \delta_2 + \gamma_2) I_2, \\ R_2^{'} &= \gamma_2 I_2 - \mu_2 R_2 + b_1 R_1 - b_2 R_2, \\ W_2^{'} &= \varepsilon_2 (I_2 - W_2). \end{cases} \tag{2}$$

The total human population and the total bacteria concentration are $N(t) = S_1(t) + I_1(t) + S_2(t) + I_2(t) + R_1(t) + R_2(t)$ and $W(t) = W_1(t) + W_2(t)$, respectively.

Once $S_1, I_1, W_1, S_2, I_2, W_2$ are obtained from the first, second, fourth, fifth, sixth and eighth equations of the system (2), the functions R_1 and R_2 are readily given by the third and seventh equations of the system (2). Thus without loss of generality, we are led to the following reduced system

$$\begin{cases} S_1^{'} &= A_1 - \lambda_1 S_1 W_1 - \beta_1 S_1 I_1 - (\mu_1 + a_1) S_1 + a_2 S_2, \\ I_1^{'} &= \lambda_1 S_1 W_1 + \beta_1 S_1 I_1 - (\mu_1 + \delta_1 + \gamma_1) I_1, \\ S_2^{'} &= A_2 - \lambda_2 S_2 W_2 - \beta_2 S_2 I_2 - (\mu_2 + a_2) S_2 + a_1 S_1, \\ I_2^{'} &= \lambda_2 S_2 W_2 + \beta_2 S_2 I_2 - (\mu_2 + \delta_2 + \gamma_2) I_2, \\ W_1^{'} &= \varepsilon_1 (I_1 - W_1), \\ W_2^{'} &= \varepsilon_2 (I_2 - W_2). \end{cases} \tag{3}$$

Table 1 summarizes the model variables and parameters in patch i $(i = 1, 2)$.

Table 1: Variables and parameters with units for the extended SIWR system (2)

Symbols	Definitions	Units
S_i	Susceptible individuals	$individual$
I_i	Infected individuals	$individual$
R_i	Recovered individuals	$individual$
B_i	Pathogen concentration in water	$cell.ml^{-1}$
$\lambda_{b,i}$	Water-to-human per capita contact rate	$cell^{-1}.ml^{-1}.day^{-1}$
β_i	Human-to-human per capita contact rate	$individual^{-1}.day^{-1}$
μ_i	Natural death rate of individuals	day^{-1}
γ_i	Recovered rate of individuals	day^{-1}
δ_i	Disease death rate of individuals	day^{-1}
α_i	Pathogen shedding rate (human-water contact rate)	$cell.ml^{-1}.day^{-1}.individual^{-1}$
ε_i	Net pathogen decay rate	day^{-1}
A_i	Recruitment of susceptible individuals	$individual.day^{-1}$
a_i	Migration rate of susceptible individuals to patch i	day^{-1}
b_i	Migration rate of recovered individuals to patch i	day^{-1}

3. Mathematical analysis

3.1. Basic properties

In this subsection, we study the basic properties of the solutions of the model system (3), which are essential in the proofs of stability results.

Theorem 3.1. *The system (3) is a dynamical system on the biologically feasible compact domain,*

$$\Omega = \left\{(S_1, I_1, W_1, S_2, I_2, W_2) \in \mathbb{R}^6_+ \ / \ N \leq \frac{A}{\mu_0}, \ \ W \leq \frac{\overline{\varepsilon} A}{\underline{\varepsilon}\mu_0}\right\}.$$

Proof of Theorem 3.1: The proof is provided in two steps.

Step 1: we prove that the solutions $(S_1(t), I_1(t), W_1(t), s_2(t), I_2(t), W_2(t))$ of system (3) corresponding to initial conditions such that $S_1(0) > 0$, $S_2(0) > 0$, $I_1(0), W_1(0), I_2(0), W_2(0) \geq 0$, are non-negative. First of all, since the first and third equations of the system (3) are first order linear equations with respect to the variables S_1 and S_2 , it is easy to see that, $S_1(t) > 0$ if and only if $S_2(t) > 0$. With this remark in mind, we shall prove below that $S_1(t) > 0$ for $t \geq 0$. To this end, put $t_1^0 = \sup\{t > 0, S_1(t) > 0\}$ and $t_2^0 = \sup\{t > 0, S_2(t) > 0\}$.

If $t_1^0 = +\infty$ or $t_2^0 = +\infty$, we use the above mentioned remark to conclude that both $S_1(t)$ and $S_2(t)$ are positive for all $t \geq 0$.

If $t_1^0 < \infty$ and $t_2^0 < \infty$, we are going to prove that this leads to a contradiction. By a continuity argument, the solution functions $S_1(t)$ and $S_2(t)$ change sign at least once in the intervals $J_1 = [t_1^0, +\infty)$ and $J_2 = [t_2^0, +\infty)$, respectively. Denote by $t_1^m \in J_1$ and $t_2^m \in J_2$ the first real numbers such that $S_1(t_1^m) = 0$ and $S_2(t_2^m) = 0$, respectively. We then have

$$\forall\, t,\ 0 < t < t_1^{m_1},\ S_1(t) > 0, S_1(t_1^m) = 0 \quad \text{and} \quad \forall\, t,\ 0 < t < t_2^{m_2}, \quad S_2(t) > 0,\ S_2(t_2^m) = 0. \tag{4}$$

Without loss of generality, suppose that $t_1^m \leq t_2^m$. Then, from system (3), we have

$$S_1^{'}(t_1^m) = A_1 + a_2 S_2(t_1^m) > 0. \tag{5}$$

Equation (5) implies that there exists a positive number $t_1^{m_1} > t_1^m$ such that

$$S_1(t) > 0,\ \forall\ 0 < t < t_1^{m_1}. \tag{6}$$

Putting the relations (4) and (6) together and using the continuity of $S_1(t)$, we conclude that t_1^m is an extremum (more precisely, a minimum) of $S_1(t)$. Moreover, since $S_1(t)$ is a differentiable function on $\mathbb{R}$, one has $S_1^{'}(t_1^m) = 0$. This is a contradiction to (5). Therefore, $t_1^0 = +\infty$, which implies that $t_2^0 = +\infty$ as well.

To prove that $I_1(t), W_1(t), I_2(t), W_2(t) \geq 0$ for all $t \geq 0$, whenever $I_1(0), W_1(0), I_2(0), W_2(0) \geq 0$, we rewrite the corresponding equations in (3) in the form

$$x^{'}(t) = \mathcal{M}x(t), \tag{7}$$

where $x(t) = (I_1(t), W_1(t), I_2(t), W_2(t))^T$, $\mathcal{M} = \begin{pmatrix} -\theta_1 + \beta_1 S_1 & \lambda_1 S_1 & 0 & 0 \\ \varepsilon_1 & -\varepsilon_1 & 0 & 0 \\ 0 & 0 & -\theta_2 + \beta_2 S_2 & \lambda_2 S_2 \\ 0 & 0 & \varepsilon_2 & -\varepsilon_2 \end{pmatrix}$,

with $\theta_1 = \mu_1 + \delta_1 + \gamma_1$ and $\theta_2 = \mu_2 + \delta_2 + \gamma_2$. With $S_1(t) > 0$, $S_2(t) > 0$ as established above, $\mathcal{M}$ is a Metzler matrix (i.e., a non-negative off-diagonal entries). Thus (7) is a monotone system. Therefore $\mathbb{R}^4_+$ is invariant under the flow of system (7). This completes the proof of the positivity of the solutions and the fact that $N(t) > 0$ for all $t > 0$, whenever $N(0) > 0$.

Step 2: we prove that $N(t)$, the total population of humans at time t, and $W(t)$, the total concentration of pathogens at time t satisfy the boundedness property $0 \leq N(t) \leq \dfrac{A}{\mu_0}$ and $0 \leq W(t) \leq \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0}$, where, $A = A_1 + A_2$, $\mu_0 = min\{\mu_1, \mu_2\}$, $\underline{\varepsilon} = \min\{\varepsilon_1, \varepsilon_2\}$ and $\overline{\varepsilon} = \max\{\varepsilon_1, \varepsilon_2\}$, whenever $0 \leq N(0) \leq \dfrac{A}{\mu_0}$ and $0 \leq W(0) \leq \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0}$,

By adding the equations of the system (2), we obtain the conservation law

$$N' = A - \mu_1 N_1 - \mu_2 N_2 - \delta_1 I_1 - \delta_2 I_2 \leq A - \mu_0 N, \tag{8}$$

Applying the Gronwall inequality to Eq. (8) yields

$$N(t) \leq \frac{A}{\mu_0} + \left(N(0) - \frac{A}{\mu_0}\right) e^{-\mu_0 t}, \quad \forall\ t \geq 0, \tag{9}$$

which implies that $0 \leq N(t) \leq A/\mu_0$ for all $t \geq 0$ if $N(0) \leq A/\mu_0$. Furthermore, it follows from the fifth and sixth equations of (3) and Eq. (9) that we have the relation

$$W' \leq \frac{\overline{\varepsilon}A}{\mu_0} - \underline{\varepsilon}W,$$

to which another application of Gronwall inequality gives the bounds

$$0 \leq W(t) \leq \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0} + \left(W(0) - \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0}\right) e^{-\overline{\varepsilon}t} \leq \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0}, \quad \forall t \geq 0,$$

whenever $W(0) \leq \frac{\overline{\varepsilon}A}{\underline{\varepsilon}\mu_0}$.

Combining Step 1 and Step 2, Theorem 3.1 follows from the classical theory of dynamical systems.

□

Remark 3.2. *As explained earlier, Theorem 3.1 implies similar results for the full model (2) thanks to the third and seventh equations of (2) from where it can be seen that $R_1(t) \geq 0$ if and only if $R_2(t) \geq 0$.*

3.2. **The disease-free equilibrium**

The disease-free equilibrium (DFE) for an epidemiological metapopulation model is an equilibrium such that the disease is absent in all the patches. Thus, if $E_0 = (S_1^0, I_1^0, W_1^0, S_2^0, I_2^0, W_2^0)$ is the DFE of model system (3), then $I_1^0 = I_2^0 = 0$. As a consequence of the fifth and sixth equations of (3), $W_1^0 = W_2^0 = 0$ with S_1^0 and S_2^0 being the solutions of the system of equations

$$\begin{cases} A_1 - (\mu_1 + a_1)S_1^0 + a_2 S_2^0 &= 0, \\ A_2 - (\mu_2 + a_2)S_2^0 + a_1 S_1^0 &= 0, \end{cases}$$

which has the unique solution

$$(E_0)\begin{cases} S_1^0 &= \dfrac{A_1(\mu_2+a_2)+a_2A_2}{\mu_1\mu_2+\mu_1a_2+\mu_2a_1}, \\ \\ S_2^0 &= \dfrac{A_2(\mu_1+a_1)+a_1A_1}{\mu_1\mu_2+\mu_1a_2+\mu_2a_1}. \end{cases} \tag{10}$$

In order to investigate the stability properties of the disease-free equilibrium, we need to compute the reproduction/threshold number $\mathcal{R}_0$ of system (3). To this end, we apply the method in [33], with (I_1, I_2, W_1, W_2) and (S_1, S_2) being the infected and uninfected classes, respectively. The vectors $\mathcal{F} = (\beta_1 S_1 I_1 + \lambda_1 S_1 W_1, \beta_2 S_2 I_2 + \lambda_2 S_2 W_2, 0, 0)^T$ and $\mathcal{V} = (\theta_1 I_1, \theta_2 I_2, -\varepsilon_1 I_1 + \varepsilon_1 W_1, -\varepsilon_2 I_2 + \varepsilon_2 W_2)^T$ represent the new infection terms and the remaining transfer terms, respectively. Their Jacobian matrices evaluated at the DFE are given by

$$F = \begin{pmatrix} \beta_1 S_1^0 & 0 & \lambda_1 S_1^0 & 0 \\ 0 & \beta_2 S_2^0 & 0 & \lambda_2 S_2^0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \theta_1 & 0 & 0 & 0 \\ 0 & \theta_2 & 0 & 0 \\ -\varepsilon_1 & 0 & \varepsilon_1 & 0 \\ 0 & -\varepsilon_2 & 0 & \varepsilon_2 \end{pmatrix}.$$

