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Research article

Global stability of an age-structured infection model in vivo with two compartments and two routes

Tsuyoshi Kajiwara[1], **Toru Sasaki**[2] **and Yoji Otani**[3,*]

[1] Graduate School of Environmental and Life Sciences, Okayama University, Japan
[2] Faculty of Environmental and Life Science, Okayama University, Japan
[3] School of Engineering, Okayama University, Japan

* **Correspondence:** Email: sasaki@okayama-u.ac.jp.

Abstract: In this paper, for an infection age model with two routes, virus-to-cell and cell-to-cell, and with two compartments, we show that the basic reproduction ratio R_0 gives the threshold of the stability. If $R_0 > 1$, the interior equilibrium is unique and globally stable, and if $R_0 \leq 1$, the disease free equilibrium is globally stable. Some stability results are obtained in previous research, but, for example, a complete proof of the global stability of the disease equilibrium was not shown. We give the proof for all the cases, and show that we can use a type reproduction number for this model.

Keywords: global stability; two routes of infection; two compartments; type reproduction number; lyapunov functional

1. Introduction

Until recent years, models for in-host infection had been considered with only one compartment. On the other hand, Qesmi et al. [1, 2] proposed models for hepatitis B and C infections. Their models have two components of infection, for example, liver cells and blood. The model in [1] is an ordinary differential equation model, and that in [2] is an age-structured model. They used models which incorporate the effect of absorption of pathogens into uninfected cells, and showed that a backward bifurcation can occur under some conditions. In Kajiwara et al. [3], the global stability of the interior equilibrium for the same ordinary differential model in [1] is shown using a Lyapunov function under some condition on parameters.

Recently, a cell-to-cell infection route for within-host infection is also paid much attention to. For example, Hübner et al. [4] suggest that HIV infection is enhanced by cell-cell adhesions. For models with two routes of infection, virus-to-cell and cell-to-cell infections, the stability analysis is done (Pourbashash et al. [5] for an ordinary differential equation model, Lai et al. [6] for a model with time delay). Wang et al. [7] considered an age-structured model with two routes of infection, and constructed a Lyapunov functional for their model. Wu et al. [8] proposed a model that considers two infection routes and two virus strains. They transformed the system into integro-differential equations, and proved some local stability and persistence results.

Models that consider both a cell-to-cell infection route and two compartments were investigated by, for example, Cheng et al. [9] and Wu and Zhao [10]. Cheng et al. [9] extended the model of [7] to a 2-compartment model as in Qesmi et al. [1, 2]. They formulated the model as an abstract Cauchy problem, and analyzed the model. They defined a quantity R_0, which is similar to the basic reproduction number but is not equal to it. They showed that if the quantity R_0 is greater than 1, there exists an interior equilibrium, and showed that a uniform persistence result holds if $R_0 > 1$. They showed the global stability results only for some restricted cases. They treated the case where the infection route is unique for each compartment, and also treated the case where there exist two infection routes under some restriction on parameters by using the asymptotic stability theory. Cheng et al. [9] did not use a Lyapunov functional, and did not present a general result on the global stability for their model. Wu et al. [10] proposed models with two compartments, two infection routes, two virus strains and an age-structure. They showed some stability results, and proved a persistence result in the case $R_0 > 1$. However they suggested the stability of the infection steady state by numerical simulations, and its mathematical proof was not given there.

In this paper, we formulate the model proposed in Cheng et al. [9] as an integral equation model. We show that the quantity R_m in Cheng et al. [9] is the type reproduction number (Roberts and Heesterbeek [11]) for the class of pathogens, and R_m determines the exact order relation between the basic reproduction number and 1. We prove qualitative properties, for example, asymptotic smoothness, and show a persistence result which is necessary to the definition and calculation of Lyapunov functionals. We follow the method in Smith and Thieme [12]. Moreover, we construct Lyapunov functionals for the cases $R_0 > 1$ and $R_0 \leq 1$. We then show that the unique interior equilibrium is globally asymptotically stable (GAS) if $R_0 > 1$, and the disease free equilibrium (DFE) is globally asymptotically stable if $R_0 \leq 1$, using an argument over the alpha-limit sets of total solutions in the compact attractor.

