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A REACTION-DIFFUSION MODEL FOR NESTED WITHIN-HOST AND BETWEEN-HOST DYNAMICS IN AN ENVIRONMENTALLY-DRIVEN INFECTIOUS DISEASE*

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Abstract A reaction-diffusion model for nested within-host and between-host dynamics in an environmentally-driven infectious disease is proposed. The model is composed of the within-host virus infectious fast time model of ordinary differential equations and the between-host disease transmission slow time model of reaction-diffusion equations. The isolated fast model has been investigated in previous literature, and the main results are summarized. For the isolated slow model, the well-posedness of solutions, and the basic reproduction number R_b are obtained. When $R_b \leq 1$, the model only has the disease-free equilibrium which is globally asymptotically stable, and when $R_b > 1$ the model has a unique endemic equilibrium which is globally asymptotically stable. For the nested slow model, the positivity and boundedness of solutions, the basic reproduction number R_c and the existence of equilibrium are firstly obtained. Particularly, the nested slow model can exist two positive equilibrium when $R_c < 1$ and a unique endemic equilibrium when $R_c > 1$. When $R_c < 1$ the disease-free equilibrium is locally asymptotically stable, and when $R_c > 1$ and an additional condition is satisfied the unique endemic equilibrium is locally asymptotically stable. When there are two positive equilibria, then a positive equilibria is locally asymptotically stable under an additional condition and the other one is unstable, which implies that the nested slow model occurs the backward bifurcation at $R_c = 1$. Lastly, numerical examples are given to verify the main conclusions. The research shows that the nested slow model has more complex dynamical behavior than the corresponding isolated slow model.

Keywords Reaction-diffusion equation, nested model, basic reproduction number, stability, backward bifurcation.

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1. Introduction

Infectious diseases have emerged in many countries around the world, for example: SARS, MERS, COVID-19, etc. (see [4, 10, 14, 32, 35]). Infectious diseases severely harm human health, economic development, and social stability. Therefore, the research of infectious diseases has attracted much attention.

Many researchers have considered various viral infection models and obtained many practical conclusions (see [7,8,11–13,15,18,30,37]). Especially for the research of environmental driven infectious diseases, many researchers have come up with new insights by analyzing the epidemic dynamics from two different levels of cell and population. See, for example, Feng et al. [11–13], Cen et al. [7], Mideo et al. [30], Coombs et al. [8], and the references cited therein.

In [11–13], a class of coupling within-host and between-host epidemic dynamical model is considered.

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = A - \beta ES - \mu S, \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = \beta ES - (\mu + \alpha)I, \\ \dfrac{\mathrm{d}E}{\mathrm{d}t} = \theta IV(s)(1 - E) - \gamma E, \end{cases} \tag{1.1}$$

$$\begin{cases} \dfrac{\mathrm{d}T}{\mathrm{d}s} = \Lambda - kVT - mT, \\ \dfrac{\mathrm{d}T^*}{\mathrm{d}s} = kVT - (m + d)T^*, \\ \dfrac{\mathrm{d}V}{\mathrm{d}s} = g(E(t)) + pT^* - cV. \end{cases} \tag{1.2}$$

Here, model (1.1) describes the dynamics of disease transmission between the hosts and the corresponding time variable is t, model (1.2) describes the dynamics of virus infection in the host and the corresponding time variable is s. The process of virus infection in the host is much faster than the process of disease transmission between the hosts. Therefore, it can be considered that the process of virus infection in the host is a fast time-varying process, and the process of disease transmission between the hosts is a slow time-varying process. In other words, the time variable t in model (1.1) is a slow time variable, and the time variable s in model (1.2) is a fast time variable. However, we further see that there is a fast time term $V(s)$ in slow time model (1.1), and a slow time term $E(t)$ in fast time model (1.2), so model (1.1)-(1.2) is the nested model of fast and slow time interaction. In [11, 12] the singular perturbation theory in [5] is used to analyze slow submodel (1.1) and fast submodel (1.2). According to the analysis results of the two submodels, the dynamic behavior of nested models (1.1)-(1.2) is further analyzed.

Inspired by the above research works, in [39] the authors proposed a discrete-time analog for coupled within-host and between-host dynamics in environmentally driven infectious disease. The system is composed of the discrete fast time subsystem of virus infection in the host and the discrete slow time subsystem of disease transmission between the hosts. The authors separately investigated the dynamic behavior of the isolated fast system, isolated slow system, and coupled slow system. Recently, in [22] the authors proposed an age-structured model for coupling within-host and between-host dynamics in environmentally-driven infectious diseases. The model is composed of the fast time ordinary differential submodel of virus infection in the host and the age-dependent partial differential submodel of disease transmission between the hosts. Firstly, the isolated fast model and the isolated slow model are discussed. On this basis, the dynamic properties of the coupled slow model are deeply analyzed.

Since the population density in different regions is different, the contact rate among individuals is also different. Therefore, the number of the infected with a certain infectious disease is usually related to geographical factors (see [31, 34]). In recent years, the theory of reaction-diffusion equations has become one of the core theories for studying the spread of infectious disease in a spatial region. Many scholars have studied different types of reaction-diffusion epidemic models, see for example [3, 6, 9, 20, 21, 23, 24, 26, 28, 29, 36, 41, 43] and the references cited therein. In particular, Luo et al. [23] proposed a reaction-diffusion multi-group SIR epidemic model with nonlinear incidence. In the spatially heterogeneous environment, the authors established the threshold criteria for the global asymptotic stability of disease-free equilibrium and the uniform persistence of solutions. In the homogeneous space, the authors obtained the global asymptotic stability of disease-free and endemic equilibrium by constructing suitable Lyapunov functions.

So far, it can be seen that almost all the existing studies of epidemic models with reaction-diffusion are about the SIS or SIR model (see [3, 6, 9, 20, 23, 41]) and rarely about the SIE (Susceptible-Infected-Environmental contamination) model. According to the knowledge of epidemiology in [25], it can be known that the best time to control the epidemic is the early stage of its spread. However, in the early stage of the spread of the epidemic, the statistics of the epidemic only show the number of patients in a certain province or city, and the coverage of the data was too small (see [1, 33]). Therefore, the homogeneous reaction-diffusion epidemic model is more convenient and more applicable than the heterogeneous reaction-diffusion epidemic model in the early stage of the spread of the epidemic.

Based on the above discussion, we construct a reaction-diffusion model for nested within-host and between-host dynamics in an environmentally-driven infectious disease, the model is given as below

$$\begin{cases} \dfrac{\partial}{\partial t}S(t,x) = D_1\triangle S(t,x) + A - \beta ES - \mu S, \\ \dfrac{\partial}{\partial t}I(t,x) = D_2\triangle I(t,x) + \beta ES - (\mu+\alpha)I, \\ \dfrac{\partial}{\partial t}E(t,x) = D_3\triangle E(t,x) + \theta IV(1-E) - \gamma E, \end{cases} \tag{1.3}$$

$$\begin{cases} \dfrac{\mathrm{d}T}{\mathrm{d}s} = \Lambda - kVT - mT, \\ \dfrac{\mathrm{d}T^*}{\mathrm{d}s} = kVT - (m+d)T^*, \\ \dfrac{\mathrm{d}V}{\mathrm{d}s} = g(E(t,x)) + pT^* - cV, \end{cases} \tag{1.4}$$

where $x \in \Omega$, $\Omega \subset R^n$ is a bounded domain with the smooth boundary $\partial\Omega$ and $x = (x_1, x_2, ..., x_n)$, $n \geq 1$ is an integer. $S(t,x)$, $I(t,x)$, $E(t,x)$ denote the numbers of susceptible and infectious individuals, the level of environmental contamination at slow time t, and spatial location x, respectively. $T(s)$, $T^*(s)$, and $V(s)$ denote the densities of healthy cells and infected cells and the viral load at fast time s, respectively; $\Delta = \Sigma_{i=1}^n \frac{\partial^2}{\partial x_i^2}$ denotes the Laplace operator. D_j $(j = 1, 2, 3)$ denote the diffusive rate of the susceptible, infected and the level of environmental contamination, respectively.

In model (1.3), A denotes the supplement rate of susceptible persons. β is the infection rate of susceptible people in a polluted environment. μ denotes the natural mortality rate of the total population. α is the induced mortality rate of infectious individuals. θ denotes the emission rate of contamination from the infected to the environment. γ is the clearance rate of environmental contamination. It is assumed that the rate of environmental contamination is proportional to the number of infected individuals and the virus load V within a host, which has the form θIV. In model (1.4), function $g(E)$ denotes an added rate in the change of virus load due to the continuous ingestion of viruses by the host from a contaminated environment. Λ is the recruitment rate of healthy cells. k denotes the infection rate of cells. m and d denote the natural and infection-induced mortality rates of infected cells, respectively. p is the virus reproduction rate by an infected cell. c denotes the within-host mortality rate of viruses. Our purpose in the article is to study the dynamic behavior of model (1.3)-(1.4).

The structure of this paper is as follows. In Section 2, some main results for the within-host fast time model are summarized. In Section 3, the between-host isolated slow time model is discussed. The well-posedness of solutions, including the nonnegativity and ultimate boundedness, is established. The basic reproduction number R_b is calculated. Furthermore, we obtain the global asymptotic stability of disease-free and endemic equilibrium. In Section 4, the nested between-host slow time model is discussed. Here, we first obtain the positivity and boundedness of solutions, the basic reproduction number R_c and the existence of equilibrium. Particularly, the nested slow model can have two positive equilibrium when $R_c < 1$. The locally asymptotic stability of disease-free equilibrium is proved when $R_c < 1$, and the locally asymptotic stability of unique endemic equilibrium is obtained when $R_c > 1$ and an additional condition is satisfied. The locally asymptotic stability of a positive equilibrium under an additional condition and the instability of the other one are established when there is two positive equilibrium, which shows that the nested between-host slow time reaction-diffusion epidemic model produces the backward bifurcation at $R_c = 1$. In Section 5, the numerical examples verify the main conclusions obtained in Section 4. Lastly, in Section 6, we draw a concise conclusion.

2. Within-host fast time model

For within-host fast time model (1.4), it is usually assumed that its state changes very quickly. Therefore, during the dynamic change of model (1.4), slow time model (1.3) will maintain the original state. Thus, we assume that the level of environmental contamination $E(t,x)$ is a constant E, and $0 \le E \le 1$, where $E = 0$ means there is no virus in the environment, $0 < E < 1$ represents there is the virus in the environment, and $E = 1$ is that the contamination reaches its maximum in the environment. Thus, model (1.4) becomes an isolated within-host fast time model of virus infection.

The function $g(E)$ of model (1.4) is assumed to satisfy the following assumption.

(**H**) $g(E)$ is nonnegative and two order continuously differentiable on $[0,1]$, $g(0) = 0$, $g'(E) > 0$ and $g''(E) \le 0$ for all $0 \le E \le 1$.

One of the simplest forms for $g(E)$ considered in [11–13] is the linear function $g(E) = aE$, where a is a positive constant.

It is assumed that any solution $(T(s), T^*(s), V(s))$ of model (1.4) satisfies the following initial conditions:

$$T(0) > 0, T^*(0) > 0, V(0) > 0. \tag{2.1}$$

The complete dynamical properties of model (1.4) have been established in [11–13]. We here summarize the main conclusions as follows.