Then, the reproduction number $\mathcal{R}_0$ of system (3) is the spectral radius of the next generation matrix FV^{-1}, i.e

$$\mathcal{R}_0 = \rho(FV^{-1}) = \max\{\mathcal{R}_0^{(1)}, \mathcal{R}_0^{(2)}\},$$

where

$$\mathcal{R}_0^{(1)} = \frac{(\lambda_1+\beta_1)[A_1(\mu_2+a_2)+a_2A_2]}{\theta_1(\mu_1\mu_2+\mu_1a_2+\mu_2a_1)} = \frac{(\lambda_1+\beta_1)}{\theta_1}S_1^0, \tag{11}$$

and

$$\mathcal{R}_0^{(2)} = \frac{(\lambda_2+\beta_2)[A_2(\mu_1+a_1)+a_1A_1]}{\theta_2(\mu_1\mu_2+\mu_1a_2+\mu_2a_1)} = \frac{(\lambda_2+\beta_2)}{\theta_2}S_2^0. \tag{12}$$

Remark 3.3. • *Notice that, on the one hand, when patch 1 and patch 2 are completely disconnected/isolated, their corresponding basic reproduction numbers are given by the expressions* $\widetilde{\mathcal{R}_0^{(1)}} = \dfrac{(\lambda_1+\beta_1)A_1}{\theta_1\mu_1}$ *and* $\widetilde{\mathcal{R}_0^{(2)}} = \dfrac{(\lambda_2+\beta_2)A_2}{\theta_2\mu_2}$. *On the other hand, if the infection exists in a single patch i which is connected to patch $j \neq i$ through movement of susceptible individuals, this process of migration is reflected in the disease-free equilibrium, and consequently in the disease thresholds quantities. This modifies the isolated basic reproduction numbers* $\widetilde{\mathcal{R}_0^{(i)}}$ *above, and gives rise to "patch specific" reproduction numbers* $\mathcal{R}_0^{(i)}$, $i = 1, 2$, *shown in (11) and (12).*

- *From Eqs. (11) and (12), we have*

$$\frac{\partial\mathcal{R}_0^{(1)}}{\partial a_1} = -\mu_2\frac{\mathcal{R}_0^{(1)}}{\mu_1\mu_2+\mu_1a_2+\mu_2a_1} < 0, \quad \text{and} \quad \frac{\partial\mathcal{R}_0^{(1)}}{\partial a_2} = \mu_2\frac{(\lambda_1+\beta_1)}{\theta_1}\frac{(a_1A_1+a_1A_2+\mu_1A_2)}{(\mu_1\mu_2+\mu_1a_2+\mu_2a_1)^2} > 0$$

$$\frac{\partial\mathcal{R}_0^{(2)}}{\partial a_2} = -\mu_1\frac{\mathcal{R}_0^{(2)}}{\mu_1\mu_2+\mu_1a_2+\mu_2a_1} < 0, \quad \text{and} \quad \frac{\partial\mathcal{R}_0^{(2)}}{\partial a_1} = \mu_1\frac{(\lambda_2+\beta_2)}{\theta_2}\frac{(a_2A_2+a_2A_1+\mu_2A_1)}{(\mu_1\mu_2+\mu_1a_2+\mu_2a_1)^2} > 0.$$

Thus, $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$ are monotonically decreasing and increasing functions in the argument a_1, respectively. The "direction" of the monotonicity of the functions $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$ in the argument a_2 changes. This suggests that the prevalence of the disease will decrease in patch i and increase in patch j whenever a large proportion of individual moves from patch i to patch j.

The relevance of the reproduction number is due to the following result established in [3].

Proposition 3.4. *The disease-free equilibrium E_0 is locally asymptotically stable in Ω if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.*

The biological implication of Proposition 3.4 is that, a sufficiently small flow of infectious individuals will not generate outbreak of the disease unless $\mathcal{R}_0 > 1$. For a better control on the disease, the global asymptotic stability (GAS) of the DFE is needed. Actually, enlarging the basin of attraction of E_0 to be the entire Ω is, for the model under consideration a more challenging task involving relatively new types of Lyapunov functions [29, 30, 36], as detailed below. We start with the following result, which is instrumental here and after.

Lemma 3.5. *For the four parameters μ_1, μ_2, a_1 and a_2 of system (3), there exist two positive constants m_1, m_2 such that the quadratic form:*

$$F(x, y) = m_1(\mu_1 + a_1)x^2 - (m_1a_2 + m_2a_1)xy + m_2(\mu_2 + a_2)y^2,$$

is positive definite.

Proof: A outline of the proof of Lemma 3.5 can be found in [29, 30, 36]. However, due to the importance of this lemma in what follows, we provide here a more detailed proof.

Since $F(x, y)$ is a quadratic form, it is enough to prove that there exist two positive real numbers m_1 and m_2 such that its Hessian matrix M_F in any basis (here we choose the canonical basis for simplicity) of $\mathbb{R}^2$ is positive definite. In fact,

$$\begin{aligned} \det(M_F) &= m_1m_2(\mu_1 + a_1)(\mu_2 + a_2) - \tfrac{1}{4}(m_1a_2 + m_2a_1)^2, \\ &= -\tfrac{1}{4}\left((m_1a_2 + m_2a_1)^2 - 4m_1m_2(\mu_1 + a_1)(\mu_2 + a_2)\right) = \tfrac{1}{4}Q(m_1, m_2) \end{aligned}$$

where $Q(m_1, m_2) = m_1^2a_2^2 + m_2^2a_1^2 - 2m_1m_2[2(\mu_1\mu_2 + \mu_2a_1 + \mu_1a_2) + a_1a_2]$. But $\det(M_Q) = -([2(\mu_1\mu_2 + \mu_2a_1 + \mu_1a_2) + a_1a_2]^2 - a_1^2a_2^2) < 0$. This implies that Q is degenerate (i.e, neither positive definite, nor negative definite). Therefore, there exist two positive constants m_1 and m_2 such that $Q(m_1, m_2) < 0$. For these values of m_1 and m_2, $\det(M_F)$ will be positive. This completes the proof.

□

Theorem 3.6. *The disease-free equilibrium E_0 of system (3) is globally asymptotically stable in Ω whenever $\mathcal{R}_0^{(1)} \leq 1$ and $\mathcal{R}_0^{(2)} \leq 1$.*

Proof: With m_1 and m_2 being two real numbers satisfying Lemma 3.5, we associate the following linear combination of quadratic and linear Lyapunov functions in Ω:

$$\begin{aligned} V_0 &= m_1\left(\frac{\left(S_1 - S_1^0\right)^2}{2} + S_1^0I_1 + S_1^0\left(\frac{\theta_1 - \beta_1S_1^0}{\varepsilon_1}\right)W_1\right) \\ &+ m_2\left(\frac{\left(S_2 - S_2^0\right)^2}{2} + S_2^0I_2 + S_2^0\left(\frac{\theta_2 - \beta_2S_2^0}{\varepsilon_2}\right)W_2\right), \end{aligned}$$

Note that the conditions $\mathcal{R}_0^{(1)} \leq 1$ and $\mathcal{R}_0^{(2)} \leq 1$ imply that

$$\theta_1 - \beta_1S_1^0 > 0 \quad \text{and} \quad \theta_2 - \beta_2S_2^0 > 0.$$

With this in mind, V_0 is a Lyapunov function as we now show. Let $x = S_1 - S_1^0$ and $y = S_2 - S_2^0$. Then, it can be shown after some algebraic re-arrangements that the derivative of V_0 along the trajectories of model system (3) satisfies

$$\begin{aligned} V_0' &= -m_1(\mu_1 + a_1)x^2 + m_1a_2xy - m_1(\lambda_1W_1 + \beta_1I_1)x^2 \\ &\quad -m_1(\lambda_1W_1 + m_1\beta_1I_1)x^2 - m_1\theta_1(1 - \mathcal{R}_0^{(1)})W_1S_1^0 \\ &\quad -m_2(\mu_2 + a_2)y^2 + m_2a_1xy - m_2(\lambda_2W_2 + \beta_2I_2)y^2 \\ &\quad -m_2(\lambda_2W_2 + m_2\beta_2I_2)y^2 - m_2\theta_2(1 - \mathcal{R}_0^{(2)})W_2S_2^0, \\ &= -F(x, y) - m_1(\lambda_1W_1 + m_1\beta_1I_1)x^2 - m_1\theta_1(1 - \mathcal{R}_0^{(2)})W_1S_1^0 \\ &\quad -m_2\lambda_2W_2y^2 - m_2\beta_2I_2y^2 - m_2\theta_2(1 - \mathcal{R}_2^{(0)})W_2S_2^0. \end{aligned}$$

In view of Lemma 3.5, where $F(x,y) > 0$, we have $V_0^{'} \leq 0$ as expected. Moreover, the largest invariant set contained in $\mathcal{E}_0 = \{(S_1, I_1, W_1, S_2, I_2, W_2) \in \Omega / \ V_0^{'} = 0\}$ is the disease-free equilibrium $\{E_0\}$. The global stability of E_0 follows from LaSalle invariance principle [21, 22]. This completes the proof.

□

Remark 3.7. *Theorem 3.6 is stated in [28], but the proof is incorrect. The authors made the assumption that the initial state is in* $\Gamma = \left\{(S_1, I_1, W_1, S_2, I_2, W_2) \in \Omega / \ S_1 \leq S_1^0, \ \ S_2 \leq S_2^0\right\}$. *Therefore, their proof only shows that the disease-free equilibrium is globally asymptotically stable in* Γ.

Note that Γ *is a positively invariant set under the flow of system (3) in view of the uniqueness of the solution of model (3), and of the fact that* $(S_1^0, 0, 0, S_2^0, 0, 0)$ *is an equilibrium solution.*

3.3. **Endemic equilibria**

We investigate the endemic equilibria of system (3). In the process, we clarify and prove two claims in [28] regarding the existence of endemic equilibria. The main result reads as follows, in terms of the usual threshold parameters $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$ and additional threshold parameters $\mathcal{T}_1 = \dfrac{(\lambda_1+\beta_1)}{\theta_1(\mu_1+a_1)}\left[A_1 + \dfrac{a_2\theta_2}{\lambda_2+\beta_2}\right]$, and $\mathcal{T}_2 = \dfrac{(\lambda_2+\beta_2)}{\theta_2(\mu_2+a_2)}\left[A_2 + \dfrac{a_1\theta_1}{\lambda_1+\beta_1}\right]$, reformulated in (16) and (17) below.

Theorem 3.8. *System (3) has two boundary equilibria and one interior equilibrium. More precisely:*

- *The patch-1 disease-free equilibrium* E^* *in (13) below exists whenever* $\mathcal{R}_0^{(1)} > 1$ *and* $\mathcal{R}_0^{(2)} \leq 1$, *while the patch-2 possesses the disease-free equilibrium* E^{**} *in (14) below whenever* $\mathcal{R}_0^{(2)} > 1$ *and* $\mathcal{R}_0^{(1)} \leq 1$.
- *The interior equilibrium* $\overline{E}$ *in (15) below exists whenever* $\mathcal{T}_1 > 1$ *and* $\mathcal{T}_2 > 1$.