2. Foundation

In this section, we present fundamental results of the model, the basic reproductive number and the type reproduction number, and compactness arguments.

2.1. The model

We assume that the number of compartments is two, and assign numbers 1 and 2 to each compartment. We denote by T_j the amount of the uninfected cells in the jth compartment and denote by $i_j(t, a)$ the infection age density of the infected cells in the jth compartment. We denote by V the amount of the pathogens. Since blood circulates quickly, we assume that V is common for each compartment.

We consider the following age-structured model with two compartments presented in Cheng et al. [9]:

$$
\begin{aligned}
\frac{\mathrm{d}T_1}{\mathrm{d}t} &= f_1(T_1(t)) - \beta_{11}T_1(t)V(t) - \beta_{12}T_1(t)\int_0^\infty p_1(a)i_1(t,a)\,\mathrm{d}a,\\
\frac{\partial i_1(t,a)}{\partial t} + \frac{\partial i_1(t,a)}{\partial a} &= -(\delta_1(a)+m_1)i_1(t,a),\\
\frac{\mathrm{d}T_2}{\mathrm{d}t} &= f_2(T_2(t)) - \beta_{21}T_2(t)V(t) - \beta_{22}T_2(t)\int_0^\infty p_2(a)i_2(t,a)\,\mathrm{d}a,\\
\frac{\partial i_2(t,a)}{\partial t} + \frac{\partial i_2(t,a)}{\partial a} &= -(\delta_2(a)+m_2)i_2(t,a),\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= \int_0^\infty q_1(a)i_1(t,a)\,\mathrm{d}a + \int_0^\infty q_2(a)i_2(t,a)\,\mathrm{d}a - cV,\\
i_1(t,0) &= \beta_{11}T_1(t)V(t) + \beta_{12}T_1(t)\int_0^\infty p_1(a)i_1(t,a)\,\mathrm{d}a,\\
i_2(t,0) &= \beta_{21}T_2(t)V(t) + \beta_{22}T_2(t)\int_0^\infty p_2(a)i_2(t,a)\,\mathrm{d}a,\\
T_1(0) &= T_{10} > 0, \quad i_1(0,a) = i_{10}(a) \in \mathrm{L}^1([0,\infty),\mathbb{R}_+),\\
T_2(0) &= T_{20} > 0, \quad i_2(0,a) = i_{20}(a) \in \mathrm{L}^1([0,\infty),\mathbb{R}_+),\\
V(0) &= V_0 \in \mathbb{R}_+ = \{\, x \in \mathbf{R} \mid x \geq 0 \,\}.
\end{aligned}
\tag{2.1}
$$

The constants β_{jk}, m_j and c are positive for each $j = 1, 2$ and $k = 1, 2$. For the growth function $f_j(x)$ of uninfected cells, we assume that $f_j(x)$ is a differentiable function with the properties

$$f_j(0) > 0, \quad f_j'(x) < 0, \quad f_j(\overline{T}_j) = 0$$

for each j, where $\overline{T}_j$ is a positive constant. We moreover assume that there exist constants A_j and B_j such that

$$f_j(s) \leqq A_j - B_j s \quad (s \geqq 0). \tag{2.2}$$

We note that the form $f_j(x) = h_j - d_j x$ is often used. The functions $p_j(a)$'s are the viral production rates of an infected cell with infection age a in the jth compartment, and $q_j(a)$'s are the viral release rates of an infected cell with age a in the jth compartment. We assume that the non-negative functions $p_j(a)$, $q_j(a)$ and $\delta_j(a)$ are Lipschitz continuous, and that $p_j(a)$ and $q_j(a)$ are essentially bounded on $(0,\infty)$. For the definition of the Lyapunov functionals, we moreover assume that the functions $ap_j : a \mapsto ap_j(a)$ and $aq_j : a \mapsto aq_j(a)$ satisfy