Lemma 2.1. *Any solution $\big(T(s), T^*(s), V(s)\big)$ of model (1.4) with initial conditions (2.1) is positive for all $s \geq 0$, and ultimately bounded. Furthermore, $\limsup_{s\to\infty}(T(s) + T^*(s)) \leq T_0$, $\limsup_{s\to\infty} V(s) \leq \frac{p\Lambda+gm}{mc}$, where $T_0 = \frac{\Lambda}{m}$ and $g = \max_{0\leq E\leq 1}\{g(E)\}$.*

The within-host reproduction number is defined by

$$R_w = \frac{kpT_0}{c(m+d)}.$$

Lemma 2.2. *When $E = 0$, then model (1.4) always has infection-free equilibrium $B_0(T_0, 0, 0)$, and if $R_w > 1$, model (1.4) has a unique infectious equilibrium $B^*(\check{T}, \check{T}^*, \check{V})$.*

$$\check{T} = \frac{c(m+d)}{kp}, \quad \check{T}^* = \frac{cm}{pk}(R_w - 1), \quad \check{V} = \frac{pmT_0}{c(m+d)}\Big(1 - \frac{1}{R_w}\Big).$$

Lemma 2.3. *When $0 < E \leq 1$, then model (1.4) always has a unique infectious equilibrium $B_1(\check{T}(E), \check{T}^*(E), \check{V}(E))$, where*

$$\begin{aligned} \check{V}(E) &= \frac{1}{c}[g(E) + \frac{pm}{(m+d)}(T_0 - \check{T}(E))], \\ \check{T}^*(E) &= \frac{m}{m+d}(T_0 - \check{T}(E)), \\ \check{T}(E) &= \frac{1}{2}(a_1(E) - \sqrt{a_1^2(E) - 4a_2}), \end{aligned} \tag{2.2}$$

where $a_1(E) = \frac{(m+d)g(E)}{pm} + T_0(1 + \frac{1}{R_w})$ and $a_2 = \frac{T_0^2}{R_w}$. Furthermore,

$$\lim_{E\to 0^+} B_1(\check{T}(E), \check{T}^*(E), \check{V}(E)) = \begin{cases} B_0(T_0, 0, 0), & \text{if} \quad R_w \leq 1, \\ B^*(\check{T}, \check{T}^*, \check{V}), & \text{if} \quad R_w > 1. \end{cases}$$

On the global asymptotic stability of the infection-free and infectious equilibrium of model (1.4), the following conclusions have been established.

Theorem 2.1. *Let $E = 0$ in model (1.4).*

(i) If $R_w \leq 1$, then infection-free equilibrium B_0 is globally asymptotically stable;

(ii) If $R_w > 1$, then infectious equilibrium B^* is globally asymptotically stable.

Theorem 2.2. *Let $0 < E \leq 1$ in model (1.4), then infectious equilibrium $B_1(\check{T}(E), \check{T}^*(E), \check{V}(E))$ is globally asymptotically stable.*

3. Between-host isolated slow model

In this section, we assume that environmental contamination does not affect the viral infection in the host, that is, $E = 0$. In this way, in fast time model (1.4), $V(s)$ will quickly stabilize to its equilibrium position $\check{V}$, and we have that $\check{V} > 0$ if $R_w > 1$ and $\check{V} = 0$ if $R_w \leq 1$.

For slow time model (1.3), we first see that $\check{V} = 0$ will result in $E(t) \to 0$ as $t \to \infty$ from the third equation of model (1.3). It implies that the disease will extinct between the hosts. Therefore, in this section we always assume $R_w > 1$ and viral concentration $V(s)$ is a positive constant V. Thus, model (1.3) becomes an isolated between-host disease transmission model.

From the biological background of model (1.3), it is assumed that any solution $(S(t,x), I(t,x), E(t,x))$ satisfies the following initial condition:

$$0 < S(0,x) = \phi_1(x),\ 0 \leq I(0,x) = \phi_2(x),\ 0 \leq E(0,x) = \phi_3(x) \leq 1$$

and homogeneous Neumann boundary condition:

$$\frac{\partial}{\partial n}S(t,x) = \frac{\partial}{\partial n}I(t,x) = \frac{\partial}{\partial n}E(t,x) = 0, x \in \partial\Omega, t \geq 0,$$

where $\phi_i(x)(i = 1,2,3)$ is the nonnegative Hölder continuous bounded functions defined on $\overline{\Omega}$, and $\frac{\partial}{\partial n}$ denotes the outward normal derivative on $\partial\Omega$.

Denote by $Y = C(\overline{\Omega}, R)$ the Banach space of all continuous functions $\phi : \overline{\Omega} \to R$ with the supremum norm $\|\phi\| = \sup_{x\in\overline{\Omega}} |\phi(x)|$. Let $Y_+ = C(\overline{\Omega}, R_+)$ be the positive cone of Y. Then (Y, Y_+) is an ordered Banach space. Additionally, denote $X = Y \times Y \times Y$ with the norm $\|\phi\|_X = \max\{\|\phi_1\|, \|\phi_2\|, \|\phi_3\|\}$, where $\phi = (\phi_1, \phi_2, \phi_3) \in X$ with $\phi_i \in Y$ $(i = 1,2,3)$. Let $X_+ = Y_+ \times Y_+ \times Y_+$ be the positive cone of X.

As a preliminary, the following scalar reaction-diffusion model is considered:

$$\begin{aligned} \frac{\partial}{\partial t}u(t,x) =& \widehat{D}\triangle u(t,x) + \vartheta - \varrho u(t,x), x \in \Omega, t > 0, \\ \frac{\partial}{\partial n}u(t,x) =& 0, x \in \partial\Omega, t > 0, \end{aligned} \tag{3.1}$$

where $\widehat{D}$, ϑ and ϱ are positive constants. From Lemma 1 in [21], we obtain the following result.

Lemma 3.1. *Model (3.1) admits a unique positive equilibrium $u_0(x) = \frac{\vartheta}{\varrho}$, which is globally asymptotically stable in $C(\overline{\Omega}, R_+)$.*

3.1. Well-posedness

We denote by $T_k(t) : C(\overline{\Omega}, R) \to C(\overline{\Omega}, R)$ the C_0 semigroup associated with $D_k\triangle - g_k(k = 1,2,3)$ subjects to the Neumann boundary condition, where $g_1 = \mu$, $g_2 = \mu + \alpha$ and $g_3 = \gamma$, respectively.

Denote

$$\begin{cases} F_1(\phi)(x) = A - \beta\phi_3(x)\phi_1(x), \\ F_2(\phi)(x) = \beta\phi_3(x)\phi_1(x), & x \in \Omega, \\ F_3(\phi)(x) = \theta\phi_2(x)V(1 - \phi_3(x)), \end{cases}$$

where $\phi = (\phi_1, \phi_2, \phi_3) \in X_+$. We define $u(t, \cdot, \phi) = (S(t, \cdot, \phi), I(t, \cdot, \phi), E(t, \cdot, \phi))$ the solution of model (1.3) with initial value function $\phi = (\phi_1, \phi_2, \phi_3) \in X_+$, then model (1.3) can be rewritten as the following integral equations:

$$\begin{cases} S(t, \cdot, \phi) = T_1(t)\phi_1 + \displaystyle\int_0^t T_1(t-s)F_1(S(s, \cdot, \phi_1))ds, \\ I(t, \cdot, \phi) = T_2(t)\phi_2 + \displaystyle\int_0^t T_2(t-s)F_2(I(s, \cdot, \phi_2))ds, \quad t > 0, \\ E(t, \cdot, \phi) = T_3(t)\phi_3 + \displaystyle\int_0^t T_3(t-s)F_3(E(s, \cdot, \phi_3))ds. \end{cases} \tag{3.2}$$

According to Corollary 4 of in [27], it can be seen that model (3.2) satisfies the subtangential condition. Thus, the following lemma is valid.

Lemma 3.2. *For any initial function $\phi = (\phi_1, \phi_2, \phi_3) \in X_+$ with $0 \le \phi_3 \le 1$, model (1.3) has a unique nonnegative mild solution $u(t, \cdot, \phi) = (S(t, \cdot, \phi), I(t, \cdot, \phi), E(t, \cdot, \phi)) \in X_+$ on the interval of existence $[0, \tau_\infty)$ and $\tau_\infty \le \infty$. Additionally, this solution is a classical solution.*

On the existence and ultimate boundedness of global solutions, and the existence of global attractor for model (1.3), the following results have been established.

Theorem 3.1. *For any initial function $\phi = (\phi_1, \phi_2, \phi_3) \in X_+$ with $0 \le \phi_3 \le 1$, model (1.3) has a unique nonnegative solution $u(t, \cdot, \phi) = (S(t, \cdot, \phi), I(t, \cdot, \phi), E(t, \cdot, \phi)) \in X_+$ defined on $[0, \infty)$ and this solution is also ultimately bounded. Additionally, $0 \le E(t, \cdot, \phi) \le 1$ for all $t \ge 0$ and $x \in \overline{\Omega}$.*

Proof. Adopting the similar method introduced in Section 2 in [2] or Chapter 3 in [19], we obtain the existence of the global solution. Let $u(t, \cdot, \phi) = (S(t, \cdot, \phi), I(t, \cdot, \phi), E(t, \cdot, \phi)) \in X_+$ be a nonnegative solution of model (1.3) with the interval of existence $[0, \tau_\infty)$ by Lemma 3.2. Suppose that $\tau_\infty < \infty$, then we have $\|u(t, \cdot, \phi)\|_X \to \infty$ as $t \to \tau_\infty$ by Theorem 2 in [25]. From the first equation of model (1.3), we have

$$\frac{\partial}{\partial t} S(t, \cdot, \phi) \le D_1 \triangle S(t, \cdot, \phi) + A - \mu S(t, \cdot, \phi), \ t \in [0, \tau_\infty), \ x \in \Omega. \tag{3.3}$$

By the comparison principle and Lemma 3.1, it follows that there exists a constant $P_1 > 0$ such that $S(t, \cdot, \phi) \le P_1$ for all $t \in [0, \tau_\infty)$ and $x \in \overline{\Omega}$.

Consider the third equation of model (1.3). Let $Q(E) = \theta IV(1-E) - \gamma E$. Since $Q(0) = \theta IV \ge 0$ and $Q(1) = -\gamma < 0$, we can obtain that $E = 1$ and $E = 0$ are the upper and lower solutions of the third equation of model (1.3), respectively (see Definition 2.4.3 in [42]). Therefore, it is known from Theorem 2.4.6 in [42] that for the solution $u(t, \cdot, \phi) = (S(t, \cdot, \phi), I(t, \cdot, \phi), E(t, \cdot, \phi))$, as long as the initial value $0 \le \phi_3 \le 1$, then there is $0 \le E(t, \cdot, \phi) \le 1$ for all $t \in [0, \tau_\infty)$ and $x \in \overline{\Omega}$.