Proof: Patch-2 disease free (or patch-1 boundary) equilibrium $E^* = (S_1^*, I_1^*, W_1^*, S_2^*, I_2^*, W_2^*)$, where $I_2^* = W_2^* = 0$, solves the system

$$\begin{cases} A_1 - \lambda_1 S_1^* W_1^* - \beta_1 S_1^* I_1^* - (\mu_1 + a_1) S_1^* + a_2 S_2^* = 0, \\ A_2 - (\mu_2 + a_2) S_2^* + a_1 S_1^* = 0, \\ \lambda_1 S_1^* W_1^* + \beta_1 S_1^* I_1^* - \theta_1 I_1^* = 0, \\ \varepsilon_1 (I_1^* - W_1^*) = 0, \end{cases}$$

Thus, the unique solution is

$$(E^*) \begin{cases} S_1^* = \dfrac{\theta_1}{\lambda_1+\beta_1}, \quad I_1^* = \dfrac{[A_1(\mu_2+a_2) + a_2A_2](\mathcal{R}_0^{(1)} - 1)}{\theta_1(\mu_2+a_2)\mathcal{R}_0^{(1)}}, \quad W_1^* = I_1^*, \\ \\ S_2^* = \dfrac{A_2(\lambda_1+\beta_1) + a_1\theta_1}{(\lambda_1+\beta_1)(\mu_2+a_2)}, \quad I_2^* = W_2^* = 0. \end{cases} \tag{13}$$

Note that I_1^* is positive if $\mathcal{R}_0^{(1)} > 1$. Similarly, patch-1 disease-free (or patch-2 boundary) equilibrium $E^{**} = \left(S_1^{**}, I_1^{**}, W_1^{**}, S_2^{**}, I_2^{**}, W_2^{**}\right)$ with $I_1^{**} = W_1^{**} = 0$, solves the system

$$\begin{cases} A_1 - (\mu_1 + a_1) S_1^{**} + a_2 S_2^{**} = 0, \\ A_2 - \lambda_2 S_2^{**} W_2^{**} - \beta_2 S_2^{**} I_2^{**} - (\mu_2 + a_2) S_2^{**} + a_1 S_1^{**} = 0, \\ \lambda_2 S_2^{**} W_2^{**} + \beta_2 S_2^{**} I_2^{**} - \theta_2 I_2^{**} = 0, \\ \varepsilon_2 (I_2^{**} - W_2^{**}) = 0, \end{cases}$$

which has the unique solution

$$(E^{**}) \begin{cases} S_1^{**} = \dfrac{A_1(\lambda_2+\beta_2) + a_2\theta_2}{(\lambda_2+\beta_2)(\mu_1+a_1)}, \quad I_1^{**} = W_1^{**} = 0, \\ \\ S_2^{**} = \dfrac{\theta_2}{\lambda_2+\beta_2}, \quad I_2^{**} = \dfrac{[A_2(\mu_1+a_1) + a_1A_1](\mathcal{R}_0^{(2)} - 1)}{\theta_2(\mu_1+a_1)\mathcal{R}_0^{(2)}}, \quad W_2^{**} = I_2^{**}. \end{cases} \tag{14}$$

We stress that I_2^{**} is positive whenever $\mathcal{R}_0^{(2)} > 1$.

The endemic (or interior) equilibrium $\overline{E} = (\overline{S}_1, \overline{I}_1, \overline{W}_1, \overline{S}_2, \overline{I}_2, \overline{W}_2)$ is the steady state of model system (3) for which all the infectious states are positive. It satisfies the equations

$$\begin{cases} A_1 - \lambda_1 \overline{S}_1 \overline{W}_1 - \beta_1 \overline{S}_1 \overline{I}_1 - (\mu_1 + a_1)\overline{S}_1 + a_2 \overline{S}_2 = 0, \\ \lambda_1 \overline{S}_1 \overline{W}_1 + \beta_1 \overline{S}_1 \overline{I}_1 - \theta_1 \overline{I}_1 = 0, \\ \varepsilon_1(\overline{I}_1 - \overline{W}_1) = 0, \\ A_2 - \lambda_2 \overline{S}_2 \overline{W}_2 - \beta_2 \overline{S}_2 \overline{I}_2 - (\mu_2 + a_2)\overline{S}_2 + a_1 \overline{S}_1 = 0, \\ \lambda_2 \overline{S}_2 \overline{W}_2 + \beta_2 \overline{S}_2 \overline{I}_2 - \theta_2 \overline{I}_2 = 0, \\ \varepsilon_2(\overline{I}_2 - \overline{W}_2) = 0, \end{cases}$$

and is uniquely found to be

$$(\bar{E}) \begin{cases} \overline{S}_1 = S_1^* = \dfrac{\theta_1}{\lambda_1 + \beta_1}, \quad \overline{I}_1 = \overline{W}_1 = \dfrac{(\mu_1 + a_1)}{(\lambda_1 + \beta_1)}(\mathcal{T}_1 - 1), \\ \\ \overline{S}_2 = S_2^{**} = \dfrac{\theta_2}{\lambda_2 + \beta_2}, \quad \overline{I}_2 = \overline{W}_2 = \dfrac{(\mu_2 + a_2)}{(\lambda_2 + \beta_2)}(\mathcal{T}_2 - 1). \end{cases} \tag{15}$$

Notice that the additional thresholds can be expressed in terms of the boundary steady states as follows:

$$\mathcal{T}_1 = \frac{(\lambda_1 + \beta_1)}{\theta_1} S_1^{**} = \frac{S_1^{**}}{S_1^0} \mathcal{R}_0^{(1)}, \tag{16}$$

and

$$\mathcal{T}_2 = \frac{(\lambda_2 + \beta_2)}{\theta_2} S_2^{*} = \frac{S_2^{*}}{S_2^0} \mathcal{R}_0^{(2)}. \tag{17}$$

□

Moreover, the threshold parameters are partially related through the following result.

Proposition 3.9. *If $\mathcal{T}_1 > 1$ and $\mathcal{T}_2 > 1$, then $\mathcal{R}_0^{(1)} > 1$ and $\mathcal{R}_0^{(2)} > 1$.*

Proof: Note that $\mathcal{T}_1 > 1$ and $\mathcal{T}_2 > 1$ are equivalent to

$$K_1 = A_1 - (\mu_1 + a_1)\frac{\theta_1}{\lambda_1 + \beta_1} + a_2 \frac{\theta_2}{\lambda_2 + \beta_2} = A_1 - (\mu_1 + a_1)\frac{S_1^0}{\mathcal{R}_0^{(1)}} + a_2 \frac{S_2^0}{\mathcal{R}_0^{(2)}} > 0$$

and

$$K_2 = A_2 - (\mu_2 + a_2)\frac{\theta_2}{\lambda_2 + \beta_2} + a_1 \frac{\theta_1}{\lambda_1 + \beta_1} = A_2 - (\mu_2 + a_2)\frac{S_2^0}{\mathcal{R}_0^{(2)}} + a_1 \frac{S_1^0}{\mathcal{R}_0^{(1)}} > 0,$$

respectively. Furthermore, since $K_1 > 0$ and $K_2 > 0$, one has

$$(\mu_2 + a_2)K_1 + a_2 K_2 > 0 \qquad \text{and} \qquad (\mu_1 + a_1)K_2 + a_1 K_1 > 0. \tag{18}$$

Replacing in (18), K_1 and K_2 by their expressions given above, direct computations show that the inequalities in (18) are equivalent to $\mathcal{R}_0^{(1)} > 1$ and $\mathcal{R}_0^{(2)} > 1$. This completes the proof.

□

Remark 3.10.

1. *Under the assumption "the infectious individuals migrate", there exit no boundary equilibria, contrary to the claim in [28]. Furthermore, our assumption leads to an explicit expression of the interior equilibrium.*
2. *In view of the method in [3, 33], it is easy to check that $\mathcal{R}_0^{(1)}$ is the threshold parameter of patch 1, when patch 2 is disease free, while $\mathcal{T}_1$ is the threshold parameter of the model (3) when the disease is endemic in patch 2. A similar interpretation applies to $\mathcal{R}_0^{(2)}$ and $\mathcal{T}_2$. Moreover, in line with the classical metapopulation setting, the threshold quantity $\mathcal{T}_i$ measures the ability of a disease to invade patch i from the endemic patch j, $(j \neq i)$ [28, 29].*

We conclude this section by investigating the stability of the boundary endemic equilibrium E^*.

Proposition 3.11. *Assume that $\mathcal{R}_0^{(1)} > 1$ and $\mathcal{R}_0^{(2)} \leq 1$. Then the boundary equilibrium E^* of system (3) is locally asymptotically stable if $\mathcal{T}_2 \leq 1$ and unstable if $\mathcal{T}_2 > 1$.*

Proof: Instead of applying the Center Manifold Theory in [8] that would restrict the LAS of E^* to the values of $\mathcal{T}_1$ and $\mathcal{T}_2$ near 1, we use an alternative approach that avoids this restriction. The characteristic polynomial $P^*(X)$ of the Jacobian matrix of model system (3) evaluated at the boundary equilibrium E^* is provided in Appendix A.1 and can be written as

$$P^*(X) = P_0(X)P_1(X), \tag{19}$$

where

$$P_0(X) = X^2 + D_1X + D_0 \qquad \text{and} \qquad P_1(X) = X^4 + B_3X^3 + B_2X^2 + B_1X + B_0, \tag{20}$$

with

$$D_1 = \varepsilon_2 + \theta_2 - \beta_2 S_2^* \qquad \text{and} \qquad D_0 = \varepsilon_2(\theta_2 - \lambda_2 S_2^* - \beta_2 S_2^*), \tag{21}$$

and

$$\begin{aligned} B_3 &= \mu_1 + a_1 + \mu_2 + a_2 + \varepsilon_1 + (\lambda_1 + \beta_1)I_1^* + \lambda_1 S_1^* > 0, \\ B_2 &= (\mu_1\mu_2 + \mu_1 a_1 + \mu_2 a_1) + (\mu_2 + a_2 + \theta_1 + \varepsilon_1)(\lambda_1 + \beta_1)I_1^* + (\varepsilon_1 + \lambda_1 S_1^*)(\mu_1 + a_1 + \mu_2 + a_2) > 0, \\ B_1 &= (\mu_1\mu_2 + \mu_1 a_1 + \mu_2 a_1)(\varepsilon_1 + \lambda_1 S_1^*) + (\theta_1 + \varepsilon_1 + \theta_1\varepsilon_1)(\mu_2 + a_2)(\lambda_1 + \beta_1)I_1^* > 0, \\ B_0 &= \varepsilon_1\theta_1(\mu_2 + a_2)(\lambda_1 + \beta_1)I_1^* > 0. \end{aligned} \tag{22}$$

Using the expression of $\mathcal{T}_2$ in Eq. (17), Eq. (21) becomes

$$D_0 = \varepsilon_2(\theta_2 - \lambda_2 S_2^* - \beta_2 S_2^*) = \varepsilon_2\theta_2(1 - \mathcal{T}_2) \text{ and } D_1 \geq \varepsilon_2 + \theta_2 - \beta_2 S_2^* - \lambda_2 S_2^* = \varepsilon_2 + \theta_2(1 - \mathcal{T}_2). \tag{23}$$

Thus, $D_0 > 0$ whenever $\mathcal{T}_2 > 1$, which implies that E^* is unstable. If $\mathcal{T}_2 \leq 1$, all the roots of P_0 have negative real parts. Equally all the roots of P_1 have negative real parts. This results from the Routh-Hurwitz criteria and the inequality

$$B_1B_2B_3 > B_1^2 + B_0B_3^2. \tag{24}$$

which is proved in Appendix A.2. This implies that E^* is locally asymptotically stable. This achieves the proof.

□

Proposition 3.11 is improved by the next theorem, which is a competitive-exclusion-principle-type result whose proof is postponed to Appendix A.3.

Theorem 3.12. *If $\mathcal{R}_0^{(1)} > 1$, $\mathcal{R}_0^{(2)} \leq 1$ and $\mathcal{T}_2 \leq 1$, then the boundary equilibrium E^* of system (3) is globally asymptotically stable in the region Ω, without the manifold $\{I_1 = W_1 = 0\}$.*

Similarly, we have the following stability results for the boundary equilibrium E^{**}.

Proposition 3.13. *Assume $\mathcal{R}_0^{(2)} > 1$ and $\mathcal{R}_0^{(1)} \leq 1$, then the boundary equilibrium E^{**} of system (3) is locally asymptotically stable if $\mathcal{T}_1 \leq 1$ and unstable if $\mathcal{T}_1 > 1$.*

Theorem 3.14. *If $\mathcal{R}_0^{(2)} > 1$, $\mathcal{R}_0^{(1)} \leq 1$ and $\mathcal{T}_1 \leq 1$, then the boundary equilibrium E^{**} of system (3) is globally asymptotically stable in the region Ω, without the manifold $\{I_2 = W_2 = 0\}$.*

As for the stability of the interior endemic equilibrium, its local asymptotic stability is established as in the proof of Proposition 3.11, though the computations are long. The proof of its GAS is postponed to Appendix A.4.