$$ap_j,\ aq_j \in L^1([0,\infty)). \tag{2.3}$$

Define $\sigma_j(a)$ by

$$\sigma_j(a) = e^{-\int_0^a (\delta_j(b)+m_j)\,\mathrm{d}b}.$$

Since $\delta_j(a)$ is continuous, $\sigma_j(a)$ is differentiable. For $j = 1, 2$, put

$$J_j[i_j] = \int_0^\infty p_j(a)i_j(a)\,\mathrm{d}a,$$

where $i_j(\cdot) \in \mathrm{L}^1([0,\infty))$ and put

$$J_j(t) = J_j[i_j(t,a)] = \int_0^\infty p_j(a) i_j(t,a)\,\mathrm{d}a,$$

where $i_j(t,a)$ is an element of a solution of (2.1). The functions $J_j(t)$ represents the forces of infection at each component. It is possible to integrate $i_j(t,a)$ along their characteristic curves:

$$i_j(t,a) = \begin{cases} \sigma_j(a)(\beta_{j1}T_j(t-a)V(t-a) + \beta_{j2}T_j(t-a)J_j(t-a)) & t \geq a, \\ \frac{\sigma_j(a)}{\sigma_j(a-t)} i_{j0}(a-t) \quad t < a, & (j = 1,2). \end{cases} \tag{2.4}$$

We note that the value of $i_j(t,a)$ can be recovered from T_j, V, J_j and the initial value $i_{j0}(\cdot)$. We define a set $\tilde{X}$ by

$$\tilde{X} = \mathbb{R} \times \mathrm{L}^1([0,\infty),\mathbb{R}) \times \mathbb{R} \times \mathrm{L}^1([0,\infty),\mathbb{R}) \times \mathbb{R},$$

with the ordinary product topology.

We take $u = (T_{10}, i_{10}(\cdot), T_{20}, i_{20}(\cdot), V_0) \in \tilde{X}$, and use u as the initial condition. We translate the original differential equation model (2.1) into an integral equation model. First it holds

$$\begin{aligned} \frac{\mathrm{d}T_j}{\mathrm{d}t} =& f_j(T_j) - \beta_{j1}T_j(t)V(t) - \beta_{j2}T_j(t)J_j(t), \quad (j=1,2), \\ J_j(t) =& \int_0^\infty p_j(a) i_j(t,a)\,\mathrm{d}a \\ =& \int_0^t p_j(a)\sigma_j(a)(\beta_{j1}T_j(t-a)V(t-a) + \beta_{j2}T_j(t-a)J_j(t-a))\,\mathrm{d}a \\ &+ \int_t^\infty p_j(a)\frac{\sigma_j(a)}{\sigma_j(a-t)} i_{j0}(a-t)\,\mathrm{d}a, \quad (j=1,2), \\ \frac{\mathrm{d}V}{\mathrm{d}t} =& \int_0^\infty q_1(a) i_1(t,a)\,\mathrm{d}a + \int_0^\infty q_2(a) i_2(t,a)\,\mathrm{d}a - cV(t) \\ =& \int_0^t q_1(a)(\sigma_1(a)(\beta_{11}T_1(t-a)V(t-a) + \beta_{12}T_1(t-a)J_1(t-a)))\,\mathrm{d}a \\ &+ \int_0^t q_2(a)(\sigma_2(a)(\beta_{21}T_2(t-a)V(t-a) + \beta_{22}T_2(t-a)J_2(t-a)))\,\mathrm{d}a \\ &+ \int_t^\infty q_1(a)\frac{\sigma_1(a)}{\sigma_1(a-t)} i_{10}(a-t)\,\mathrm{d}a + \int_t^\infty q_2(a)\frac{\sigma_2(a)}{\sigma_2(a-t)} i_{20}(a-t)\,\mathrm{d}a \\ &- cV(t). \end{aligned} \tag{2.5}$$