Therefore, we further obtain

$$\frac{\partial}{\partial t} I(t, \cdot, \phi) \le D_2 \triangle I(t, \cdot, \phi) + \beta P_1 - (\mu + \alpha) I(t, \cdot, \phi), t \in [0, \tau_\infty), \ x \in \Omega.$$

The comparative model is considered as follows

$$\begin{cases} \dfrac{\partial}{\partial t} Z(t,\cdot,\phi) = D_2 \triangle Z(t,\cdot,\phi) + \beta P_1 - (\mu+\alpha) Z(t,\cdot,\phi),\ t>0,\ x\in\Omega, \\ \dfrac{\partial}{\partial n} Z(t,\cdot,\phi) = 0,\ t>0,\ x\in\partial\Omega. \end{cases}$$

It follows from the comparison principle and Lemma 3.1 that there exists a constant $P_2 > 0$ such that $I(t,\cdot,\phi) \le P_2$ for all $t \in [0,\tau_\infty)$ and $x \in \overline{\Omega}$. Thus, we finally get a contradiction with $\|u(t,\cdot,\phi)\|_X \to \infty$ as $t \to \tau_\infty$. Therefore, $\tau_\infty = \infty$, and the global existence of $u(t,\cdot,\phi)$ is derived.

Now we will prove that the solution is ultimately bounded. In fact, from inequality (3.3) and Lemma 3.1, we get $\limsup_{t\to\infty} S(t,\cdot,\phi) \le \frac{A}{\mu}$ uniformly for $x \in \overline{\Omega}$, which implies that $S(t,\cdot,\phi)$ is ultimately bounded. For any constant $\varepsilon > 0$ there is a $t_1 > 0$ such that $S(t,\cdot,\phi) < \frac{A}{\mu} + \varepsilon$ for all $t \ge t_1$ and $x \in \overline{\Omega}$. Thus, we also have

$$\frac{\partial}{\partial t} I(t,\cdot,\phi) \le D_2 \triangle I(t,\cdot,\phi) + \beta(\frac{A}{\mu} + \varepsilon) - (\mu+\alpha) I(t,\cdot,\phi),\ t \ge t_1,\ x\in\Omega.$$

Again using the comparison principle and Lemma 3.1 we obtain $\limsup_{t\to\infty} I(t,\cdot,\phi) \le \frac{\beta(\frac{A}{\mu}+\varepsilon)}{\mu+\alpha}$ uniformly for $x \in \overline{\Omega}$, which implies that $I(t,x)$ is ultimately bounded. This completes the proof. □

We denote $X_+^* = \{\phi = (\phi_1,\phi_2,\phi_3) \in X_+, 0 \le \phi_3 \le 1\}$. According to Theorem 3.4.8 in [17] and Theorem 3.1, we know that all nonnegative solutions $u(t,\cdot,\phi) = (S(t,\cdot,\phi), I(t,\cdot,\phi), E(t,\cdot,\phi))$ of model (1.3) with $\phi \in X_+^*$ generate a solution semiflow $\Phi(t) : X_+^* \to X_+^*$ with $\Phi(t)\phi = u(t,\cdot,\phi)$ for all $t \ge 0$. In addition, as a consequence of Theorem 3.1, the following conclusion is introduced.

Corollary 3.1. *The solution semiflow $\Phi(t) : X_+^* \to X_+^*$ of model (1.3) has a compact and global attractor.*

3.2. Stability of equilibrium

The between-host reproduction number for the isolated slow model is defined by

$$R_b = \frac{\beta\theta V S_0}{(\mu+\alpha)\gamma},$$

where $S_0 = \frac{A}{\mu}$. On the existence of equilibrium, we have the following conclusion.

Lemma 3.3. *Model (1.3) always has the disease-free equilibrium $W_0 = (S_0, 0, 0)$, and when $R_b > 1$ model (1.3) also has an endemic equilibrium $W^* = (S^*, I^*, E^*)$ with*

$$S^* = \frac{[\beta A\theta V + (\mu+\alpha)\gamma\beta]}{\beta\theta V(\beta+\mu)},\ I^* = \frac{\beta A\theta V - (\mu+\alpha)\mu\gamma}{(\mu+\alpha)\theta V(\beta+\mu)},\ E^* = \frac{\beta A\theta V - (\mu+\alpha)\mu\gamma}{\beta A\theta V + (\mu+\alpha)\gamma\beta}.$$

The proof of Lemma 3.3 is simple, we hence omit it here. Now, we investigate the stability of equilibrium W_0 and W^*. We can establish the following result.

Theorem 3.2. (i) *If $R_b \le 1$, then disease-free equilibrium W_0 is globally asymptotically stable in X_+^*;*

(ii) *If $R_b > 1$, then endemic equilibrium W^* is globally asymptotically stable in X_+^*.*

Proof. With regard to conclusion (i). The Lyapunov function $H_1(t)$ is defined as below

$$H_1(t) = \int_\Omega [(S - S_0 - S_0 \ln \frac{S}{S_0}) + I + \frac{(\mu+\alpha)}{\theta V} E] dx.$$

The derivative of $H_1(t)$ along solution W_0 of model (1.3) is given by

$$\begin{aligned}\frac{dH_1(t)}{dt} &= \int_\Omega \{(1 - \frac{S_0}{S})[D_1 \triangle S(t,x) + A - \beta ES - \mu S] + D_2 \triangle I(t,x) + \beta ES \\ &\quad - (\mu+\alpha) I + \frac{(\mu+\alpha)}{\theta V}[D_3 \triangle E(t,x) + \theta IV(1-E) - \gamma E]\} dx.\end{aligned}$$

By the divergence theorem (see Theorem 3.3 in [16]), we get

$$\begin{aligned}\frac{dH_1(t)}{dt} &= \int_\Omega [\mu S_0 (2 - \frac{S}{S_0} - \frac{S_0}{S}) + \frac{(\mu+\alpha)\gamma}{\theta V}(R_b - 1)E \\ &\quad - (\mu+\alpha) IE - S_0 D_1 \frac{\|\nabla S\|^2}{S^2}] dx.\end{aligned}$$

When $R_b \leq 1$, we have $\frac{dH_1(t)}{dt} \leq 0$. Additionally, $\frac{dH_1(t)}{dt} = 0$ implies $S = S_0$. From the first equation of model (1.3) we have $E = 0$. From the third equation of model (1.3) we further have $I = 0$. Thus, W_0 is globally asymptotically stable by the LaSalle's invariance principle.

With regard to conclusion (ii). The Lyapunov function $H_2(t)$ is defined as below

$$\begin{aligned}H_2(t) &= \int_\Omega [(S - S^* - S^* \ln \frac{S}{S^*}) + (I - I^* - I^* \ln \frac{I}{I^*}) \\ &\quad + \frac{(\mu+\alpha)}{\theta V(1-E^*)}(E - E^* - E^* \ln \frac{E}{E^*})] dx.\end{aligned}$$

The derivative of $H_2(t)$ along solution W^* of model (1.3) is given by

$$\begin{aligned}\frac{dH_2(t)}{dt} &= \int_\Omega \{(1 - \frac{S^*}{S})[D_1 \triangle S(t,x) + A - \beta ES - \mu S] \\ &\quad + (1 - \frac{I^*}{I})[D_2 \triangle I(t,x) + \beta ES - (\mu+\alpha) I] \\ &\quad + \frac{(\mu+\alpha)}{\theta V(1-E^*)}(1 - \frac{E^*}{E})[D_3 \triangle E(t,x) + \theta IV(1-E) - \gamma E]\} dx.\end{aligned}$$

By the divergence theorem (see Theorem 3.3 in [16]), we further obtain

$$\begin{aligned}\frac{dH_2(t)}{dt} &= \int_\Omega [\mu S^* (2 - \frac{S}{S^*} - \frac{S^*}{S}) + (\mu+\alpha) I^* (3 - \frac{S^*}{S} - \frac{E^* I}{E I^*} - \frac{ESI^*}{E^* S^* I}) \\ &\quad - \frac{(\mu+\alpha) I (E - E^*)^2}{(1-E^*)E} - S^* D_1 \frac{\|\nabla S\|^2}{S^2} - I^* D_2 \frac{\|\nabla I\|^2}{I^2} \\ &\quad - \frac{(\mu+\alpha) E^*}{\theta V(1-E^*)} D_3 \frac{\|\nabla E\|^2}{E^2}] dx.\end{aligned}$$

Notably, $H_2'(t) \leq 0$. Furthermore, $H_2'(t) = 0$ if and only if $(S, I, E) = (S^*, I^*, E^*)$. Thus, W^* is globally asymptotically stable by the LaSalle's invariance principle. This completes the proof. □

Remark 3.1. From the conclusions given in Theorem 3.2, we see that isolated between-host slow time reaction-diffusion epidemic model (1.3) possess complete dynamical properties.

4. Nested between-host slow model

Now, we consider slow time model (1.3) with the assumption which the environmental contamination has an impact on viral infection in the host, i.e., $0 < E \leq 1$ in fast time model (1.4). In this way, $V(s)$ in model (1.4) will quickly stabilize to its equilibrium position $\check{V}(E)$, and this equilibrium position depends on E. Thus, we can take $V(s) = \check{V}(E)$ in model (1.3), and further acquire the following nested between-host slow time model:

$$\begin{cases} \dfrac{\partial}{\partial t} S(t,x) = D_1 \triangle S(t,x) + A - \beta E S - \mu S, \\ \dfrac{\partial}{\partial t} I(t,x) = D_2 \triangle I(t,x) + \beta E S - (\mu+\alpha) I, \\ \dfrac{\partial}{\partial t} E(t,x) = D_3 \triangle E(t,x) + \theta I \check{V}(E)(1-E) - \gamma E. \end{cases} \tag{4.1}$$

In Section 2, we obtain that any solution $(T(s), T^*(s), V(s))$ of model (1.4) has the limit

$$\lim_{s\to\infty} (T(s), T^*(s), V(s)) = \begin{cases} (T_0, 0, 0), & \text{if } E = 0, R_w \leq 1; \\ (\check{T}, \check{T}^*, \check{V}), & \text{if } E = 0, R_w > 1; \\ (\check{T}(E), \check{T}^*(E), \check{V}(E)), & \text{if } 0 < E \leq 1. \end{cases}$$

Denote

$$B^*(E) = (\check{T}(E), \check{T}^*(E), \check{V}(E)) = \begin{cases} (T_0, 0, 0), & \text{if } E = 0, R_w \leq 1; \\ (\check{T}, \check{T}^*, \check{V}), & \text{if } E = 0, R_w > 1; \\ (\check{T}(E), \check{T}^*(E), \check{V}(E)), & \text{if } 0 < E \leq 1. \end{cases}$$

It is clear that

$$\check{V}(0) = \lim_{E\to 0} \check{V}(E) = \begin{cases} 0, & R_w \leq 1, \\ \dfrac{m(R_w - 1)}{k}, & R_w > 1. \end{cases}$$

In this section, for the convenience of discussions we always assume $R_w > 1$. Thus, we have $\check{V}(0) = \frac{m(R_w-1)}{k}$.

On the well-posedness of solutions of model (4.1), we have the following result which is similar to isolated slow model (1.3).