Proposition 3.15. *If $\mathcal{T}_1 > 1$ and $\mathcal{T}_2 > 1$, then the endemic equilibrium $\overline{E}$ of system (3) is locally asymptotically stable.*

Theorem 3.16. *If $\mathcal{T}_1 > 1, \mathcal{T}_2 > 1$ and the values of the parameters of system (3) are such that*

$$A_1 - \lambda_1 \overline{S}_1 \overline{I}_1 \geq 0 \qquad \text{and} \qquad A_2 - \lambda_2 \overline{S}_2 \overline{I}_2 \geq 0, \tag{25}$$

then, the interior endemic equilibrium $\overline{E}$ of system (3) is globally asymptotically stable in the interior of Ω.

Remark 3.17. *The following comments are in order from the biological point of view.*

1. *The inequalities in (25) are satisfied if the following two conditions are met:*
   a) *The outflow of susceptible individuals from any patch matches the inflow in the same patch in the following specific sense : $a_1 \overline{S}_1 = a_2 \overline{S}_2$.*
   b) *All epidemiological parameters in a given patch are equal to their analogues in the other patch.*
2. *In all the results above, where the stability of the equilibria involves threshold quantities other than the classical reproduction number, we can say that the value $\mathcal{R}_0 = 1$ is not always a forward bifurcation point of our model (3) as it is the case for most epidemic models [14, 19, 20, 24, 31]. Additional thresholds, namely $\mathcal{T}_1$ and $\mathcal{T}_2$ are needed to prove the existence and stability of endemic equilibria.*
3. *Investigating the GAS of $\overline{E}$ in the case when condition (25) is not met is an issue of interest. In this regard, numerical simulations below suggest that $\overline{E}$ is GAS.*

4. Numerical simulations

In this section, we give numerical simulations that support the theory presented in the previous sections. The simulations are produced by MatLab. While the parameters in patch 1 are mostly taken from [9, 32], we have assumed them accordingly in patch 2.

Table 2: Numerical values for the parameters of system (3)

Parameters	Estimates	Parameters	Estimates
λ_1	Variable	δ_1	0.03 day^{-1}
λ_2	variable	δ_2	0.034 day^{-1}
β_1	0.000022 $individuals^{-1}.day^{-1}$	α_1	50 $cells.day^{-1}.individuals^{-1}$
β_2	0.000025 $individuals^{-1}.day^{-1}$	α_2	52 $cells.day^{-1}.individuals^{-1}$
μ_1	0.09 day^{-1}	ε_1	0.8 day^{-1}
μ_2	0.03 day^{-1}	ε_2	0.7 day^{-1}
γ_1	0.33 day^{-1}	A_1	40 $individuals.day^{-1}$
γ_2	0.035 day^{-1}	A_2	5 $individuals.day^{-1}$
a_1	0.032 day^{-1}	a_2	0.013 day^{-1}

Figure 2, an illustration of Theorem 3.6, shows the GAS of the disease-free equilibrium for the infected individuals and bacteria cells in each patch using various initial conditions when $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$ and $\beta_2 = 0.000025$ (so that $\mathcal{R}_0^{(1)} = 07367 < 1$ and $\mathcal{R}_0^{(2)} = 0.6861 < 1$. It is seen on this figure that the disease disappears in the two patches when $\mathcal{R}_0 \leq 1$.

Fig.3 and Fig.4 illustrate the GAS of boundary equilibria. With $\lambda_1 = 0.00014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$ and $\beta_2 = 0.000025$ (so that $\mathcal{R}_0^{(1)} = 7.2041 > 1$, $\mathcal{R}_0^{(2)} = 0.6861 < 1$, $\mathcal{T}_1 = 7.576 > 1$ and $\mathcal{T}_2 = 0.2708 < 1$), Fig.3 displays the GAS of the patch 1 boundary equilibrium E^* as demonstrated in Theorem 3.12, while with $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.00002$ and $\beta_2 = 0.000025$ (so that $\mathcal{R}_0^{(1)} = 0.7367 < 1$, $\mathcal{R}_0^{(2)} = 5.9712 > 1$, $\mathcal{T}_1 = 0.6675 < 1$ and $\mathcal{T}_2 = 7.4714 > 1$) Fig.4 shows the GAS of the patch 2 boundary equilibrium E^{**} as proved in Theorem 3.14.

Figure 5 shows the GAS of the interior equilibrium for the parameter values $\lambda_1 = 0.00014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.00002$ and $\beta_2 = 0.000025$ so that $\mathcal{R}_0^{(1)} = 7.2041 > 1$, $\mathcal{R}_0^{(2)} = 5.9712 > 1$, $\mathcal{T}_1 = 6.5274 > 1$ and $\mathcal{T}_2 = 2.357 > 1$. This illustrates Theorem 3.16.

Further, numerical simulations are carried out to investigate the role of human movements in the system (3). Model system (3) is simulated in two cases below, with the initial conditions $S_1(0) = 1000$, $I_1(0) = 50$, $W_1(0) = 750$, $S_2(0) = 1500$, $I_2(0) = 70$ and $W_2(0) = 800$.

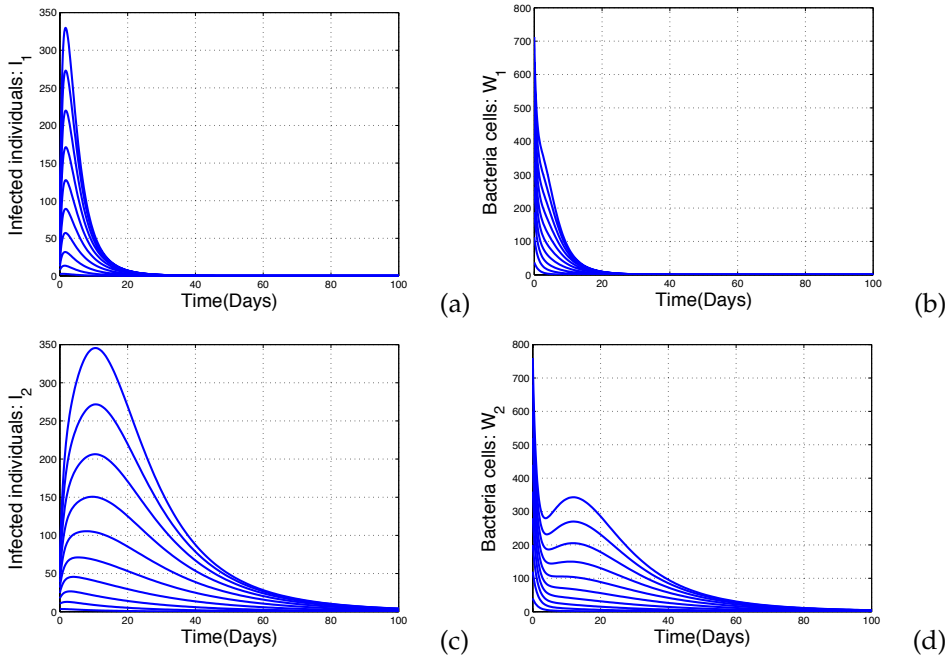

Figure 2: GAS of the DFE for $\mathcal{R}_0 \leq 1$(Theorem 3.6): $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$ and $\beta_2 = 0.000025$ so that $\mathcal{R}_0^{(1)} = 07367 < 1$ and $\mathcal{R}_0^{(2)} = 0.6861 < 1$.

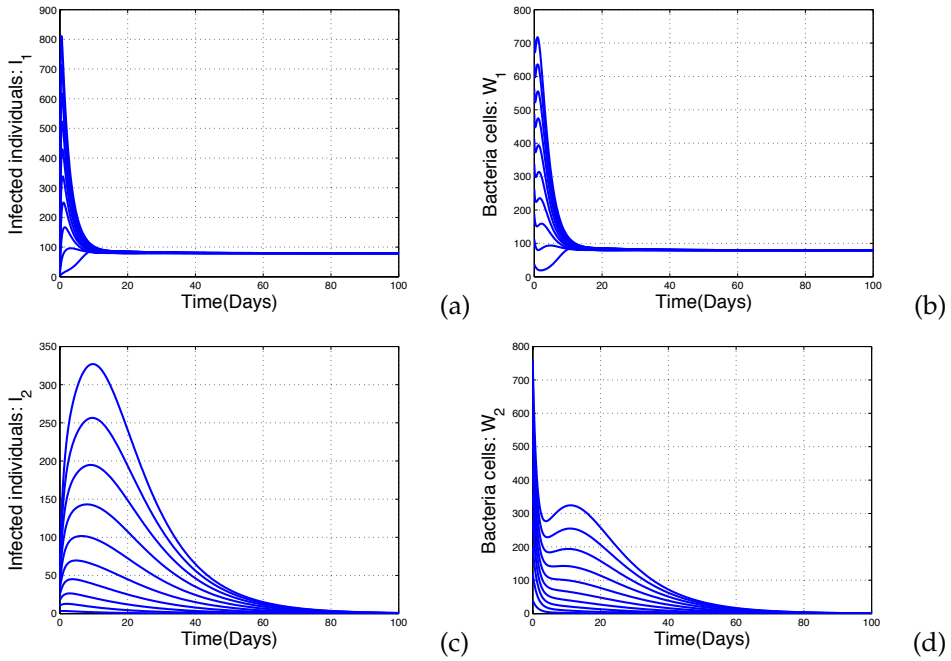

Figure 3: GAS of the boundary endemic equilibrium E^* (Theorem 3.12): $\lambda_1 = 0.00014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$ and $\beta_2 = 0.000025$ so that $\mathcal{R}_0^{(1)} = 7.2041 > 1$, $\mathcal{R}_0^{(2)} = 0.6861 < 1$, $\mathcal{T}_1 = 7.576 > 1$ and $\mathcal{T}_2 = 0.2708 < 1$.

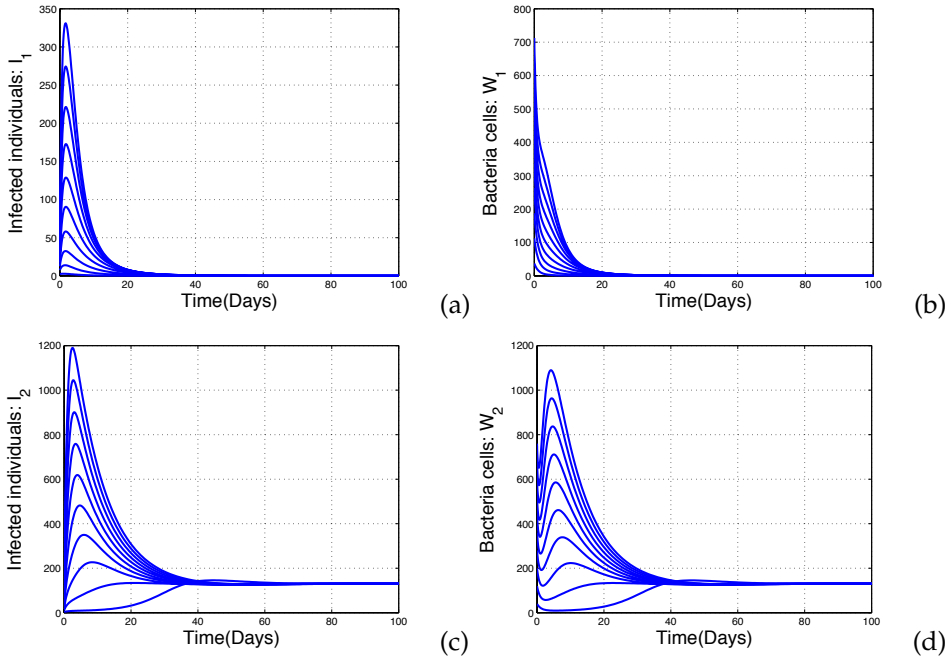

Figure 4: GAS of the boundary endemic equilibrium E^{**} (Theorem 3.14): $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.00002$ and $\beta_2 = 0.000025$ so that $\mathcal{R}_0^{(1)} = 0.7367 < 1$, $\mathcal{R}_0^{(2)} = 5.9712 > 1$, $\mathcal{T}_1 = 0.6675 < 1$ and $\mathcal{T}_2 = 7.4714 > 1$.