Using the method of variation of the constant, we get the following integral equation model:

$$
\begin{aligned}
T_j(t) =& T_{j0} + \int_0^t \Big(f_j(T_j(s)) - \beta_{j1} T_j(s) V(s) - \beta_{j2} T_j(s) J_j(s) \Big)\, \mathrm{d}s, \quad (j = 1, 2), \\
J_j(t) =& \int_0^t p_j(a)\sigma_j(a)(\beta_{j1} T_j(t-a) V(t-a) + \beta_{j2} T_j(t-a) J_j(t-a))\, \mathrm{d}a \\
& + \int_t^\infty p_j(a) \frac{\sigma_j(a)}{\sigma_j(a-t)} i_{j0}(a-t)\, \mathrm{d}a, \quad (j = 1, 2), \\
V(t) =& e^{-ct} V_0 + e^{-ct} \int_0^t e^{cs} \Bigg(\int_0^s q_1(a)(\sigma_1(a)(\beta_{11} T_1(s-a) V(s-a) + \beta_{12} T_1(s-a) J_1(s-a)))\, \mathrm{d}a \\
& + \int_0^s q_2(a)(\sigma_2(a)(\beta_{21} T_2(s-a) V(s-a) + \beta_{22} T_2(s-a) J_2(s-a)))\, \mathrm{d}a \\
& + \int_s^\infty q_1(a) \frac{\sigma_1(a)}{\sigma_1(a-s)} i_{10}(a-s)\, \mathrm{d}a + \int_s^\infty q_2(a) \frac{\sigma_2(a)}{\sigma_2(a-s)} i_{20}(a-s)\, \mathrm{d}a \Bigg)\, \mathrm{d}s.
\end{aligned} \tag{2.6}
$$

Theorem 2.1. *A local solution of* (2.6) *exists uniquely.*

Proof. The proof is similar to that of Proposition 1 in [13]. We use the Banach fixed point theorem in the space

$$
\begin{aligned}
H_\tau =& \{(T_1, T_2, J_1, J_2, V) \in C[0, \tau]^5; \\
& |T_1 - T_{10}| \leqq M, |T_2 - T_{20}| \leqq M, |J_1 - J_{10}| \leqq M, |T_2 - T_{20}| \leqq M, |V - V_0| \leqq M\}
\end{aligned}
$$

where M and τ are positive numbers, τ being chosen sufficiently small later. We can define the integral operator from H to itself by (2.6), if we take τ small enough. Moreover the operator defines the contractive map for small enough τ. Thus we can use the Banach fixed point theorem to complete the proof.

Let $u = (T_{10}, i_{10}(\cdot), T_{20}, i_{20}(\cdot), V_0) \in \tilde{X}$. We denote by $(0, \tau(u))$ the maximum existence interval of the solution u of (2.6) such that $u(0) = u_0$.

The following theorem is proved in Cheng, Dong and Takeuchi [9] (Lemma 1). We note that the equations for i_j and V are common.

Theorem 2.2. *Let* $u_0 = (T_{10}, i_{10}(\cdot), T_{20}, i_{20}(\cdot), V_0)$ *and assume* $T_{j0} > 0$, $i_{j0}(\cdot) \in \mathrm{L}^1([0, \infty), \mathbb{R}_+))$ *and* $V_0 \geq 0$. *Then for* $0 < t < \tau(u)$, *the all components of solution* u *with* $u(0) = u_0$ *take nonnegative values.*

We give a complete metric on $(0, \infty)$ which gives the usual topology on it as in [13] and put

$$
X = (0, \infty) \times \mathrm{L}^1([0, \infty), \mathbb{R}_+) \times (0, \infty) \times \mathrm{L}^1([0, \infty), \mathbb{R}_+) \times \mathbb{R}_+
$$

with the product topology.

By a standard method using differential inequalities, we can show that each solution is bounded as long as it exists.