Lemma 4.1. *For any initial function $\phi = (\phi_1, \phi_2, \phi_3) \in X_+$ with $0 \leq \phi_3 \leq 1$, model (4.1) has a unique nonnegative solution $W(t,\cdot,\phi) = (S(t,\cdot,\phi), I(t,\cdot,\phi), E(t,\cdot,\phi)) \in X_+$ defined on $[0,\infty)$ and this solution is also ultimately bounded. Furthermore, $0 \leq E(t,\cdot,\phi) \leq 1$ for all $t \geq 0$ and $x \in \overline{\Omega}$.*

4.1. Existence of equilibrium

The basic reproduction number for the nested between-host slow model is defined by

$$R_c = \frac{\beta\theta\check{V}(0)S_0}{\gamma(\mu+\alpha)}.$$

The function is defined as below

$$F(E) = (1-E)\check{V}(E),\ G(E) = \frac{\gamma(\mu+\alpha)E}{\theta A} + \frac{\gamma(\mu+\alpha)\mu}{\beta\theta A}, \tag{4.2}$$

where $\check{V}(E)$ is defined in (2.2). Furthermore, we define $H(E) = F(E) - G(E)$ and $H_M = \max_{0\le E\le 1}\{H(E)\}$.

On the existence of nonnegative equilibrium of model (4.1), we have the following result.

Lemma 4.2. *Assume $R_w > 1$. Then we have*

(i) Model (4.1) always has the disease-free equilibrium $W_0 = (S_0, 0, 0)$ with $S_0 = \frac{A}{\mu}$;

(ii) Model (4.1) has a unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ if and only if one of the following conditions holds
(a) $R_c > 1$; (b) $R_c = 1$ and $H_M > 0$; (c) $R_c < 1$ and $H_M = 0$;

(iii) Model (4.1) has two positive equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$ if and only if the following condition holds
(d) $R_c < 1$ and $H_M > 0$;

(iv) Model (4.1) has only disease-free equilibrium $W_0 = (S_0, 0, 0)$ if and only if the following condition holds
(e) $H_M < 0$; (f) $R_c = 1$ and $H_M = 0$.

Proof. It is obvious that model (4.1) always has disease-free equilibrium $W_0 = (\frac{A}{\mu}, 0, 0)$. The positive equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ satisfies equation

$$\begin{cases} A - \beta\widetilde{E}\widetilde{S} - \mu\widetilde{S} = 0, \\ \beta\widetilde{E}\widetilde{S} - (\mu+\alpha)\widetilde{I} = 0, \\ \theta\widetilde{I}\check{V}(\widetilde{E})(1-\widetilde{E}) - \gamma\widetilde{E} = 0. \end{cases}$$

By computing, we obtain $\widetilde{S} = \frac{A}{\beta\widetilde{E}+\mu}$, $\widetilde{I} = \frac{\beta\widetilde{E}A}{(\mu+\alpha)(\beta\widetilde{E}+\mu)}$, and $\widetilde{E} \in (0,1)$ satisfying

$$\check{V}(\widetilde{E})(1-\widetilde{E}) = \frac{\gamma(\mu+\alpha)\widetilde{E}}{\theta A} + \frac{\gamma(\mu+\alpha)\mu}{\beta\theta A}.$$

Thus, $\widetilde{E}$ is a solution of equation $F(E) = G(E)$ with $0 < E < 1$, where $F(E)$ and $G(E)$ are given in (4.2). Equivalently, $\widetilde{E}$ is a zero of function $H(E)$.

By calculating we have

$$H(0) = \check{V}(0)(1 - \frac{1}{R_c}),\ H(1) = -\frac{\gamma(\mu+\alpha)}{\theta A} - \frac{\gamma(\mu+\alpha)\mu}{\beta\theta A} < 0.$$

When $0 < E < 1$, from (2.2) we have

$$H^{''}(E) = -\frac{2}{c}[g^{'}(E) - \frac{mp}{(m+d)}\check{T}^{'}(E)] + \frac{(1-E)}{c}[g^{''}(E) - \frac{mp}{(m+d)}\check{T}^{''}(E)].$$

From assumption (**H**) and (2.2) we acquire $a_1'(E) > 0$ and $a_1''(E) < 0$, then

$$\check{T}^{'}(E) = \frac{1}{2}a_1'(E)\Big(1 - \frac{a_1(E)}{\sqrt{a_1^2(E) - 4a_2}}\Big) < 0,$$
$$\check{T}^{''}(E) = \frac{1}{2}a_1^{''}(E)[1 - \frac{a_1(E)}{\sqrt{a_1^2(E) - 4a_2}}] + \frac{1}{2}(a_1^{'}(E))^2\frac{4a_2}{[a_1^2(E) - 4a_2]^{\frac{3}{2}}} > 0.$$

Hence, the second derivative $H^{''}(E) < 0$ for all $0 < E \leq 1$. This shows that $H(E)$ is an upper convex function in $0 < E \leq 1$.

Assume that condition (a) holds, then owing to $R_c > 1$, $H(E) = 0$ has a unique positive root $\widetilde{E} \in (0,1)$. Therefore, endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ exists and is unique.

If condition (b) holds, then from $R_c = 1$, we have $H(0) = 0$. By $H_M > 0$, we easily see that $H(E) = 0$ has a unique positive root $\widetilde{E} \in (0,1)$. Hence, endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ exists and is unique.

If condition (c) holds, then from $R_c < 1$ we have $H(0) < 0$. By $H_M = 0$, we see that $H(E) = 0$ has a unique positive root $\widetilde{E} \in (0,1)$. Hence, endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ also exists and is unique.

If condition (d) holds, by $H_M > 0$ and $R_c < 1$, we get $H(0) < 0$. Hence $H(E) = 0$ has only two positive roots. Thus, model (4.1) has only two endemic equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$.

If condition (e) holds. From $H_M < 0$, we see that $H(E) = 0$ has no root. Therefore, there is only disease-free equilibrium $W_0 = (\frac{A}{\mu}, 0, 0)$.

At last, if condition (f) holds, then from $H_M = 0$ and $R_c = 1$, we obtain $H(0) = 0$. Hence $H(E) < 0$ for all $E \in (0,1]$. It follows that $H(E) = 0$ has a unique root $\widetilde{E} = 0$, and then there is only disease-free equilibrium $W_0 = (\frac{A}{\mu}, 0, 0)$. This completes the proof. □

Remark 4.1. Comparing Lemma 4.2 with previous Lemma 3.3, we see that the existence of equilibrium for nested slow model (4.1) is more complex than isolated slow time model (1.3). Particularly, when the basic reproduction number less than 1, model (1.3) has only the disease-free equilibrium, but model (4.1) have two positive equilibria.

4.2. Stability of equilibrium

From Lemma 4.2, we see that nested slow model (4.1) may have a unique endemic equilibrium or two positive equilibrium depending on parameter values. This shows that the nested slow model may have complex dynamical behavior. Therefore, in this section, we will investigate the local stability of these equilibria. We choose the spatial domain $\Omega = [0, \pi]$ mainly for the simplified calculation and for convenience of carrying out demonstrating numerical results. Generally, closed interval $[a, b]$ can be transformed to $[0, \pi]$ by a translation and rescaling. For this case, we have that the operator $\Delta = \frac{\partial^2}{\partial x^2}$.

Theorem 4.1. *(i) If $R_c < 1$, then disease-free equilibrium W_0 of model (4.1) is locally asymptotically stable;*

(ii) If $R_c > 1$, then equilibrium W_0 is unstable.

Proof. Let $M_* = (S_*, I_*, E_*)$ be any equilibrium of model (4.1) and $N_0 = \{0, 1, 2, 3...\}$. Linearizing model (4.1) at equilibrium M_*, we get

$$\frac{\partial M(t,x)}{\partial t} = D\frac{\partial^2 M(t,x)}{\partial x^2} + L_1(M(t,x)), \tag{4.3}$$

where $M(t,x) = (M_1(t,x), M_2(t,x), M_3(t,x))^T$ and

$$D = \begin{pmatrix} D_1 & 0 & 0 \\ 0 & D_2 & 0 \\ 0 & 0 & D_3 \end{pmatrix}$$

and $L_1 : X_+^* \to R^3$ is defined by

$$L_1(M(t,x)) \\ = \begin{pmatrix} -(\beta E_* + \mu)M_1(t,x) - \beta S_* M_3(t,x) \\ \beta E_* M_1(t,x) - (\mu + \alpha)M_2(t,x) + \beta S_* M_3(t,x) \\ (\theta \check{V}(E_*)(1 - E_*))M_2(t,x) + [\theta I_* \check{V}'(E_*)(1 - E_*) - \theta I_* \check{V}(E_*) - \gamma]M_3(t,x) \end{pmatrix}.$$

Taking $M(t,x) = e^{\delta t} y_1(x)$ into system (4.3), we obtain

$$\delta y_1 - D\Delta y_1 - L_1(y_1) = 0, y_1 \in dom(\Delta)\backslash\{0\}, dom(\Delta) \subset X. \tag{4.4}$$

From the properties of Laplacian operator in [38, 40] defined in space X with homogeneous Neumann boundary conditions, the operator $\frac{\partial^2}{\partial x^2}$ has the eigenvalues $-l^2$, where $l \in N_0$ is the wave velocity, with the corresponding eigenfunctions on X are $\varphi_l^1 = (\gamma_l, 0, 0)^T$, $\varphi_l^2 = (0, \gamma_l, 0)^T$ and $\varphi_l^3 = (0, 0, \gamma_l)^T$, where $\gamma_l = cos(lx)$ and sequence $\{\varphi_l^1, \varphi_l^2, \varphi_l^3\}_{l=0}^{\infty}$ composes a basis of space X. Therefore, any element $y_1 \in X$ can be expanded as a Fourier series in the form.

$$y_1 = \sum_{l=0}^{\infty} Y_{1l}^T \begin{pmatrix} \varphi_l^1 \\ \varphi_l^2 \\ \varphi_l^3 \end{pmatrix}, \text{ where } Y_{1l}^T = \begin{pmatrix} \langle y_1, \varphi_l^1 \rangle \\ \langle y_1, \varphi_l^2 \rangle \\ \langle y_1, \varphi_l^3 \rangle \end{pmatrix}, \tag{4.5}$$

and for any $l \in N_0$ and $i = 1, 2, 3$, $\langle y_1, \varphi_l^i \rangle$ is defined to be the inner product of y_1 and φ_l^i in space X. We have for any $l \in N_0$,

$$L_1(Y_{1l}^T \begin{pmatrix} \varphi_l^1 \\ \varphi_l^2 \\ \varphi_l^3 \end{pmatrix}) = L_1(Y_{1l}^T) \begin{pmatrix} \varphi_l^1 \\ \varphi_l^2 \\ \varphi_l^3 \end{pmatrix}, \Delta y_1 = -\sum_{l=0}^{\infty} l^2 Y_{1l}^T \begin{pmatrix} \varphi_l^1 \\ \varphi_l^2 \\ \varphi_l^3 \end{pmatrix}. \tag{4.6}$$

It follows from the third equation of (4.1) that

$$\theta I_* = \frac{\gamma E_*}{\check{V}(E_*)(1-E_*)} = \frac{\gamma E_*}{F(E_*)}. \tag{4.7}$$

Thus,

$$\theta I_*[\check{V}'(E_*)(1-E_*) - \check{V}(E_*)] - \gamma = \theta I_* F'(E_*) - \gamma = \frac{-\gamma[F(E_*) - E_* F'(E_*)]}{F(E_*)}.$$

From (4.5)-(4.7), equation (4.4) is equivalent to

$$\sum_{l=0}^{\infty} Y_{1l}^T \begin{bmatrix} c_{11} & 0 & \beta S_* \\ -\beta E_* & c_{22} & -\beta S_* \\ 0 & -\theta F(E_*) & c_{33} \end{bmatrix} \begin{pmatrix} \varphi_l^1 \\ \varphi_l^2 \\ \varphi_l^3 \end{pmatrix} = 0,$$

where $c_{11} = \delta + D_1 l^2 + \beta E_* + \mu$, $c_{22} = \delta + D_2 l^2 + \mu + \alpha$ and $c_{33} = \delta + D_3 l^2 + \frac{\gamma[F(E_*) - E_* F'(E_*)]}{F(E_*)}$. Therefore, we finally obtain the characteristic equation as follows£º

$$\begin{vmatrix} c_{11} & 0 & \beta S_* \\ -\beta E_* & c_{22} & -\beta S_* \\ 0 & -\theta F(E_*) & c_{33} \end{vmatrix} = 0,\ l \in N_0, \tag{4.8}$$

where δ denotes the eigenvalue.