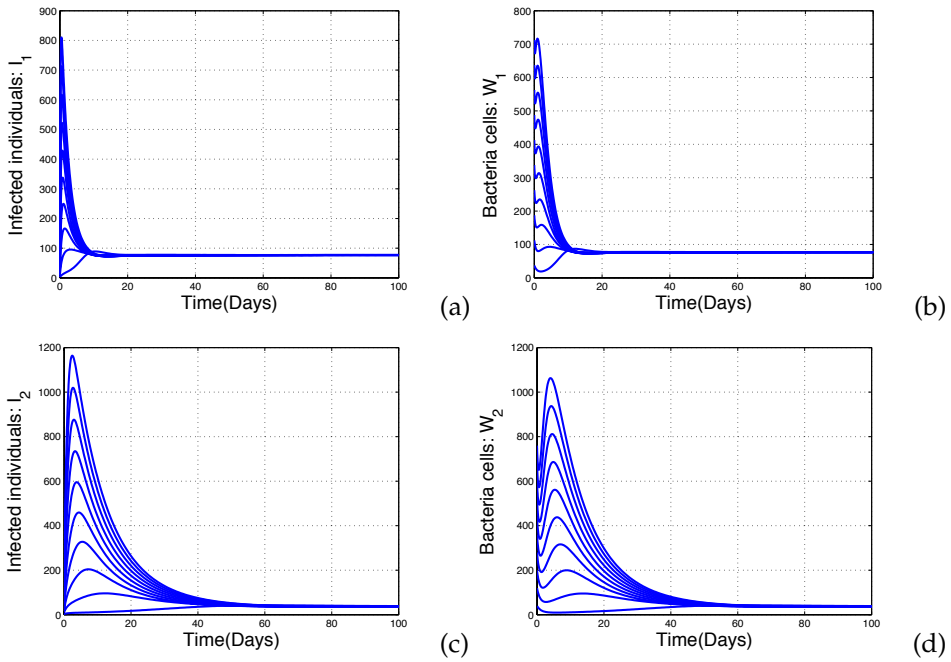

Figure 5: GAS of the interior endemic equilibrium $\overline{E}$ (Theorem 3.16): $\lambda_1 = 0.00014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.00002$ and $\beta_2 = 0.000025$ so that $\mathcal{R}_0^{(1)} = 7.2041 > 1$, $\mathcal{R}_0^{(2)} = 5.9712 > 1$, $\mathcal{T}_1 = 6.5274 > 1$ and $\mathcal{T}_2 = 2.357 > 1$.

- *Case 1.* We consider the hypothetical scenario where cholera begins to spread between a high prevalence endemic region (patch 1) and a low prevalence region where a minor outbreak could be eradicated (patch 2). We choose $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$, $\beta_2 = 0.000025$ and $a_2 = 0.013$. Figures 6 (a) and (b) correspond to the cases $a_1 = a_2$ (so that $\mathcal{R}_0^{(1)} = 7.8689 > 1$, $\mathcal{R}_0^{(2)} = 0.5067 < 1$, $\mathcal{T}_1 = 9.3076 > 1$ and $\mathcal{T}_2 = 0.1878 < 1$), $a_1 = 20a_2$ and $a_1 = 50a_2$, respectively. They illustrate that allowing migration from patch 1 to patch 2 could lead to a larger prevalence of cholera in patch 2. This suggests that limiting the movement of individuals from an infected patch to a non-infected patch is a good way to fight against the disease.

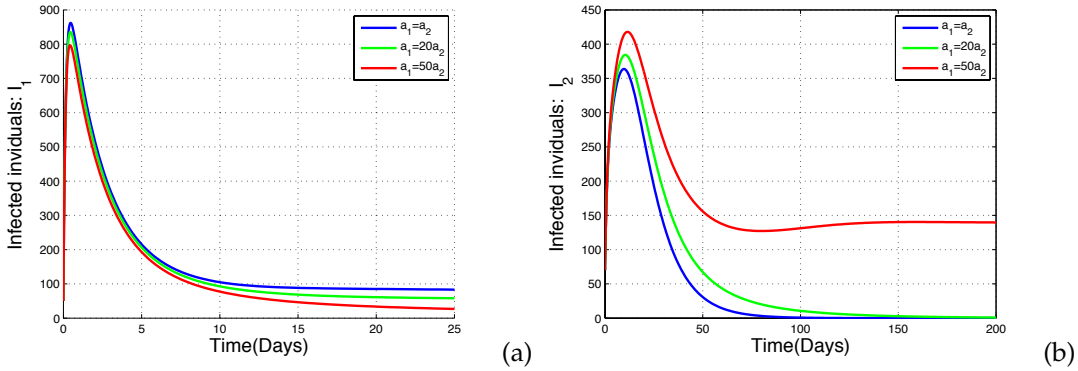

Figure 6: Impact of susceptible individuals movement from a high prevalence patch: with a_1 proportional to $a_2 = 0.013$, $\lambda_1 = 0.000014$, $\beta_1 = 0.000022$, $\lambda_2 = 0.000002$, $\beta_2 = 0.000025$, $a_2 = 0.013$ so that $\mathcal{R}_0^{(1)} = 7.8689 > 1$, $\mathcal{R}_0^{(2)} = 0.5067 < 1$, it is observed that, increasing continuously the movement of susceptible individuals from a high prevalence patch 1 (a) to a lower prevalence patch 2 can finally increase the prevalence in patch 2 to reach the endemic level as illustrates in (b).

- *Case 2.* We consider the case when many susceptible individuals move from patch 1 to patch 2. Simulation results showing the effect of increasing the migration rate from patch 1 to patch 2 are given in Fig.7. As expected, there is an increase of the number of infected individuals in patch 2, and a decrease of the number of infected individuals in patch 1. This fact is further displayed in Fig.8 in accordance with the Remark 3.3 regarding the monotonicity of the threshold parameters $\mathcal{R}_0^1$ and $\mathcal{R}_0^2$.

5. Discussion and conclusion

The point of departure of this work is to acknowledge the complexity of taking into account the movement of humans in the modeling of cholera. In some of the existing models in the literature, the difficulty is overcome through questionable assumptions such as the water movement as migration [12], the patch model without human movement [4], the patch model with displacement of infected individuals and no migration of recovered individuals [28].

In this work, we have considered a two patch model in which the following factors of movements are incorporated: (a) a more general demographic structure, (b) the difference of demographic structure and disease transmission between the two patches and (c) the difference between the dispersal rates of susceptible individuals, which simulates the process of disease control.

Our findings on the long term dynamics of the system can be summarized as follows:

1. we computed the disease-free equilibrium and the reproduction number $\mathcal{R}_0$ as the maximum of the threshold parameters $\mathcal{R}_0^{(i)}$ that determine, the outcome of the disease in each patch i. Furthermore, three unique endemic equilibria are computed explicitly: two boundary equilibria in terms of $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$; one interior equilibrium in terms of two additional quantities $\mathcal{T}_1$ and $\mathcal{T}_2$ where $\mathcal{T}_i$ is a threshold parameter of the model when the disease is endemic in the order patch. The latter threshold quantities are in agreement with the

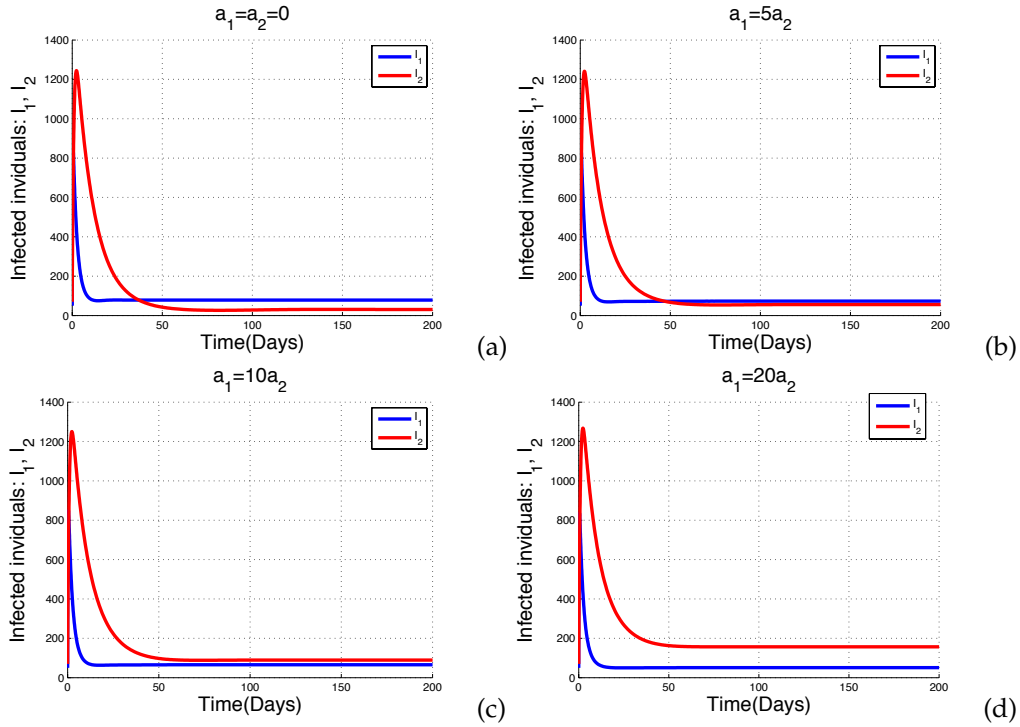

Figure 7: Effects of varying the migration rates of susceptible individuals: with initially $\mathcal{R}_0^{(1)} > \mathcal{R}_0^{(2)} > 1$, it is observed that, increasing the movement of susceptible individuals from a high prevalence endemic patch 1 to a lower prevalence endemic patch 2 can reverse the trend ($1 < \mathcal{R}_0^{(1)} < \mathcal{R}_0^{(2)}$) by lowering the prevalence in patch 1, and increasing it in patch 2.

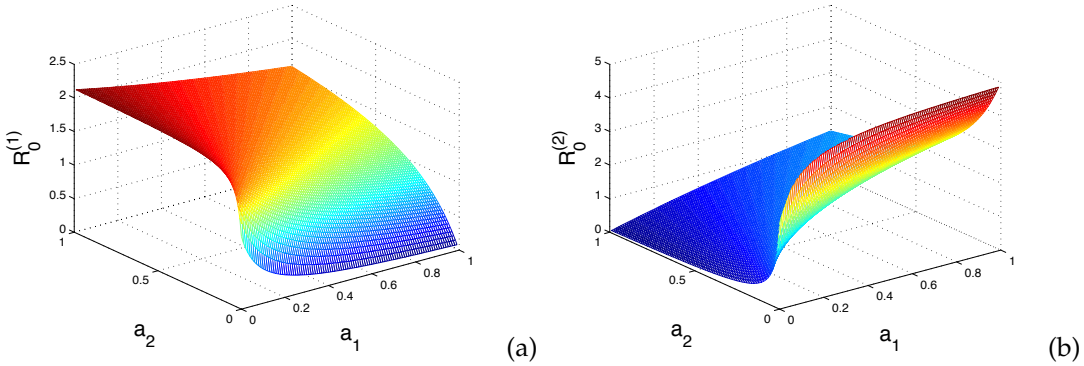

Figure 8: $\mathcal{R}_0^{(1)}$ and $\mathcal{R}_0^{(2)}$ as a function of a_1 and a_2: clearly $\mathcal{R}_0^{(1)}$ is a decreasing function of a_1 and an increasing function of a_2, (b) $\mathcal{R}_0^{(2)}$ is a decreasing function of a_2 and an increasing function of a_1. This illustrates Remark 3.3.

classical metapopulation setting where they measure the ability of a disease to invade patch i from the endemic patch j, ($j \neq i$) [28, 29].