Lemma 2.3. *The positive orbit of each bounded subset of X is bounded.*

Proof. This lemma is shown by using differential inequalities as in [13]. We consider

$$W_j(t) = T_j(t) + \int_0^\infty i_j(t,a)\,\mathrm{d}a$$

for $i = 1, 2$. Then, by (2.4), we have

$$\begin{aligned} W_j(t) = T_j(t) + &\int_0^t \beta_{j1} T_j(t-a) V(t-a) \sigma_j(a)\,\mathrm{d}a + \int_0^t \beta_{j2} T(t-a) J_j(t-a) \sigma_j(a)\,\mathrm{d}a \\ &+ \int_0^\infty \frac{\sigma_j(b+t)}{\sigma_j(b)} i_{j0}(b)\,\mathrm{d}b. \end{aligned}$$

From this, we can obtain

$$\frac{\mathrm{d}W_j}{\mathrm{d}t} = f_j(T_j(t)) - \int_0^\infty (\delta_j(a) + m_j) i_j(t,a)\,\mathrm{d}a \leqq f_j(T_j(t)) - m_j \int_0^\infty i_j(t,a)\,\mathrm{d}a.$$

Thus, using (2.2), we can show that W_j is bounded, and hence T_j and i_j are also bounded.

By the equation for V in (2.1) and by the fact that i_j is bounded in L^1, it is easy to show that V is bounded, because q_i's are assumed to be essentially bounded.

By Lemma 2.3, each solution to (2.1) is bounded as long as it exists. Then it holds $\tau(u) = \infty$ for each $u \in X$. As in Kajiwara et al. [13], we can define a semiflow on the phase space X corresponding to the solutions of the equation.

Definition 2.4. *We define a semiflow $\{S_t\}_{t\geq 0}$ on X satisfying $S_t(u) = u(t)$ for each $u \in X$, where $u(t)$ is the solution of* (2.1) *with $u(0) = u$.*

As in [13], $\{S_t\}_{t\geq 0}$ is a continuous semiflow on the phase space X.

2.2. Equilibria and reproduction numbers

Following Cheng et al. [9], put

$$M_j = \int_0^\infty p_j(a)\sigma_j(a)\,\mathrm{d}a, \quad N_j = \int_0^\infty q_j(a)\sigma_j(a)\,\mathrm{d}a, \quad (j = 1, 2),$$

and put

$$\begin{aligned} \mathcal{R}_1 &= \mathcal{R}_{11} + \mathcal{R}_{12}, \text{ where } \mathcal{R}_{11} = \frac{\beta_{11} N_1}{c} \overline{T}_1, \ \mathcal{R}_{12} = \beta_{12} M_1 \overline{T}_1, \\ \mathcal{R}_2 &= \mathcal{R}_{21} + \mathcal{R}_{22}, \text{ where } \mathcal{R}_{21} = \frac{\beta_{21} N_2}{c} \overline{T}_2, \ \mathcal{R}_{22} = \beta_{22} M_2 \overline{T}_2, \\ \mathcal{R}_m &= \frac{\mathcal{R}_{11}}{1 - \mathcal{R}_{12}} + \frac{\mathcal{R}_{21}}{1 - \mathcal{R}_{22}} \qquad \text{for } \mathcal{R}_{12} < 1, \mathcal{R}_{22} < 1. \end{aligned}$$

We consider them using the notion of type reproduction numbers. We assume the population is divided into n host-types, and firstly focus on one of the host-types. The infection spreads from one infected individual of the first host-type around other host-types, and finally produces infected individuals of the first host-type. The average number of the secondary infected individual of the first host-type is called the type reproduction number [11, 14].

To consider the next generation matrix and the type reproduction number, we call the class of pathogens, the class of infected cells in compartment 1 and the class of infected cells in compartment 2, 0th-class, first-class and second-class respectively. We denote by t_{pq} $(p, q = 0, 1, 2)$ the average number of pathogens or infected cells directly created in the pth class from qth class at DFE. Put

$$K = \begin{bmatrix} t_{00} & t_{01} & t_{02} \\ t_{10} & t_{11} & t_{12} \\ t_{20} & t_{21} & t_{22} \end{bmatrix}.$$

Then K is the next generation matrix (NGM), and the spectral radius of K is the basic reproductive number R_0 of the model.