Denote $K(E) = F(E) - EF'(E)$. Since $\check{V}'(E) = \frac{1}{c}[g'(E) - \frac{mp}{(m+d)}\check{T}'(E)] > 0$ and $\check{V}''(E) = \frac{1}{c}[g''(E) - \frac{mp}{(m+d)}\check{T}''(E)] < 0$, we get $F''(E) = \check{V}''(E)(1-E) - 2\check{V}'(E) < 0$. Thus, $K'(E) = -EF''(E) > 0$ for $0 < E \le 1$. By $K(0) = \frac{m(R_w - 1)}{k} > 0$, we have $K(E) > 0$ for $0 < E \le 1$.

Notably, the characteristic equation of model (4.1) at equilibrium $W_0 = (S_0, 0, 0)$ can be obtained from (4.8) as follows

$$(\delta + D_1 l^2 + \mu)[(\delta + D_2 l^2 + \mu + \alpha)(\delta + D_3 l^2 + \gamma) - \beta S_0 \theta \check{V}(0)] = 0, \tag{4.9}$$

where $l \in N_0$. It is shown that one root of equation (4.9) is $\delta_1 = -(D_1 l^2 + \mu) < 0$. The remaining two roots δ_2 and δ_3 are obtained by the following equation

$$\delta^2 + [(D_2 + D_3)l^2 + \mu + \alpha + \gamma]\delta + (D_2 l^2 + \mu + \alpha)(D_3 l^2 + \gamma) - \beta S_0 \theta \check{V}(0) = 0. \tag{4.10}$$

Consider conclusion (i), when $R_c < 1$, then $(\mu + \alpha)\gamma - \beta S_0 \theta \check{V}(0) > 0$, we get

$$\begin{cases} \delta_2 + \delta_3 = -[(D_2 + D_3)l^2 + \mu + \alpha + \gamma] < 0, \\ \delta_2 \delta_3 = D_2 D_3 L^4 + D_2 l^2 \gamma + (\mu + \alpha) D_3 l^2 + (\mu + \alpha)\gamma - \beta S_0 \theta \check{V}(0) > 0. \end{cases}$$

Hence, two roots of equation (4.10) have negative real parts. Thus, W_0 is locally asymptotically stable.

Consider conclusion (ii), when $R_c > 1$, then $(\mu+\alpha)\gamma - \beta S_0\theta\check{V}(0) < 0$, we have

$$\begin{cases} \delta_2+\delta_3 = -[(D_2+D_3)l^2+\mu+\alpha+\gamma] < 0, \\ \delta_2\delta_3 = D_2D_3l^4 + D_2l^2\gamma + (\mu+\alpha)D_3l^2 + (\mu+\alpha)\gamma - \beta S_0\theta\check{V}(0). \end{cases}$$

It is clear that there is an integer number $l_1 \geq 0$ such that if $l < l_1$ then $\delta_2\delta_3 < 0$, if $l = l_1$ then $\delta_2\delta_3 \leq 0$ and if $l > l_1$ then $\delta_2\delta_3 > 0$. Therefore, when $l \leq l_1$ equation (4.10) has a positive root, which indicates that W_0 is unstable. This completes the proof. □

To discuss the stability of endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$, positive equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$ for model (4.1), we need to introduce the following assumptions.

(**A**) $F'(\widetilde{E}) \leq 0$; (**B**) $D_1 = D_2$ and $\widetilde{E} \leq \frac{\mu^2}{\beta\alpha}$; (**C**) $F'(\widetilde{E}_2) \leq 0$.

Theorem 4.2. (i) *Assume that* (**A**) *and one of conditions* (a) *and* (b) *in Lemma 4.2 hold. Then endemic equilibrium* $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ *of model (4.1) is locally asymptotically stable;*

(ii) *Assume that* (**B**) *and condition* (c) *in Lemma 4.2 hold. Then endemic equilibrium* $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ *of model (4.1) is locally asymptotically stable.*

Proof. From (4.8), the characteristic equation of model (4.1) at equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E})$ can be calculated as follows

$$\delta^3 + j_2(\widetilde{W})\delta^2 + j_1(\widetilde{W})\delta + j_0(\widetilde{W}) = 0, \tag{4.11}$$

where

$$\begin{aligned} j_2(\widetilde{W}) =&(D_1+D_2+D_3)l^2 + \frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + \mu + \alpha + \beta\widetilde{E} + \mu > 0, \\ j_1(\widetilde{W}) =&(D_1l^2 + \beta\widetilde{E} + \mu)(D_2l^2 + \mu + \alpha + D_3l^2 + \frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}) \\ &+ (D_2l^2+\mu+\alpha)(D_3l^2 + \frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}) - \beta\theta\widetilde{S}F(\widetilde{E}), \\ j_0(\widetilde{W}) =&(D_1l^2 + \beta\widetilde{E} + \mu)[(D_2l^2+\mu+\alpha)(D_3l^2 + \frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}) - \beta\theta\widetilde{S}F(\widetilde{E})] \\ &+ \beta\widetilde{E}\beta\theta\widetilde{S}F(\widetilde{E}). \end{aligned}$$

Firstly, we consider conclusion (i). According to (4.7) and the second equation of model (4.1), we obtain $\widetilde{S} = \frac{(\mu+\alpha)\gamma}{\beta\theta F(\widetilde{E})}$. By the expressions of $j_1(\widetilde{W})$ and $j_0(\widetilde{W})$, we further obtain

$$\begin{aligned} j_1(\widetilde{W}) =&D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}+\mu) \\ &+ D_3l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 \\ &+ D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)D_3l^2 + \gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1], \end{aligned}$$

$$\begin{aligned} j_0(\widetilde{W}) =& D_1D_2D_3l^6 + D_1D_2l^4\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1D_3l^4(\mu+\alpha) + D_2D_3l^4(\beta\widetilde{E}+\mu) \\ &+ D_2l^2(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)(\beta\widetilde{E}+\mu)D_3l^2 + \beta\widetilde{E}\gamma(\mu+\alpha) \\ &+ D_1l^2\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})}-1] + (\beta\widetilde{E}+\mu)\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})}-1]. \end{aligned}$$

Using assumption (**A**) and the expression of $K(E)$, we have $K(\widetilde{E}) = F(\widetilde{E}) - \widetilde{E}F'(\widetilde{E}) \geq F(\widetilde{E})$. Therefore, we obtain

$$\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1 \geq 0. \tag{4.12}$$

Furthermore, we also obtain $j_1(\widetilde{W}) > 0$ and $j_0(\widetilde{W}) > 0$.

Next, we prove $j_2(\widetilde{W})j_1(\widetilde{W}) - j_0(\widetilde{W}) > 0$. By calculating, we have

$$\begin{aligned} & j_2(\widetilde{W})j_1(\widetilde{W}) - j_0(\widetilde{W}) \\ =& D_1l^2[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}+\mu) \\ &+ D_3l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 \\ &+ D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)D_3l^2] + D_2l^2[D_1D_2l^4 + D_1D_3l^4 + D_1l^2(\mu+\alpha) \\ &+ D_2l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)D_3l^2 \\ &+ (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + A_c] + D_3l^2[D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_2l^2(\beta\widetilde{E}+\mu) \\ &+ D_3l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)D_3l^2 \\ &+ (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + A_c] + \frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} \\ &+ D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}+\mu) + D_3l^2(\beta\widetilde{E}+\mu) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} \\ &+ (\mu+\alpha)D_3l^2 + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + A_c] + (\mu+\alpha)[D_1D_2l^4 + D_1D_3l^4 \\ &+ D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}+\mu) + D_3l^2(\beta\widetilde{E}+\mu) \\ &+ (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)D_3l^2 \\ &+ (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + A_c] + (\beta\widetilde{E}+\mu)[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} \end{aligned}$$

$$+ D_1 l^2(\mu+\alpha) + D_2 l^2(\beta\widetilde{E}+\mu) + D_3 l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)(\mu+\alpha)$$
$$+ D_2 D_3 l^4 + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + A_c],$$

where $A_c = \gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1]$. From (4.12) again, we further have $j_2(\widetilde{W})j_1(\widetilde{W}) - j_0(\widetilde{W}) > 0$. Based on the above discussion, all roots of equation (4.11) have negative real parts by the Routh-Hurwitz criterion. Therefore, equilibrium $\widetilde{W}$ is locally asymptotically stable.

Secondly, we consider conclusion (ii). Since $H_M = 0$, we obtain $F(\widetilde{E}) = G(\widetilde{E}) = \frac{\gamma\widetilde{E}}{\theta\widetilde{I}}$ and $F'(\widetilde{E}) = G'(\widetilde{E})$. By $\widetilde{S} = \frac{(\mu+\alpha)\widetilde{I}}{\beta\widetilde{E}}$ and the first equation of model (4.1), we obtain $\beta\widetilde{E}+\mu = \frac{\beta\theta S_0}{(\mu+\alpha)\gamma} \times \frac{\widetilde{E}\mu\gamma}{\theta\widetilde{I}}$. Therefore, we further obtain

$$(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} = \gamma\mu\frac{\beta\theta S_0}{(\mu+\alpha)\gamma}K(\widetilde{E}) = \gamma\mu\frac{\beta\theta S_0}{(\mu+\alpha)\gamma} \times \frac{\gamma(\mu+\alpha)\mu}{\beta\theta A} = \gamma\mu$$

and

$$\begin{aligned}\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1] &= -\gamma(\mu+\alpha)\frac{\widetilde{E}G'(\widetilde{E})}{G(\widetilde{E})} \\ &= -\gamma(\mu+\alpha)\frac{\frac{\gamma(\mu+\alpha)\widetilde{E}}{\theta A}}{\frac{\gamma(\mu+\alpha)\widetilde{E}}{\theta A} + \frac{\gamma(\mu+\alpha)\mu}{\beta\theta A}} = -\gamma(\mu+\alpha)\frac{\beta\widetilde{E}}{\beta\widetilde{E}+\mu}.\end{aligned}$$

Using assumption (**B**), we have $\mu^2 - \beta\widetilde{E}\alpha \ge 0$. Thus,

$$(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + \gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1] = \frac{\gamma(\mu^2 - \beta\widetilde{E}\alpha)}{\beta\widetilde{E}+\mu} \ge 0. \tag{4.13}$$