2. we proved that the disease-free equilibrium is globally asymptotically stable whenever $\mathcal{R}_0 \leq 1$. We established the global asymptotic stability of the boundary endemic equilibrium corresponding to the larger value than one of the threshold parameter $\mathcal{R}_0^{(i)}$, in agreement with the competitive exclusion principle. We showed the global asymptotic stability of the interior equilibrium when the two additional threshold parameters are greater than one. A big deal in the proof of the global results has been the construction of Lyapunov functions of gradual sophistication ranging from a linear combination of the quadratic and linear Lyapunov functions (Theorem 3.6), a linear combination of quadratic, linear and Volterra-type Lyapunov functions (Theorem 3.12 and Theorem 3.14) to a linear combination of Volterra-type Lyapunov functions (Theorem 3.16). Thus, we have successfully applied to a metapopulation model for direct and indirect transmitted diseases, the types of Lyapunov functions that were originally designed in [14, 30, 34] for direct transmitted diseases.
3. we showed computationally that limiting and allowing human movements reduces and increases the spread of the disease, respectively.

Different improvements and extensions of the model on which we are still working include:

- extension to n patches though it is not easy to handle the model;
- considering explicitly the lost of immunity of recovered individuals;
- introducing time-dependent parameters;
- considering variable mobility rates of human individuals by taking into account: the relative attractiveness, the overcrowding and the return trips.

Finally, the design of Nonstandard Finite Difference Schemes [1] is an issue of interest as it has never been considered for the patch models.

Appendices

A.1. Computation of the coefficients of $P^*(X)$ in the proof of Proposition 3.11

The characteristic polynomial $P^*(X)$ of the Jacobian matrix J^* of system (3) evaluated at the boundary equilibrium E^* is the determinant of the following matrix:

$$J^* - XI_6 = \begin{pmatrix} -\phi_1 - X & -\beta_1 S_1^* & -\lambda_1 S_1^* & a_2 & 0 & 0 \\ \varphi_1 & -\lambda_1 S_1^* - X & \lambda_1 S_1^* & 0 & 0 & 0 \\ 0 & \xi_1 & -\xi_1 - X & 0 & 0 & 0 \\ a_1 & 0 & 0 & -\mu_2 - a_2 - X & -\beta_2 S_2^* & -\lambda_2 S_2^* \\ 0 & 0 & 0 & 0 & -\lambda_2 S_2^* - X & \lambda_2 S_2^* \\ 0 & 0 & 0 & 0 & \xi_2 & -\xi_2 - X \end{pmatrix} = \begin{pmatrix} J_1^* - XI_4 & 0 \\ 0 & J_2^* - XI_2 \end{pmatrix},$$

where $\phi_1 = (\lambda_1 + \beta_1)I_1^* + \mu_1 + a_1$, $\varphi_1 = (\lambda_1 + \beta_1)I_1^*$, $J_2^* - XI_2 = \begin{pmatrix} -\lambda_2 S_2^* - X & \lambda_2 S_2^* \\ \xi_2 & -\xi_2 - X \end{pmatrix}$ and

$$J_1^* - XI_4 = \begin{pmatrix} -\phi_1 - X & -\beta_1 S_1^* & -\lambda_1 S_1^* & a_2 \\ \varphi_1 & -\lambda_1 S_1^* - X & \lambda_1 S_1^* & 0 \\ 0 & \xi_1 & -\xi_1 - X & 0 \\ a_1 & 0 & 0 & -\mu_2 - a_2 - X \end{pmatrix}.$$

Thus $P^*(X) = P_0(X)P_1(X)$, where $P_0(X) = \det(J_0^* - XI_2) = X^2 + D_1X + D_0$, with the coefficients D_0, D_1 defined in Eq. (23). For the computation of $P_1(X) = \det(J_1^* - XI_4)$, we perform successively the following linear operations on rows and columns of $(J_1^* - XI_4)$: (i)- replace column 2 by column 3 + column 2; (ii)- replace row 1 by row 2 + row 1; (iii)- replace row 2 by row 2 - row 3. Since $\theta_1 = (\lambda_1 + \beta_1)S_1^*$, one obtains

$$P_1(X) = \begin{vmatrix} \varphi_1 - \phi_1 - X & -\theta_1 - X & 0 & a_2 \\ \varphi_1 & 0 & \xi_1 + \lambda_1 S_1^* + X & 0 \\ 0 & -X & -\xi_1 - X & 0 \\ a_1 & 0 & 0 & -\mu_2 - a_2 - X \end{vmatrix}.$$

Further, we expand this determinant which respect to the last row 4 and do simple calculations which give the coefficients B_0, B_1, B_2, B_3 of $P_1(X)$ defined in Eq. (22).

□

A.2. Proof of inequality (24)

To show that the inequality (24) holds, we gather terms in $B_1B_2B_3$ and $B_1^2 + B_0B_3^2$ in such a way that it is easier to compare them. A lengthy calculation done by hand gives the following couple of expressions:

$$\begin{aligned} B_1^2 + B_0B_3^2 &= (\mu_1\mu_2 + \mu_1a_2 + \mu_2a_1)^2(\varepsilon_1 + \lambda_1 S_1^*)^2 && \text{(26a)} \\ &+ \left[\varepsilon_1\theta_1 + (\theta_1 + \varepsilon_1)(\mu_2 + a_2)\right]^2 ((\lambda_1 + \beta_1)I_1^*)^2 && \text{(26b)} \\ &+ 2\left[\varepsilon_1\theta_1 + (\theta_1 + \varepsilon_1)(\mu_2 + a_2)\right](\mu_1\mu_2 + \mu_1a_2 + \mu_2a_1)(\varepsilon_1 + \lambda_1 S_1^*)((\lambda_1 + \beta_1)I_1^*) && \text{(26c)} \\ &+ \varepsilon_1\theta_1(\mu_2 + a_2)((\lambda_1 + \beta_1)I_1^*)^3 && \text{(26d)} \\ &+ 2\varepsilon_1\theta_1(\mu_2 + a_2)(\mu_1 + a_1 + \mu_2 + a_2)(\varepsilon_1 + \lambda_1 S_1^*)((\lambda_1 + \beta_1)I_1^*) && \text{(26e)} \\ &+ 2\varepsilon_1\theta_1(\mu_2 + a_2)(\mu_1 + a_1 + \mu_2 + a_2)((\lambda_1 + \beta_1)I_1^*)^2 && \text{(26f)} \\ &+ 2\varepsilon_1\theta_1(\mu_2 + a_2)(\varepsilon_1 + \lambda_1 S_1^*)((\lambda_1 + \beta_1)I_1^*)^2. && \text{(26g)} \end{aligned}$$

and

$$
\begin{aligned}
B_1B_2B_3 &= (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)^2(\mu_1+a_1+\mu_2+a_2)((\lambda_1+\beta_1)I_1^*) && \text{(27a)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\mu_1+a_1+\mu_2+a_2)((\lambda_1+\beta_1)I_1^*)(\varepsilon_1+\lambda_1S_1^*)(\theta_1+\varepsilon_1+\mu_2+a_2) && \text{(27b)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\mu_1+a_1+\mu_2+a_2)^2(\varepsilon_1+\lambda_1S_1^*)^2 && \text{(27c)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\mu_1+a_1+\mu_2+a_2)(\varepsilon_1+\lambda_1S_1^*)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27d)}\\
&+ (\mu_1+a_1+\mu_2+a_2)((\lambda_1+\beta_1)I_1^*)^2(\theta_1+\varepsilon_1+\mu_2+a_2)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27e)}\\
&+ (\mu_1+a_1+\mu_2+a_2)^2(\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2))(\lambda_1+\beta_1)I_1^* && \text{(27f)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)^2(\varepsilon_1+\lambda_1S_1^*)^2 && \text{(27g)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\varepsilon_1+\lambda_1S_1^*)^2((\lambda_1+\beta_1)I_1^*)(\theta_1+\varepsilon_1+\mu_2+a_2) && \text{(27h)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\mu_1+a_1+\mu_2+a_2)(\varepsilon_1+\lambda_1S_1^*)^3 && \text{(27i)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\varepsilon_1+\lambda_1S_1^*)((\lambda_1+\beta_1)I_1^*)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27j)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)^2(\varepsilon_1+\lambda_1S_1^*)((\lambda_1+\beta_1)I_1^*) && \text{(27k)}\\
&+ (\varepsilon_1+\lambda_1S_1^*)((\lambda_1+\beta_1)I_1^*)^2(\theta_1+\varepsilon_1+\mu_2+a_2)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27l)}\\
&+ (\mu_1+a_1+\mu_2+a_2)(\varepsilon_1+\lambda_1S_1^*)^2((\lambda_1+\beta_1)I_1^*)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27m)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\varepsilon_1+\lambda_1S_1^*)((\lambda_1+\beta_1)I_1^*)^2(\theta_1+\varepsilon_1+\mu_2+a_2) && \text{(27n)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)(\mu_1+a_1+\mu_2+a_2)(\varepsilon_1+\lambda_1S_1^*)^2((\lambda_1+\beta_1)I_1^*) && \text{(27o)}\\
&+ (\mu_1\mu_2+\mu_1a_2+\mu_2a_1)((\lambda_1+\beta_1)I_1^*)^2\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27p)}\\
&+ ((\lambda_1+\beta_1)I_1^*)^3(\theta_1+\varepsilon_1+\mu_2+a_2)\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right] && \text{(27q)}\\
&+ (\mu_1+a_1+\mu_2+a_2)(\varepsilon_1+\lambda_1S_1^*)((\lambda_1+\beta_1)I_1^*)^2\left[\varepsilon_1\theta_1+(\theta_1+\varepsilon_1)(\mu_2+a_2)\right], && \text{(27r)}
\end{aligned}
$$

To show that $B_1B_2B_3-(B_1^2+B_0B_3^2)>0$, we proceed by inspection to conclude that all the terms in $(B_1^2+B_0B_3^2)$ are present in $B_1B_2B_3$.

(26a) is present in (27c), so that (27c)- (26a)> 0.
(26b) is present in (27e), (27l) and (27r), so that (27e)+ (27l) + (27r)- (26b) >0.
(26c) is present in (27h) and (27j), so that (27h) + (27j)- (26c) > 0.
(26d) is present in (27f), so that (27f) - (26d) > 0.
(26e) is present in (27l), so that (27l) - (26e) > 0.
(26f) is present in (27q), so that (27q) - (26f) > 0.
(26g) is present in (27f) and (27m), so that (27f) + (27m)- (26g) > 0.
(26h) is present in (27e) and (27r), so that (27e) + (27r)- (26h) > 0.
(26i) is present in (27l), so that (27l) - (26i) > 0.

Putting all these expressions together, we have $B_1B_2B_3-(B_1^2+B_0B_3^2)>0$.

□

A.3. Proof of Theorem 3.12 and Theorem 3.14

We deal with Theorem 3.12, the proof being similar for Theorem 3.14.

We set $\Omega_1=\{(S_1,I_1,W_1,S_2,I_2,W_2)\in\Omega/\ I_1>0,\ W_1>0\}$ and consider the following combined linear-quadratic-Volterra-type Lyapunov function in Ω_1:

$$
\begin{aligned}
L_1 &= m_1\left[\frac{(S_1-S_1^*)^2}{2}+S_1^*\left(I_1-I_1^*\ln I_1\right)+\frac{\lambda_1(S_1^*)^2}{\varepsilon_1}\left(W_1-I_1^*\ln W_1\right)\right]\\
&+ m_2\left[\frac{\left(S_2-S_2^*\right)^2}{2}+S_2^*I_2+S_2^*\left(\frac{\theta_2-\beta_2S_2^*}{\varepsilon_2}\right)W_2\right],
\end{aligned}
\tag{28}
$$

where the numbers m_1 and m_2 are chosen according to Lemma 3.5.