Lemma 2.5. *For the elements of K, we have*

$$t_{00} = 0, \quad t_{12} = 0, \quad t_{21} = 0, \quad t_{10}t_{01} = \mathcal{R}_{11}, \quad t_{20}t_{02} = \mathcal{R}_{21}, \quad t_{11} = \mathcal{R}_{12}, \quad t_{22} = \mathcal{R}_{22}.$$

Proof. It is trivial that $t_{00} = 0$, $t_{12} = 0$ and $t_{21} = 0$.

The quantity $t_{10}t_{01}$ is the average number of pathogens newly created in compartment 1 from a pathogen at DFE. At time t, the population size of pathogens which exist at $t = 0$ is written as $V(t) = V_0 e^{-ct}$. We denote the number of pathogens by $\tilde{V}(t)$ which are newly created in compartment 1 until time t. Since $\tilde{V}(0) = 0$, it holds

$$\begin{aligned}\tilde{V}(\infty) = & \int_0^\infty \frac{\mathrm{d}\tilde{V}}{\mathrm{d}t}\,\mathrm{d}t = \beta_{11} \int_0^\infty \int_0^t q_1(a)\sigma_1(a)\overline{T}_1 V(t-a)\,\mathrm{d}a\,\mathrm{d}t \\ =&\beta_{11}\overline{T}_1 \int_0^\infty q_1(a)\sigma_1(a)\,\mathrm{d}a \cdot \int_0^\infty V(t)\,\mathrm{d}t = \frac{\beta_{11}N_1\overline{T}_1}{c}V_0 = \mathcal{R}_{11}V_0,\end{aligned}$$

then $t_{01}t_{10} = \mathcal{R}_{11}$. Similarly, $t_{02}t_{20} = \mathcal{R}_{21}$.

We consider t_{11} and t_{22}. We denote by $i_j(t, 0)$ the age density at $a = 0$ of infected cells created directly from an infected cell in compartment j. By the boundary condition, it holds

$$i_j(t, 0) = \beta_{j2}\overline{T}_j \int_0^\infty p_j(a)i_j(t, a)\mathrm{d}a.$$

Then

$$\begin{aligned}i_j(t, 0) =&\beta_{j2}\overline{T}_j \int_0^t p_j(a)i_j(t, a)\,\mathrm{d}a + \beta_{j2}\overline{T}_j \int_t^\infty p_j(a)i_j(t, a)\,\mathrm{d}a \\ =& \int_0^t \beta_{j2}\overline{T}_j p_j(a)\sigma_j(a)i_j(t-a, 0)\,\mathrm{d}a + \int_t^\infty \beta_{j2}\overline{T}_j p_j(a)\frac{\sigma_j(a)}{\sigma_j(a-t)}i_{j0}(a-t, 0)\,\mathrm{d}a.\end{aligned} \tag{2.7}$$

Put

$$\psi(t) = i_j(t, 0), \quad K(a) = \beta_{j2}\overline{T}_j p_j(a)\sigma_j(a), \quad g(t) = \int_t^\infty \beta_{j2}\overline{T}_j p_j(a)\frac{\sigma_j(a)}{\sigma_j(a-t)}i_{j0}(a-t, 0)\,\mathrm{d}a,$$

then (2.7) is written as

$$\psi(t) = \int_0^t K(a)\psi(t-a)\,\mathrm{d}a + g(t). \tag{2.8}$$

This is a renewal equation with respect to $\psi(t)$, and the basic reproductive number R_0^1 of (2.8) is calculated as

$$R_0^1 = \int_0^\infty K(a)\,\mathrm{d}a.$$

Since t_{11} is equal to R_0^1,

$$t_{11} = \beta_{12}\overline{T}_1 M_1 = \mathcal{R}_{12}.$$

Similarly, $t_{22} = \mathcal{R}_{22}$.