By (4.13), we further have

$$\begin{aligned}j_1(\widetilde{W}) =& D_1 D_2 l^4 + D_1 D_3 l^4 + D_1 l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1 l^2(\mu+\alpha) + D_2 l^2(\beta\widetilde{E}+\mu) \\ &+ D_3 l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2 D_3 l^4 + D_2 l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} \\ &+ (\mu+\alpha)D_3 l^2 + \gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1] + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} > 0.\end{aligned}$$

By simplifying, we obtain

$$\begin{aligned}j_0(\widetilde{W}) =& D_1 D_2 D_3 l^6 + D_1 D_2 l^4\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1 D_3 l^4(\mu+\alpha) + D_2 D_3 l^4(\beta\widetilde{E}+\mu) \\ &+ D_2 l^2(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + (\mu+\alpha)(\beta\widetilde{E}+\mu)D_3 l^2 \\ &+ D_1 l^2\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1] + (\beta\widetilde{E}+\mu)\gamma(\mu+\alpha)\frac{K(\widetilde{E})}{F(\widetilde{E})} - \mu\gamma(\mu+\alpha).\end{aligned}$$

From $\beta\widetilde{E}+\mu=\frac{\beta\theta S_0}{(\mu+\alpha)\gamma}\mu F(\widetilde{E})$, $F(\widetilde{E})=G(\widetilde{E})$ and $F'(\widetilde{E})=G'(\widetilde{E})$, we obtain

$$\begin{aligned}&(\beta\widetilde{E}+\mu)\gamma(\mu+\alpha)\frac{K(\widetilde{E})}{F(\widetilde{E})}-\mu\gamma(\mu+\alpha)\\ =&\gamma\mu(\mu+\alpha)\{\frac{\beta\theta S_0}{(\mu+\alpha)\gamma}[G(\widetilde{E})-\widetilde{E}G'(\widetilde{E})]-1\}\\ =&\gamma\mu(\mu+\alpha)\{\frac{\beta\theta S_0}{(\mu+\alpha)\gamma}\times\frac{\gamma(\mu+\alpha)\mu}{\beta\theta A}-1\}=0.\end{aligned}$$

Thus, by $D_1=D_2$ in assumption (**B**) we further obtain

$$\begin{aligned}j_0(\widetilde{W})=&D_1D_2D_3l^6+D_1D_2l^4\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+D_1D_3l^4(\mu+\alpha)+D_1l^2\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})}-1]\\ &+D_2D_3l^4(\beta\widetilde{E}+\mu)+D_2l^2(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+(\mu+\alpha)(\beta\widetilde{E}+\mu)D_3l^2\\ =&D_1^2D_3l^6+D_1^2l^4\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+D_1D_3l^4(\mu+\alpha)+D_2D_3l^4(\beta\widetilde{E}+\mu)\\ &+(\mu+\alpha)(\beta\widetilde{E}+\mu)D_3l^2+D_1l^2\{\gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})}-1]+(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}\}.\end{aligned}$$

By (4.13), we have $j_0(\widetilde{W})>0$.

Next, we prove $j_2(\widetilde{W})j_1(\widetilde{W})-j_0(\widetilde{W})>0$. By calculating, we obtain

$$\begin{aligned}&j_2(\widetilde{W})j_1(\widetilde{W})-j_0(\widetilde{W})\\ =&D_1l^2[D_1D_2l^4+D_1D_3l^4+D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+D_1l^2(\mu+\alpha)+D_2l^2(\beta\widetilde{E}+\mu)\\ &+D_3l^2(\beta\widetilde{E}+\mu)+(\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+(\beta\widetilde{E}+\mu)(\mu+\alpha)+D_2D_3l^4\\ &+D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+(\mu+\alpha)D_3l^2]+D_2l^2[D_1D_2l^4+D_1D_3l^4+D_1l^2(\mu+\alpha)\\ &+D_2l^2(\beta\widetilde{E}+\mu)+(\beta\widetilde{E}+\mu)(\mu+\alpha)+D_2D_3l^4+D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}\\ &+(\mu+\alpha)D_3l^2+B_c]+D_3l^2[D_1D_3l^4+D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+D_2l^2(\beta\widetilde{E}+\mu)\\ &+D_3l^2(\beta\widetilde{E}+\mu)+(\beta\widetilde{E}+\mu)(\mu+\alpha)+D_2D_3l^4+D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}\\ &+(\mu+\alpha)D_3l^2+B_c]+(\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+\mu+\alpha)[D_1D_2l^4+D_1D_3l^4\\ &+D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+D_1l^2(\mu+\alpha)+D_2l^2(\beta\widetilde{E}+\mu)+D_3l^2(\beta\widetilde{E}+\mu)\\ &+(\beta\widetilde{E}+\mu)(\mu+\alpha)+D_2D_3l^4+D_2l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}+(\mu+\alpha)D_3l^2+B_c]\end{aligned}$$

$$+ (\beta\widetilde{E}+\mu)[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})} + D_1l^2(\mu+\alpha)$$
$$+ D_2l^2(\beta\widetilde{E}+\mu) + D_3l^2(\beta\widetilde{E}+\mu) + (\beta\widetilde{E}+\mu)(\mu+\alpha) + D_2D_3l^4 + B_c],$$

where $B_c = \gamma(\mu+\alpha)[\frac{K(\widetilde{E})}{F(\widetilde{E})} - 1] + (\beta\widetilde{E}+\mu)\frac{\gamma K(\widetilde{E})}{F(\widetilde{E})}$. From (4.13) again, we further obtain $j_2(\widetilde{W})j_1(\widetilde{W}) - j_0(\widetilde{W}) > 0$. Based on the above discussion, all roots of equation (4.11) have negative real parts by the Routh-Hurwitz criterion. Therefore, equilibrium $\widetilde{W}$ is locally asymptotically stable. This completes the proof. □

Remark 4.2. For Theorem 4.2, we only establish the local asymptotic stability of endemic equilibrium $\widetilde{W}$ for nested slow model (4.1) when $R_c > 1$. Comparing conclusion (*ii*) of Theorem 3.2, for the nested slow model, we propose an open problem, that is, whether endemic equilibrium $\widetilde{W}$ of model (4.1) also is globally asymptotically stable when $R_c > 1$.

Theorem 4.3. *Assume that condition (d) in Lemma 4.2 holds, then positive equilibrium* $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ *of model (4.1) is unstable.*

Proof. From (4.8), the characteristic equation of model (4.1) at equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ can be established as follows

$$\delta^3 + j_2(\widetilde{W}_1)\delta^2 + j_1(\widetilde{W}_1)\delta + j_0(\widetilde{W}_1) = 0, \tag{4.14}$$

where

$$j_2(\widetilde{W}_1) =(D_1+D_2+D_3)l^2 + \frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + \mu + \alpha + \beta\widetilde{E}_1 + \mu > 0,$$
$$j_1(\widetilde{W}_1) =(D_1l^2 + \beta\widetilde{E}_1 + \mu)(D_2l^2 + \mu + \alpha + D_3l^2 + \frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)})$$
$$+ (D_2l^2 + \mu + \alpha)(D_3l^2 + \frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)}) - \beta\theta\widetilde{S}_1F(\widetilde{E}_1),$$
$$j_0(\widetilde{W}_1) =(D_1l^2 + \beta\widetilde{E}_1 + \mu)[(D_2l^2 + \mu + \alpha)(D_3l^2 + \frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)}) - \beta\theta\widetilde{S}F(\widetilde{E}_1)]$$
$$+ \beta\widetilde{E}_1\beta\theta\widetilde{S}_1F(\widetilde{E}_1).$$

By $\beta\theta\widetilde{S}_1F(\widetilde{E}_1) = \gamma(\mu+\alpha)$, we have

$$j_1(\widetilde{W}_1) =D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_1+\mu)$$
$$+ D_3l^2(\beta\widetilde{E}_1+\mu) + (\beta\widetilde{E}_1+\mu)\frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + (\beta\widetilde{E}_1+\mu)(\mu+\alpha) + D_2D_3l^4$$
$$+ D_2l^2\frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + (\mu+\alpha)D_3l^2 + \gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)} - 1]$$

and

$$j_0(\widetilde{W}_1) =D_1D_2D_3l^6 + D_1D_2l^4\frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + D_1D_3l^4(\mu+\alpha) + D_2D_3l^4(\beta\widetilde{E}_1+\mu)$$

$$+ D_2 l^2(\beta\widetilde{E}_1+\mu)\frac{\gamma K(\widetilde{E}_1)}{F(\widetilde{E}_1)} + (\mu+\alpha)(\beta\widetilde{E}_1+\mu)D_3 l^2 + \beta\widetilde{E}_1\gamma(\mu+\alpha)$$
$$+ D_1 l^2\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)}-1] + (\beta\widetilde{E}_1+\mu)\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)}-1].$$

Consider the term $\beta\widetilde{E}_1\gamma(\mu+\alpha) + (\beta\widetilde{E}_1+\mu)\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)}-1]$ in $j_0(\widetilde{W}_1)$. By $H'(\widetilde{E}_1) > 0$ and $H(\widetilde{E}_1) = 0$, we get $F'(\widetilde{E}_1) > G'(\widetilde{E}_1) > 0$ and $F(\widetilde{E}_1) = G(\widetilde{E}_1)$, then

$$\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)}-1] = -\gamma(\mu+\alpha)\frac{\widetilde{E}_1 F'(\widetilde{E}_1)}{F(\widetilde{E}_1)} < -\gamma(\mu+\alpha)\frac{\widetilde{E}_1 G'(\widetilde{E}_1)}{G(\widetilde{E}_1)}$$
$$= -\gamma(\mu+\alpha)\frac{\frac{\gamma(\mu+\alpha)\widetilde{E}_1}{\theta A}}{\frac{\gamma(\mu+\alpha)\widetilde{E}_1}{\theta A}+\frac{\gamma(\mu+\alpha)\mu}{\beta\theta A}} = -\gamma(\mu+\alpha)\frac{\beta\widetilde{E}_1}{\beta\widetilde{E}_1+\mu}.$$

Thus,

$$\beta\widetilde{E}_1\gamma(\mu+\alpha) + (\beta\widetilde{E}_1+\mu)\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_1)}{F(\widetilde{E}_1)}-1]$$
$$<\beta\widetilde{E}_1\gamma(\mu+\alpha) + (\beta\widetilde{E}_1+\mu)[-\gamma(\mu+\alpha)\frac{\beta\widetilde{E}_1}{\beta\widetilde{E}_1+\mu}] = 0.$$

It is clear that there is an integer number $l_2 \geq 0$ such that if $l \leq l_2$ then $j_0(\widetilde{W}_1) < 0$. Thus, when $l \leq l_2$, equation (4.14) has a positive root, which indicates that $\widetilde{W}_1$ is unstable. This completes the proof. □

Theorem 4.4. *Assume that* (**C**) *and condition* (*d*) *in Lemma 4.2 hold, then positive equilibrium* $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$ *of model (4.1) is locally asymptotically stable.*