The time derivative of L_1 along the trajectories of system (3) is

$$\begin{aligned} L_1^{'} &= m_1\Big[(S_1-S_1^*)(A_1-(\mu_1+a_1)S_1-\beta_1S_1I_1-\lambda_1S_1W_1+a_2S_2)\Big] \\ &+ m_1\left[S_1^*\left(1-\frac{I_1^*}{I_1}\right)(\lambda_1S_1I_1+\beta_1S_1I_1-\theta_1I_1)+\frac{\lambda_1(S_1^*)^2}{\varepsilon_1}\left(1-\frac{I_1^*}{W_1}\right)(I_1-W_1)\right] \\ &+ m_2\Big[(S_2-S_2^*)(A_2-(\mu_2+a_2)S_2-\beta_2S_2I_2-\lambda_2S_2W_2+a_1S_1)\Big] \\ &+ m_2\left[S_2^*(\beta_2S_2I_2W_2-\theta_2I_2)+S_2^*\left(\frac{\theta_2-\beta_2S_2^*}{\varepsilon_2}\right)(I_1-W_2)\right]. \end{aligned} \tag{29}$$

Note that at the boundary equilibrium E^*, one has

$$A_1=(\mu_1+a_1)S_1^*+\beta_1S_1^*I_1^*+\lambda_1S_1^*I_1^*-a_2S_2^* \qquad \text{and} \qquad A_2=(\mu_1+a_1)S_1^*-a_1S_1^*.$$

Plugging the above expressions in Eq. (29) gives

$$\begin{aligned} L_1^{'} &= -m_1(\mu_1+a_1)(S_1-S_1^*)^2+(m_1a_2+m_2a_1)(S_1-S_1^*)(S_2-S_2^*)-m_2(\mu_2+a_2)(S_2-S_2^*)^2 \\ &+ m_1\Big[\beta_1S_1^*I_1^*S_1-\beta_1(S^*)^2I_1^*+\lambda_1S_1^*I_1^*S_1-(\beta_1S_1^2-2\beta_1S_1S_1^*)I_1\Big] \\ &- m_1\Big[(\lambda_1S_1^2-2\lambda_1S_1S_1^*-\lambda_1(S_1^*)^2)W_1-\theta_1S_1^*I_1-\beta_1S_1S_1^*I_1^*+\theta_1S_1^*I_1^*\Big] \\ &+ m_1\left[\lambda_1(S_1^*)^2I_1^*-\frac{\lambda_1(S_1^*)^2I_1^*I_1}{W_1}-\frac{\lambda_1S_1^*I_1^*S_1W_1}{I_1}\right] \\ &+ m_2\Big[-\beta_2I_2(S_2^2-2S_2S_2^*+(S_2^*)^2)-\lambda_2W_2(S_2^2-2S_2S_2^*+(S_2^*)^2)\Big] \\ &+ m_2\Big[\lambda_2W_2(S_2^*)^2-\theta_2S_2^*W_2+\beta_2(S_2^*)^2W_2\Big]. \end{aligned} \tag{30}$$

Setting $x=(S_1-S_1^*)$, $y=(S_2-S_2^*)$, and keeping in mind that $\theta_1=(\lambda_1+\beta_1)S_1^*$, Eq. (30) becomes

$$\begin{aligned} L_1^{'} &= -F(x,y)-m_1\Big[\beta_1I_1x^2+\lambda_1W_2x^2\Big] \\ &+ m_1\left[2\lambda_1(S_1^*)^2I_1^*-\frac{\lambda_1(S_1^*)^2I_1^*I_1}{W_1}-\frac{\lambda_1S_1^*I_1^*S_1W_1}{I_1}\right] \\ &+ m_2\Big[-\beta_2I_2y^2-\lambda_2W_2y^2+(\lambda_2S_2^*+\beta_2S_2^*-\theta_2)S_2^*W_2\Big]. \end{aligned}$$

Putting $\lambda_1(S_1^*)^2I_1^*$ in factor in the second brackets and using the definition (17) of $\mathcal{T}_2$ in the third brackets, we have:

$$\begin{aligned} L_1^{'} &= -F(x,y)-m_1\Big[\beta_1I_1x^2+\lambda_1W_2x^2+\lambda_1(S_1^*)^2I_1^*\Big] \\ &+ m_1\left[\lambda_1(S_1^*)^2I_1^*\left(3-\frac{I_1}{W_1}-\frac{S_1^*W_1}{S_1I_1}-\frac{S_1}{S_1^*}\right)\right] \\ &- m_2\Big[\beta_2I_2y^2+\lambda_2W_2y^2+(1-\mathcal{T}_2)\theta_2S_2^*W_2\Big]. \end{aligned}$$

In view of the geometric and the arithmetic means inequality $\left(3-\frac{I_1}{W_1}-\frac{S_1^*W_1}{S_1I_1}-\frac{S_1}{S_1^*}\right)\leq 0$, the assumption $\mathcal{T}_2<1$ and the condition $F(x,y)>0$ (see Lemma 3.5), it follows that $L_1^{'}\leq 0$, which shows that, L_1 is indeed a Lyapunov function. Furthermore, the largest invariant set contained in $\mathcal{E}_*=\{(S_1,I_1,W_1,S_2,I_2,W_2)\in\Omega_1/L_1^{'}=0\}$ is the boundary endemic equilibrium E^*. Then, using the LaSalle's invariance principle [21, 22], we conclude that E^* is globally asymptotically stable in Ω_1.

With the assumptions of Theorem 3.12, we notice in passing that if a solution $(S_1(t),I_1(t),W_1(t),S_2(t),I_1(t),W_2(t))$ of system (3) is such that $I_1(t)=0$ or $W_1(t)=0$, $\forall t\geq 0$, then this solution is identically equal to the disease-free equilibrium E_0 which is unstable. This explains why we worked above with the set Ω_1 instead of Ω.

□

A.4. Proof of Theorem 3.16

For the same reason mentioned at the end of the proof of Theorem 3.12, we introduce the following subset of Ω. Let $\Omega_0=\{(S_1,I_1,W_1,S_2,I_2,W_2)\in\Omega\,/I_1>0,W_1>0,I_2>0,W_2>0\}$. Consider the

following linear combination of Volterra-type Lyapunov functions on Ω_0:

$$\begin{aligned} L &= k_1\left[S_1-\overline{S}_1\ln S_1+\left(I_1-\overline{I}_1\ln I_1\right)+\frac{\lambda_1(\overline{S}_1)}{\varepsilon_1}\left(W_1-\overline{I}_1\ln W_1\right)\right] \\ &+ k_2\left[S_2-\overline{S}_2\ln S_2+\left(I_2-\overline{I}_2\ln I_2\right)+\frac{\lambda_2(\overline{S}_2)}{\varepsilon_2}\left(W_2-\overline{I}_2\ln W_2\right)\right], \end{aligned} \tag{31}$$

where k_1 and k_2 are two positive constants to be determined shortly.

The time derivative of L along the trajectories of system (3) is

$$\begin{aligned} L' &= k_1\left[A_1-(\mu_1+a_1)S_1+a_2S_2-\frac{A_1\overline{S}_1}{S_1}+\lambda_1W_1\overline{S}_1+\beta_1\overline{S}_1I_1\right] \\ &+ k_1\left[(\mu_1+a_1)\overline{S}_1-\frac{a_2\overline{S}_1S_2}{S_1}-\theta_1I_1-\frac{\lambda_1S_1W_1\overline{I}_1}{I_1}\right] \\ &+ k_1\left[-\beta_1S_1\overline{I}_1+\theta_1\overline{S}_1+\lambda_1\overline{S}_1I_1-\lambda_1\overline{S}_1W_1+\lambda_1\overline{S}_1\overline{I}_1-\frac{\lambda_1\overline{S}_1\overline{I}_1I_1}{W_1}\right] \\ &+ k_2\left[A_2-(\mu_2+a_2)S_2+a_1S_1-\frac{A_2\overline{S}_2}{S_2}+\lambda_2W_2\overline{S}_2+\beta_2\overline{S}_2I_2\right] \\ &+ k_2\left[(\mu_2+a_2)\overline{S}_2-\frac{a_1\overline{S}_2S_1}{S_2}-\theta_2I_2-\frac{\lambda_2S_2W_2\overline{I}_2}{I_2}\right] \\ &+ k_2\left[-\beta_2S_2\overline{I}_2+\theta_2\overline{I}_2+\lambda_2\overline{S}_2I_2-\lambda_2\overline{S}_2W_2+\lambda_2\overline{S}_2\overline{I}_2-\frac{\lambda_2\overline{S}_2\overline{I}_2I_2}{W_2}\right]. \end{aligned} \tag{32}$$

At the interior equilibrium $\overline{E}$, we have the relations

$$\begin{aligned} &(\lambda_1+\beta_1)\overline{S}_1\overline{I}_1=A_1-(\mu_1+a_1)\overline{S}_1+a_2\overline{S}_2, \quad (\lambda_2+\beta_2)\overline{S}_2\overline{I}_2=A_2-(\mu_2+a_2)\overline{S}_2+a_1\overline{S}_1, \\ &\theta_1=(\lambda_1+\beta_1)\overline{S}_1, \quad \theta_2=(\lambda_2+\beta_2)\overline{S}_2, \end{aligned}$$

which reduces Eq. (32) to

$$\begin{aligned} L' &= k_1\left[2A_1-(\mu_1+a_1)S_1-\frac{A_1\overline{S}_1}{S_1}+a_2S_2+a_2\overline{S}_2-\frac{a_2\overline{S}_2S_2}{S_1}\right] \\ &+ k_1\left[-\frac{\lambda_1S_1W_1\overline{I}_1}{I_1}-\frac{\lambda_1\overline{S}_1\overline{I}_1I_1}{W_1}+\lambda_1\overline{S}_1\overline{I}_1\right] \\ &+ k_2\left[2A_2-(\mu_2+a_2)S_2-\frac{A_2\overline{S}_2}{S_2}+a_1S_1+a_1\overline{S}_1-\frac{a_1\overline{S}_1S_1}{S_2}\right] \\ &+ k_2\left[-\beta_2S_2\overline{I}_2-\frac{\lambda_2S_2W_2\overline{I}_2}{I_2}-\frac{\lambda_2\overline{S}_2\overline{I}_2I_2}{W_2}+\lambda_2\overline{S}_2\overline{I}_2\right]. \end{aligned} \tag{33}$$

We add and subtract $A_1\dfrac{S_1}{\overline{S}_1}$ and $A_2\dfrac{S_2}{\overline{S}_2}$ from the first and the third brackets of L', respectively. This yields

$$\begin{aligned} L' &= k_1\left[-A_1\left(\frac{\overline{S}_1}{S_1}+\frac{S_1}{\overline{S}_1}-2\right)+A_1\frac{S_1}{\overline{S}_1}-\beta_1S_1\overline{I}_1-(\mu_1+a_1)S_1+a_2S_2+a_2\overline{S}_2-\frac{a_2\overline{S}_2S_2}{S_1}\right] \\ &+ k_1\left[-\frac{\lambda_1S_1W_1\overline{I}_1}{I_1}-\frac{\lambda_1\overline{S}_1\overline{I}_1I_1}{W_1}+\lambda_1\overline{S}_1\overline{I}_1\right] \\ &+ k_2\left[-A_2\left(\frac{\overline{S}_2}{S_2}+\frac{S_2}{\overline{S}_2}-2\right)+A_2\frac{S_2}{\overline{S}_2}-\beta_2S_2\overline{I}_2-(\mu_2+a_2)S_2+a_1S_1+a_1\overline{S}_1-\frac{a_1\overline{S}_1S_1}{S_2}\right] \\ &+ k_2\left[-\frac{\lambda_2S_2W_2\overline{I}_2}{I_2}-\frac{\lambda_2\overline{S}_2\overline{I}_2I_2}{W_2}+\lambda_2\overline{S}_2\overline{I}_2\right]. \end{aligned} \tag{34}$$