The quantity $\mathcal{R}_m$ is a type reproduction number defined in [11].

Lemma 2.6. *We assume that $\mathcal{R}_{12} < 1$ and $\mathcal{R}_{22} < 1$. Then the type reproduction number T_V of the class of pathogens is well defined, and is equal to $\mathcal{R}_m$.*

Proof. We assume that $\mathcal{R}_{12} < 1$ and $\mathcal{R}_{22} < 1$. Then the average number of pathogens which are newly infected from V class at DFE is as follows:

$$\begin{aligned} t_{10}\sum_{p=0}^{\infty} t_{11}^p t_{01} + t_{20}\sum_{p=0}^{\infty} t_{22}^p t_{02} =& t_{10}t_{01}\sum_{p=0}^{\infty}\mathcal{R}_{22}^p + t_{20}t_{02}\sum_{p=0}^{\infty}\mathcal{R}_{33}^p \\ =& \frac{\mathcal{R}_{11}}{1-\mathcal{R}_{12}} + \frac{\mathcal{R}_{21}}{1-\mathcal{R}_{22}}. \end{aligned}$$

Then it holds $T_V = \mathcal{R}_m$.

We note that the characteristic equation of K is as follows:

$$\Lambda^3 - (\mathcal{R}_{12} + \mathcal{R}_{22})\Lambda^2 - (\mathcal{R}_{21} + \mathcal{R}_{11} - \mathcal{R}_{12}\mathcal{R}_{22})\Lambda + \mathcal{R}_{12}\mathcal{R}_{21} + \mathcal{R}_{22}\mathcal{R}_{11} = 0. \tag{2.9}$$

The quantity R_0 is the largest real solution of (2.9). Since the equation is cubic, it is not easy to calculate R_0. But, it is possible to describe the following threshold condition $R_0 > 1$ (Cheng et al. [9]).

Lemma 2.7. *$R_0 > 1$ is equivalent to the following:*

$$\mathcal{R}_1 > 1 \text{ or } \mathcal{R}_2 > 1 \text{ or } (\mathcal{R}_1 \le 1, \mathcal{R}_2 \le 1, \text{ and } \mathcal{R}_m > 1)$$

Proof. Suppose $R_0 > 1$. First, assume $\mathcal{R}_1 \le 1$, $\mathcal{R}_2 \le 1$. Since $\mathcal{R}_{12} < 1$, $\mathcal{R}_{22} < 1$, $\mathcal{R}_m = T_V$. By [11], $\mathcal{R}_m > 1$.

Conversely, assume $\mathcal{R}_j > 1$. Let K^j be the NGM of the j-compartment model. K^j is nonnegative and $K^j \le K$. Then the Perron-Frobenius eigenvalue of K is equal or greater than that of K^j, then $R_0 > 1$. If $\mathcal{R}_1 \le 1$, $\mathcal{R}_2 \le 1$, $\mathcal{R}_m > 1$, by [11] $R_0 > 1$.

The following proposition is proved in Theorem 6 of [9].

Proposition 2.8. *(Cheng et al. [9]) If $R_0 > 1$, then an interior equilibrium exists.*

We note that if $T_j^* > 0$ $(j = 1, 2)$ are specified for the interior equilibrium, then V^* and i_j^* are uniquely determined as:

$$V^* = \frac{1}{c}(f_1(T_1^*)N_1 + f_2(T_2^*)N_2), \quad i_j^*(a) = f_j(T_j^*)\sigma_j(a).$$

Lemma 2.9. *If $R_0 \le 1$, interior equilibria do not exist.*

Proof. By Theorem 4.4 in Section 4.2, if $R_0 \le 1$, then DFE is GAS and interior equilibria do not exist.

2.3. Arguments for compactness

Theorem 2.10. *The semiflow $\{ S_t \}_{t\geq 0}$ on X is point dissipative.*

Proof. It is shown using differential inequalities as in [13].