Proof. From (4.8), the characteristic equation of model (4.1) at equilibrium $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$ can be established as follows

$$\delta^3 + j_2(\widetilde{W}_2)\delta^2 + j_1(\widetilde{W}_2)\delta + j_0(\widetilde{W}_2) = 0, \tag{4.15}$$

where

$$j_2(\widetilde{W}_2) =(D_1+D_2+D_3)l^2 + \frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + \mu + \alpha + \beta\widetilde{E}_2 + \mu > 0,$$
$$j_1(\widetilde{W}_2) =(D_1 l^2+\beta\widetilde{E}_2+\mu)(D_2 l^2+\mu+\alpha+D_3 l^2+\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)})$$
$$+ (D_2 l^2+\mu+\alpha)(D_3 l^2+\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}) - \beta\theta\widetilde{S}F(\widetilde{E}_2),$$
$$j_0(\widetilde{W}_2) =(D_1 l^2+\beta\widetilde{E}_2+\mu)[(D_2 l^2+\mu+\alpha)(D_3 l^2+\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}) - \beta\theta\widetilde{S}F(\widetilde{E}_2)]$$
$$+ \beta\widetilde{E}_2\beta\theta\widetilde{S}F(\widetilde{E}_2).$$

According to (4.7) and the second equation of model (4.1), we obtain $\widetilde{S}_2 = \frac{(\mu+\alpha)\gamma}{\beta\theta F(\widetilde{E}_2)}$. From the expressions of $j_1(\widetilde{W_2})$ and $j_0(\widetilde{W_2})$, we further obtain

$$\begin{aligned}
j_1(\widetilde{W_2}) =& D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_2+\mu)\\
&+ D_3l^2(\beta\widetilde{E}_2+\mu) + (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4\\
&+ D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)D_3l^2 + \gamma(\mu+\alpha)[\frac{K(\widetilde{E}_2)}{F(\widetilde{E}_2)} - 1],\\
j_0(\widetilde{W_2}) =& D_1D_2D_3l^6 + D_1D_2l^4\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + D_1D_3l^4(\mu+\alpha) + D_2D_3l^4(\beta\widetilde{E}_2+\mu)\\
&+ D_2l^2(\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)(\beta\widetilde{E}_2+\mu)D_3l^2 + \beta\widetilde{E}_2\gamma(\mu+\alpha)\\
&+ D_1l^2\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_2)}{F(\widetilde{E}_2)} - 1] + (\beta\widetilde{E}_2+\mu)\gamma(\mu+\alpha)[\frac{K(\widetilde{E}_2)}{F(\widetilde{E}_2)} - 1].
\end{aligned}$$

Using assumption (**C**) and the definition of $K(E)$, we have $K(\widetilde{E}_2) = F(\widetilde{E}_2) - \widetilde{E}_2F'(\widetilde{E}_2) \geq F(\widetilde{E}_2)$. Therefore, we obtain

$$\frac{K(\widetilde{E}_2)}{F(\widetilde{E}_2)} - 1 \geq 0. \tag{4.16}$$

Furthermore, we also obtain $j_1(\widetilde{W_2}) > 0$ and $j_0(\widetilde{W_2}) > 0$.

Next, we prove $j_2(\widetilde{W_2})j_1(\widetilde{W_2}) - j_0(\widetilde{W_2}) > 0$. By calculating, we obtain

$$\begin{aligned}
&j_2(\widetilde{W_2})j_1(\widetilde{W_2}) - j_0(\widetilde{W_2})\\
=& D_1l^2[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_2+\mu)\\
&+ D_3l^2(\beta\widetilde{E}_2+\mu) + (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4\\
&+ D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)D_3l^2] + D_2l^2[D_1D_2l^4 + D_1D_3l^4 + D_1l^2(\mu+\alpha)\\
&+ D_2l^2(\beta\widetilde{E}_2+\mu) + (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)D_3l^2\\
&+ (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + C_c] + D_3l^2[D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + D_2l^2(\beta\widetilde{E}_2+\mu)\\
&+ D_3l^2(\beta\widetilde{E}_2+\mu) + (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)D_3l^2\\
&+ (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + C_c] + \frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}\\
&+ D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_2+\mu) + D_3l^2(\beta\widetilde{E}_2+\mu) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}
\end{aligned}$$

$$+ (\mu+\alpha)D_3l^2 + (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + C_c] + (\mu+\alpha)[D_1D_2l^4 + D_1D_3l^4$$

$$+ D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_2+\mu) + D_3l^2(\beta\widetilde{E}_2+\mu)$$

$$+ (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4 + D_2l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + (\mu+\alpha)D_3l^2$$

$$+ (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + C_c] + (\beta\widetilde{E}_2+\mu)[D_1D_2l^4 + D_1D_3l^4 + D_1l^2\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)}$$

$$+ D_1l^2(\mu+\alpha) + D_2l^2(\beta\widetilde{E}_2+\mu) + D_3l^2(\beta\widetilde{E}_2+\mu)$$

$$+ (\beta\widetilde{E}_2+\mu)(\mu+\alpha) + D_2D_3l^4 + (\beta\widetilde{E}_2+\mu)\frac{\gamma K(\widetilde{E}_2)}{F(\widetilde{E}_2)} + C_c],$$

where $C_c = \gamma(\mu+\alpha)[\frac{K(\widetilde{E}_2)}{F(\widetilde{E}_2)}-1]$. From (4.16) again, we further obtain $j_2(\widetilde{W}_2)j_1(\widetilde{W}_2) - j_0(\widetilde{W}_2) > 0$. Based on the above discussion, all roots of equation (4.15) have negative real parts by the Routh-Hurwitz criterion. Therefore, equilibrium $\widetilde{W}_2$ is locally asymptotically stable. This completes the proof. □

Remark 4.3. Theorems 4.3 and 4.4 show that when $R_c < 1$, $H_M > 0$ and the additional assumption (**C**) holds then nested slow model (4.1) occurs the backward bifurcation at disease-free equilibrium W_0.

5. Numerical examples

In this section, we give some numerical examples to verify the theoretical results obtained Theorem 4.2 and Theorem 4.4. In nested models (1.3)-(1.4), for the convenience of numerical simulations, we take the function $g(E) = aE$ with $a = 4\times10^5$ in the following examples. In addition, we choose the spatial domain is $\Omega = [0,\pi]$ and the parameters $D_3 = 0.003$, $A = 4$, $\theta = 1\times10^{-10}$, $\Lambda = 6000$, $k = 1\times10^{-6}$, $m = 0.3$ and $d = 0.2$. The parameters D_1, D_2, β, γ, α, μ, c and p are chosen as free parameters.

Example 5.1. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.005$, $\beta = 0.0006$, $\gamma = 0.02$, $\alpha = 0.0004$, $\mu = 0.0004$, $c = 54$ and $p = 1516.97438$. Furthermore, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 1 are chosen by $(4500, 1000, 0.05)$, $(12000, 1600, 0.35)$ and $(8000, 3500, 0.7)$, respectively.

By calculating we have $R_w = 1.1237 > 1$ and $R_c = 1.3915 > 1$. Model (4.1) has unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E}) = (7155.3, 1430.1, 0.2663)$. We further have $F'(\widetilde{E}) = F'(0.2663) = -49953 < 0$. Hence, assumption (**A**) is satisfied. The numerical simulations given in Figure 1 elucidate that unique endemic equilibrium $\widetilde{W}$ is locally asymptotically stable. Thus, conclusion (i) of Theorem 4.2 is verified.

Example 5.2. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.005$, $\beta = 0.008$, $\gamma = 0.02$, $\alpha = 0.0004$, $\mu = 0.001$, $c = 69.5$ and $p = 1800.58$. In addition, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 2 are chosen by $(1300, 1200, 0.1)$, $(1800, 1500, 0.25)$ and $(2700, 2400, 0.4)$, respectively.

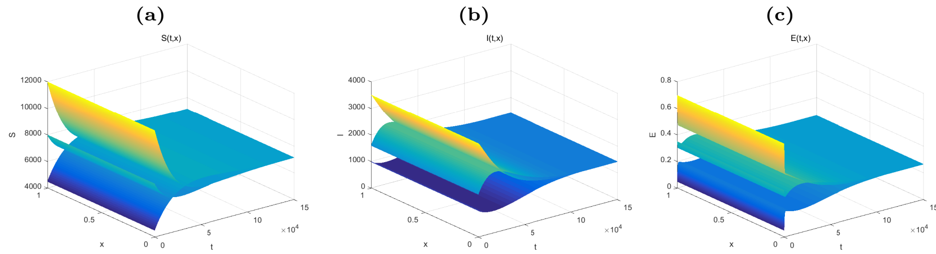

Figure 1. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}$.

By calculating we have $R_w = 1.0363 > 1$ and $R_c = 1.2447 > 1$. Model (4.1) has unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E}) = (1641, 1685, 0.1797)$. Since $F'(\widetilde{E}) = F'(0.1797) = 92.613 > 0$, assumption (**A**) is not satisfied. The numerical simulations given in Figure 2 illustrate that unique endemic equilibrium $\widetilde{W}$ is locally asymptotically stable even if assumption (**A**) is not true. Therefore, $F'(\widetilde{E}) \leq 0$ may be a purely mathematical condition used in the proof of Theorem 4.2.

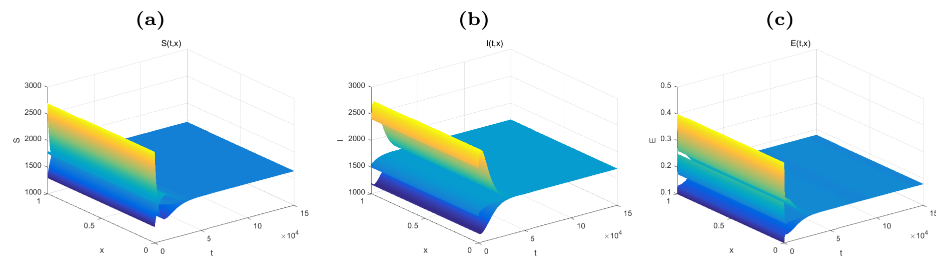

Figure 2. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}$.

Example 5.3. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.005$, $\beta = 0.0006$, $\gamma = 0.015$, $\alpha = 0.0004$, $\mu = 0.0004$, $c = 52$ and $p = 1387.8609$. Furthermore, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 3 are chosen by $(5500, 1000, 0.15)$, $(9000, 1600, 0.34)$ and $(12000, 3000, 0.6)$, respectively.

By calculating we have $R_w = 1.0676 > 1$ and $R_c = 1$. Model (4.1) has the unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E}) = (7117.5, 1446, 0.2707)$. Moreover, we also have $H_M = 3112.0544 > 0$ and $F'(\widetilde{E}) = F'(0.2707) = -37795 < 0$. Therefore, assumption (**A**) is satisfied. The numerical simulations given in Figure 3 elucidate that unique endemic equilibrium $\widetilde{W}$ is locally asymptotically stable. Hence, conclusion (i) of Theorem 4.2 is also verified.

Example 5.4. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.004$, $\beta = 0.00015$, $\gamma = 0.004$, $\alpha = 0.0004$, $\mu = 0.0004$, $c = 56$ and $p = 1456.80959$. Moreover, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 4 are chosen by $(5500, 300, 0.21)$, $(8500, 600, 0.32)$ and $(12000, 1000, 0.55)$, respectively.