Since it can also be proved that

$$A_1\frac{S_1}{\overline{S}_1}-\beta_1 S_1\bar{I}_1=\lambda_1 S_1\bar{I}_1+(\mu_1+a_1)S_1-\frac{a_2S_1\overline{S}_2}{\overline{S}_1},$$
$$A_2\frac{S_2}{\overline{S}_2}-\beta_2 S_2\bar{I}_2=\lambda_2 S_2\bar{I}_2+(\mu_2+a_2)S_2-\frac{a_1S_2\overline{S}_1}{\overline{S}_2},$$

at the interior equilibrium, Eq. (34) becomes

$$\begin{aligned}
L^{'} &= k_1\left[-A_1\left(\frac{\overline{S}_1}{S_1}+\frac{S_1}{\overline{S}_1}-2\right)-\lambda_1\overline{S}_1\bar{I}_1\left(\frac{S_1W_1}{I_1\overline{S}_1}+\frac{I_1}{W_1}-\frac{S_1}{\overline{S}_1}-1\right)\right]\\
&+ k_1\left[a_2S_2+a_2\overline{S}_2-\frac{a_2S_1\overline{S}_2}{\overline{S}_1}-\frac{a_2\overline{S}_2S_2}{S_1}\right]\\
&+ k_2\left[-A_2\left(\frac{\overline{S}_2}{S_2}+\frac{S_2}{\overline{S}_2}-2\right)-\lambda_2\overline{S}_2\bar{I}_2\left(\frac{S_2W_2}{I_2\overline{S}_2}+\frac{I_2}{W_2}-\frac{S_2}{\overline{S}_2}-1\right)\right]\\
&+ k_2\left[a_1S_1+a_1\overline{S}_1-\frac{a_1S_2\overline{S}_1}{\overline{S}_2}-\frac{a_1\overline{S}_1S_1}{S_2}\right],
\end{aligned}$$

or

$$\begin{aligned}
L^{'} &= k_1\left[\left(\lambda_1\overline{S}_1\bar{I}_1-A_1\right)\left(\frac{\overline{S}_1}{S_1}+\frac{S_1}{\overline{S}_1}-2\right)-\lambda_1\overline{S}_1\bar{I}_1\left(\frac{S_1W_1}{I_1\overline{S}_1}+\frac{I_1}{W_1}+\frac{\overline{S}_1}{S_1}-3\right)\right]\\
&+ k_1\left[a_2S_2+a_2\overline{S}_2-\frac{a_2S_1\overline{S}_2}{\overline{S}_1}-\frac{a_2\overline{S}_2S_2}{S_1}\right]\\
&+ k_2\left[\left(\lambda_2\overline{S}_2\bar{I}_2-A_2\right)\left(\frac{\overline{S}_2}{S_2}+\frac{S_2}{\overline{S}_2}-2\right)-\lambda_2\overline{S}_2\bar{I}_2\left(\frac{S_2W_2}{I_2\overline{S}_2}+\frac{I_2}{W_2}+\frac{\overline{S}_2}{S_2}-3\right)\right]\\
&+ k_2\left[a_1S_1+a_1\overline{S}_1-\frac{a_1S_2\overline{S}_1}{\overline{S}_2}-\frac{a_1\overline{S}_1S_1}{S_2}\right].
\end{aligned}\tag{35}$$

Now, the positive constants k_1 and k_2 are chosen such that

$$k_1a_2+k_2a_1\frac{\overline{S}_1}{\overline{S}_2}=k_2a_1+k_1a_2\frac{\overline{S}_2}{\overline{S}_1}=0,$$

which gives

$$k_1=a_1\overline{S_1}\qquad\text{and}\qquad k_2=a_2\overline{S}_2.$$

Then, Eq. (35) becomes

$$\begin{aligned}
L^{'} &= -a_1\overline{S}_1\left(A_1-\lambda_1\overline{S}_1\bar{I}_1\right)\left(\frac{\overline{S}_1}{S_1}+\frac{S_1}{\overline{S}_1}-2\right)-a_1\overline{S}_1\lambda_1\overline{S}_1\bar{I}_1\left(\frac{S_1W_1}{I_1\overline{S}_1}+\frac{I_1}{W_1}+\frac{\overline{S}_1}{S_1}-3\right)\\
&- a_2\overline{S}_2\left(A_2-\lambda_2\overline{S}_2\bar{I}_2\right)\left(\frac{\overline{S}_2}{S_2}+\frac{S_2}{\overline{S}_2}-2\right)-a_2\overline{S}_2\lambda_2\overline{S}_2\bar{I}_2\left(\frac{S_2W_2}{I_2\overline{S}_2}+\frac{I_2}{W_2}+\frac{\overline{S}_2}{S_2}-3\right)\\
&- a_1a_2\overline{S}_1\overline{S}_2\left(\frac{S_2}{S_1}+\frac{S_1}{S_2}-2\right).
\end{aligned}\tag{36}$$

From the arithmetic and geometric means inequality, one has

$$\left(\frac{\overline{S}_1}{S_1}+\frac{S_1}{\overline{S}_1}-2\right)\geq 0,\qquad\left(\frac{S_1W_1}{I_1\overline{S}_1}+\frac{I_1}{W_1}+\frac{\overline{S}_1}{S_1}-3\right)\geq 0\qquad\text{and}\qquad\left(\frac{S_2}{S_1}+\frac{S_1}{S_2}-2\right)\geq 0.$$

Thus, if $\left(A_1-\lambda_1\overline{S}_1\bar{I}_1\right)\geq 0$ and $\left(A_2-\lambda_2\overline{S}_2\bar{I}_2\right)\geq 0$, one has that $L^{'}\leq 0$. Once again, we conclude by the LaSalle's invariance principle [21, 22] that the interior equilibrium $\overline{E}$ is globally asymptotically stable.

□

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References

[1] R. Anguelov, J.M.-S. Lubuma, Contributions to the mathematics of the nonstandard finite difference method and applications, Numer. Methods Partial Differ. Equ. 17 (2001) 518-543.

[2] J. Arino, P. van den Driessche, Metapopulation epidemic models, Field Inst. Commun. 48 (2006) 1-13.

[3] M. Bani-Yabhoub, R. Gautam, Z. Shuai, P. van den Driessche, R. Ivanek, Reproduction numbers for infections with free-living pathogens growing in the environment, J. Biol. Dyn. 6(2) (2012) 923-940.

[4] E. Bertuzzo, S. Azaele, A. Maritan, M. Gatto, I. Rodriguez-Iturbe, A. Rinaldo, On the space-time evolution of a cholera epidemic, Water Resour. Res. 44 (2008) W01424.

[5] E. Bertuzzo, R. Casagrandi, M. Gatto, I. Rodriguez-Iturbe, A. Rinaldo, On spatially explicit models for cholera epidemics, J. R. Soc., Interface 7 (2010) 321.

[6] E. Bertuzzo, L. Mari, L. Righetto, M. Gatto, R. Casagrandi, M. Blokesch, I. Rodriguez-Iturbe, A. Rinaldo, Prediction of the spatial evolution and effects of control measures for the unfolding Haiti cholera outbreak, Geophys. Res. Lett. 38 (2011) L06403.

[7] V. Capasso, S.L. Paveri-Fontana, A mathematical model for the 1973 cholera epidemic in the European Mediterranean region, Rev. Epidemiol. Sante Publique 27 (1979) 121.

[8] C. Castillo-Chavez, B. Song, Dynamical models of tuberculosis and their application, Math. Biosci. Eng. 1 (2004) 361-404.

[9] C.T. Codeço, Endemic and epidemic dynamic of cholera: the role of the aquatic reservoir, BMC Infec. Dis. 1(1) (2001).

[10] J. Cui, Z. Wu, X. Zhou, Mathematical analysis of a cholera model with vaccination, J. Appl. Math. (2014), Article ID 324767, 16 pages, http://dx.doi.org/10.1155/2014/324767.

[11] M.C. Eisenberg, S.L. Robertson, J.H. Tien., Identifiability and estimation of multiple transmission pathways in a cholera and waterborne disease, J. Theor. Biol. 324 (2013) 84.

[12] M.C. Eisenberg, Z. Shuai, J.H. Tien, P. van den Driessche, A cholera model in a patchy environment with water and human movement, Math. Biosci. 246 (2013) 105-112.

[13] K. Goh, S. Teo, S. Lam, M. Ling, Person-to-person transmission of cholera in a psychiatric hospital, J. Infect. 20 (1990) 193-2000.

[14] H. Guo, M.H. Li, Z. Zhuai, Global stability of the endemic equilibrium of multigroup SIR epidemic models, Can. Appl. Math. Q. 14 (2006) 259.

[15] H. Guo, M.H. Li, Z. Zhuai, A graph-theoretic approach to the method of global Lyapunov functions, Proc. Amer. Math. Soc. 136 (2008) 2793.

[16] J.B. Harris, A.I. Khan, R.C. LaRocque, D.J. Dorer, F. Chowdhury, A.S.G. Faruque, D.A. Sack, E.T. Ryan, F. Qadri, S.B. Calderwood, Blood group, immunity, and risk of infection with vibrio cholerae in an area of endemicity, Infect. Immnu. 73 (2005) 7422-7427.

[17] D.M. Hartley, J.G. Morris, D.L. Smith, Hyperinfectivity: a critical element in the ability of V. cholerae to cause epidemics? PLoS Med. 3 (2006) 0063.

[18] A. Iggidr, G. Sallet, B. Tsanou, Global stability analysis of a metapopulation SIS epidemic model, Math. Pop. Stud. 19(3) (2012) 115-129.

[19] A. Korobeinikov, Lyapunov functions and global properties for SEIR and SIRS epidemic models, Math. Med. Biol. 21 (2004) 75-83.

[20] A. Korobeinikov, G. Wake, Lyapunov functions and global stability for SIR, SIRS, and SIS epidemiological models, Appl. Math. Lett. 15 (2002) 955-961.

[21] J.P. LaSalle, The stability of Dynamical Systems, Regional Conference Series in Applied Mathematics, SIAM, Philadelphia, 1976.

[22] J.P. LaSalle, S. Lefsschetz, Stability by Liapunov's Direct Method with Applications, Academic Press: New York, 1961.

[23] D.S. Merrell, S. M. Butler, Host-induced epidemic spread of the cholera bacterium. Nature 417 (2002) 642-645. doi:10.1038/nature00778.

[24] R.L. Miller Neilan, E. Schaefer, H. Gaff, K.R. Fister, S. Lenhart, Modeling optimal intervention strategies for cholera, Bull. Math. Biol. 72 (2010) 2004-2018.

[25] R.R. Mourino-Pérez, A.Z. Worden, Farooq Azam, Growth of vibrio cholerae O1 in red tide waters of California, Appl. Environ. Microbiol. 69 (2003) 6923-6931.

[26] Z. Mukandavire, S. Liao, J.Wang, H. Gaff, D.L. Smith, J.G. Morris, Jr., Estimating the basic reproduction number for the 2008-2009 cholera outbreaks in Zimbabwe, PNAS 108 (2011) 8767-8772.

[27] E.J. Nelson, J.B. Harris, J.G. Morris, S.B. Calderwood, A. Camilli, Cholera transmission: the host, pathogen and bacteriophage dynamics, Nat. Rev. Microbiol. 7 (2009) 693-702.

[28] J.B.H. Njaagarah, F. Nyabadza, A metapopulation model for cholera transmission dynamics between communities linked by migration, Appl. Math. Comput. 241 (2014) 317-331.

[29] J.J. Tewa, S. Bowong, B. Mewoli, Mathematical analysis of a two-patch model for dynamical transmission of tuberculosis, Appl. Math. Model. 36 (2012) 2466-2485.

[30] J.J. Tewa, S. Bowong, S.C. Oukouomi Noutchie, Mathematical analysis of a two-patch model of tuberculosis with stage progression, Appl. Math. Model. 36 (2012) 5792-5807.

[31] J.P. Tian, J. Wang, Global stability for cholera epidemic models, Math. Biosci. 232 (2011) 31-41.

[32] J.H. Tien, D.J.D. Earn, Multiple Transmission Pathways and Disease Dynamics in a Waterborne Pathogen Model, Bull. Math. Biol. 72 (2010) 1506-1533.

[33] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of desease transmission, Math. Biosci. 180 (2002) 29-48.

[34] W. Wang, G. Mulone, Threshold of disease transmission in a patchy, J. Math. Anal. Appl. 285 (2003) 321-335.

[35] J. Wang, S. Liao, A generalized cholera model and epidemic-endemic analysis, J. Biol. Dyn. 6 (2012) 568-589.

[36] Y. Yang, J. Wu, J. Li, Z. Ma, Global dynamics-convergence to equilibria-of epidemic patch models with immigration, Math. Com. Model. 51 (2010) 329-337.

[37] WHO, Weekly epidemiological record, August 2013, http://www.who.int/wer.

[38] T. Zhang, Q. Gou, X. Wang, Existence of traveling wave solutions for cholera model, Abstr. Appl. Anal. (2014), Article ID 201094, 11 pages, http://dx.doi.org/10.1155/2014/201094.