By calculating we have $R_w = 1.0406 > 1$ and $R_c = 0.5706 < 1$. Model (4.1) has unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E}) = (9155.8, 423.6287, 0.2471)$. We further

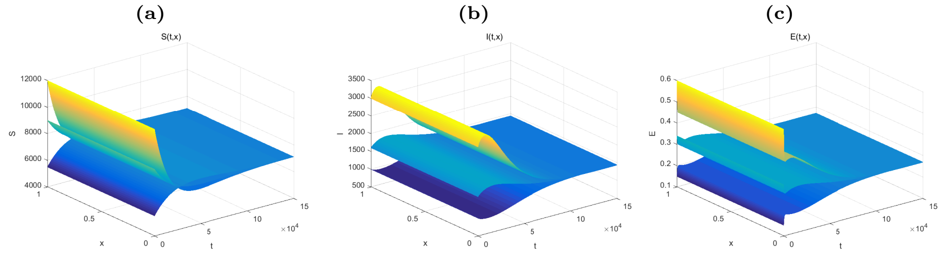

Figure 3. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}$.

have $H_M = H(0.2471) = 0$ and $\frac{\mu^2}{\beta\alpha} = 0.2667 > 0.2471$. Therefore, assumption (**B**) is satisfied. The numerical simulations given in Figure 4 illustrate that unique endemic equilibrium $\widetilde{W}$ is locally asymptotically stable. Hence, conclusion (ii) of Theorem 4.2 is verified.

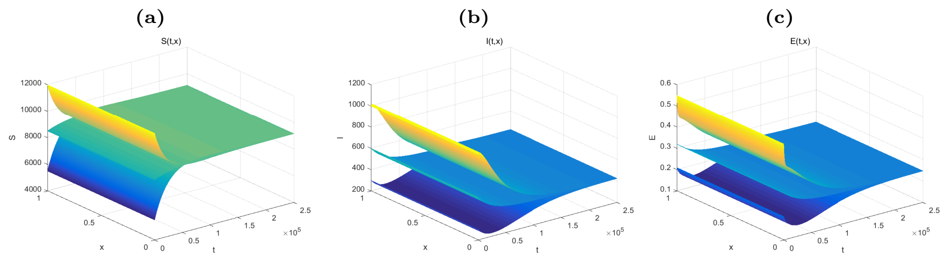

Figure 4. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}$.

Example 5.5. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.004$, $\beta = 0.0006$,$\gamma = 0.02$, $\alpha = 0.0002$, $\mu = 0.0004$, $c = 60$ and $p = 1594.29488$. In addition, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 5 are chosen by $(5500, 1500, 0.25)$, $(8000, 2500, 0.5)$ and $(9000, 3000, 0.7)$, respectively.

By calculating we have $R_w = 1.0629 > 1$ and $R_c = 0.9429 < 1$. Model (4.1) has unique endemic equilibrium $\widetilde{W} = (\widetilde{S}, \widetilde{I}, \widetilde{E}) = (6469.9, 2353.7, 0.3637)$. Moreover, we also have $H_M = H(0.3637) = 0$ and $\frac{\mu^2}{\beta\alpha} = 0.0133 < 0.3637$. Thus, assumption (**B**) is not satisfied. The numerical simulations given in Figure 5 elucidate that unique endemic equilibrium $\widetilde{W}$ is also locally asymptotically stable even if assumption (**B**) is not true. Therefore, $D_1 = D_2$ and $\widetilde{E} \le \frac{\mu^2}{\beta\alpha}$ may be purely mathematical conditions used in the proof of Theorem 4.2.

Example 5.6. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.005$, $\beta = 0.002$,$\gamma = 0.015$, $\alpha = 0.0001$, $\mu = 0.0015$, $c = 56.5$ and $p = 1430$. Besides, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 6 are chosen by $(800, 100, 0.1)$, $(1600, 900, 0.65)$ and $(2500, 1700, 0.9)$, respectively.

By calculating we have $R_w = 1.0124 > 1$ and $R_c = 0.0826 < 1$. Model (4.1)

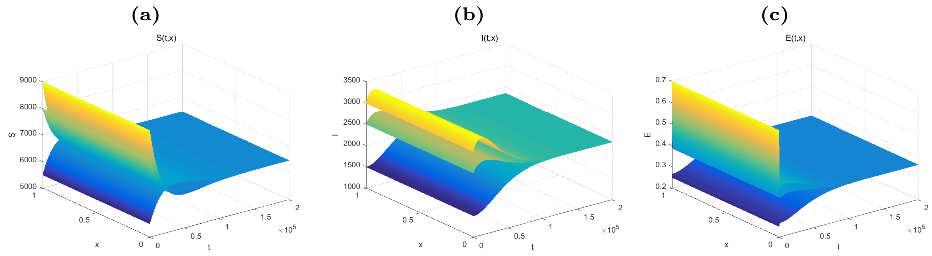

Figure 5. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}$.

has two positive equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1) = (2660.7, 0.00001, 0.0016781)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2) = (1291.5, 1289.2, 0.7986)$. We further have $H_M = 13550.41 > 0$ and $F'(\widetilde{E}_2) = F'(0.7986) = -43305.45 < 0$, then assumption (**C**) is satisfied. The numerical simulations given in Figure 6 illustrate that equilibrium $\widetilde{W}_2$ is locally asymptotically stable. Therefore, Theorem 4.4 is verified.

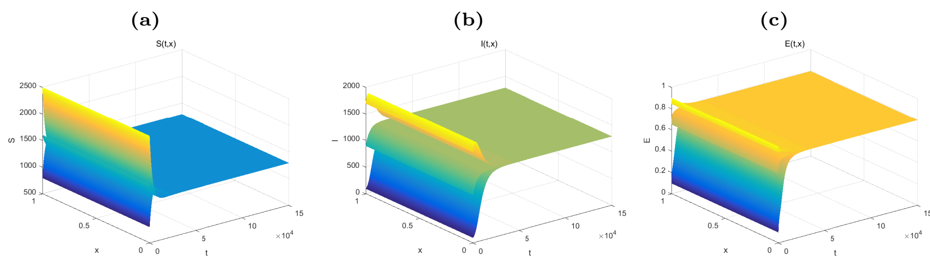

Figure 6. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}_2$.

Example 5.7. We select the surplus parameters $D_1 = 0.004$, $D_2 = 0.005$, $\beta = 0.0006$,$\gamma = 0.015$, $\alpha = 0.0001$, $\mu = 0.0015$, $c = 60$ and $p = 1510$. Besides, the initial values of solution $(S(t,x), I(t,x), E(t,x))$ in Figure 7 are chosen by $(1500, 250, 0.25)$, $(2400, 390, 0.5)$ and $(4000, 600, 0.7)$, respectively.

By calculating we have $R_w = 1.0067 > 1$ and $R_c = 0.0133 < 1$. Model (4.1) has two positive endemic equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1) = (2520.9, 0.000035, 0.144528)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2) = (2250.6, 390.0916, 0.4622)$. We further have $H_M = 1812.43$ > 0 and $F'(\widetilde{E}_2) = F'(0.4622) = 10.7235 > 0$, then assumption (**C**) is not satisfied. The numerical simulations given in Figure 7 illustrate that equilibrium $\widetilde{W}_2$ is locally asymptotically stable even if assumption (**C**) is not true. Therefore, $F'(\widetilde{E}_2) \leq 0$ may be a purely mathematical condition used in the proof of Theorem 4.4.

6. Conclusions

In this article, we investigate a reaction-diffusion model for nested within-host and between-host dynamics in an environmentally-driven infectious disease. The model

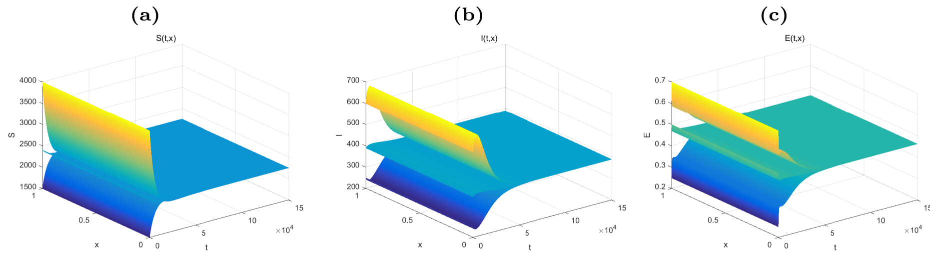

Figure 7. Dynamical behaviors of $S(t,x)$ (Fig. (a)), $I(t,x)$ (Fig. (b)) and $E(t,x)$ (Fig. (c)). The numerical simulations indicate that the solutions finally converge to the equilibrium $\widetilde{W}_2$.

is composed of a hybrid model of ordinary and partial differential equations which is divided into a within-host fast time model of ordinary differential equations and a between-host slow time reaction-diffusion model by using the singular perturbation theory in [5].

For within-host fast time model (1.4), the dynamical behavior has been investigated in [11–13]. We only summarize the main results.

For isolated between-host slow time model (1.3), we first obtain the positivity and ultimately boundedness of solutions, the basic reproduction number R_b and the existence of equilibrium. Next, the global stability of equilibrium is obtained by using the Lyapunov function method. That is, if $R_b \leq 1$, then disease-free equilibrium is globally asymptotically stable, and if $R_b > 1$, then endemic equilibrium is globally asymptotically stable.

For nested between-host slow time model (4.1), we first obtain the existence of positive equilibrium with the help of basic reproduction number R_c and H_M. Particularly, model (4.1) have a unique endemic equilibrium $\widetilde{W}$ when $R_c > 1$, and two positive equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ and $\widetilde{W}_2 = (\widetilde{S}_2, \widetilde{I}_2, \widetilde{E}_2)$ with $\widetilde{E}_1 < \widetilde{E}_2$ when $R_c < 1$ and $H_M > 0$. This shows that model (4.1) can undergo a backward bifurcation at $R_c = 1$. We further establish a series of criteria for the stability of equilibrium. Namely, disease-free equilibrium W_0 is locally asymptotically stable if $R_c < 1$, unique endemic equilibrium $\widetilde{W}$ is locally asymptotically stable if $R_c > 1$ and $F'(\widetilde{E}) \leq 0$ or $R_c = 1$, $H_M > 0$ and $F'(\widetilde{E}) \leq 0$ or $R_c < 1$, $H_M = 0$, $D_1 = D_2$ and $\widetilde{E} \leq \frac{\mu^2}{\beta\alpha}$, positive equilibrium $\widetilde{W}_1 = (\widetilde{S}_1, \widetilde{I}_1, \widetilde{E}_1)$ is unstable if $R_c < 1$ and $H_M > 0$, and positive equilibrium $\widetilde{W}_2$ is locally asymptotically stable if $R_c < 1$, $H_M > 0$ and $F'(\widetilde{E}_2) \leq 0$.

Generally, we just want the local stability of the equilibrium of model (4.1) to be only related to R_c. Therefore, some open problems can be further investigated. For example, whether we can obtain the local asymptotic stability of the equilibrium of model (4.1), even if assumptions (**A**), (**B**) and (**C**) are not true, as well as when $R_c > 1$ whether we can obtain the global asymptotic stability of unique endemic equilibrium of model (4.1). These problems are very challenging and will be solved in the future.

The main content of this paper is to study the dynamic behavior of model (1.3)-(1.4). Compared with model (1.1) of ordinary differential equations, the characteristic of partial differential equation model (1.3) is to include the mobility of the population in space. Therefore, models (1.3)-(1.4) are more practical and the conclusions of models (1.3)-(1.4) can provide more effective guidance for disease control and prevention.

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