Proposition 2.11. *The semiflow $\{ S_t \}_{t\geq 0}$ on X is asymptotically smooth.*

Proof. It is proved by the method in Demasse et al. [15] and Kajiwara et al. [16]. Let B be a forward invariant bounded subset of X. Take an infinite sequence $\{u_p\}_{p=1,2,\ldots} = ((T_1)_p), (i_1)_p, (T_2)_p, (i_2)_p, V_p)_{p=1,2,\ldots}$ in B and an infinite sequence $\{ t^p \}_{p=1,2,\ldots}$ in $\mathbb{R}_+$ with $t^p \to \infty$. For $t \geq 0$, we put $u^p(t) = S(t)u_p$. We show that $\{u^p(t^p)\}$ contains a convergent sequence. Since the bounded subset B is positively invariant, we can assume that subsequences $\{ (T_i)^p(t^p) \}_{p=1,2,\ldots}$, $\{ V^p(t^p) \}_{p=1,2,\ldots}$ $(i = 0, 1)$ of $\mathbb{R}$ are convergent. For $t \geq -t^p$ we define

$$(T_i)_p(t) = (T_i)^p(t + t^p), \quad V_p(t) = V_p(t + t^p).$$

We extend $(T_i)_p(t)$ and $V_p(t)$ $(i = 0, 1)$ for $t \leq -t^p$ continuously such that their maximums do not exceed those in $t \geq -t^p$, their Lipschitz norms are not greater than 1 and their values are zero for sufficiently small t. Since B is forward invariant, they are uniformly bounded. Moreover their Lipschitz norms are also uniformly bounded because they are elements of the solution of (2.6). Using Ascolli-Arzella Theorem for $\mathbb{R}$, we can take a subsequence which is convergent locally uniformly from $\{(T_j)^p\}_{p=1,2,\ldots}$ and $\{V^p\}_{p=1,2\ldots}$. Using the Cantor diagonal process, they contain subsequences of the same indices which converge uniformly on each compact interval, Using the Volterra expression (2.4) for $i_j(t, a)$ $(j = 1, 2)$, and by the standard arguments, we can show that $\{(i_j)_p(t_p, a)\}_{p=1,2,\ldots}$ has convergent subsequence with respect to L^1 topology for $j = 1, 2$. The semiflow $\{S_t\}_{t\geq 0}$ is asymptotically compact on each forward invariant bounded subset, then $\{S_t\}_{t\geq 0}$ is asymptotically smooth.

Lemma 2.12. *The semiflow $\{ S_t \}_{t\geq 0}$ has a compact attractor $\mathcal{A}$ for bounded subsets in X.*

Proof. The semiflow $\{S_t\}_{t\geq 0}$ is asymptotically smooth and each positive orbit of a bounded subset is bounded under $\{S_t\}_{t\geq 0}$. Then by Theorem 2.33 in [12], $\{S_t\}_{t\geq 0}$ has a compact attractor in X.

The following proposition is used to show that if a compact attractor contains only one point, it attracts all points and is locally stable. The proof is contained in [13].

Proposition 2.13. *(Simplified version of Lemma 23.7 in Sell and You [17]) Let X be a compact metric space and $\{ S_t \}_{t\geq 0}$ be a continuous semiflow on X. Assume that a compact attractor of $\{ S_t \}_{t\geq 0}$ consists of one equilibrium x^*. Then the equilibrium x^* is locally stable and is globally asymptotically stable. If there exists a persistence attractor for $\{ S_t\}_{t\geq 0}$, the unique equilibrium in the persistence attractor is globally asymptotically stable by a similar argument.*

3. Persistence

In this section, we always assume that $R_0 > 1$, and present results of the semiflow $\{ S_t \}_{t\geq 0}$.

3.1. Persistence function

The persistence result of the semiflow $\{S_t\}_{1\geq t}$ is necessary for the definition of the Lyapunov functional that will be defined in Section 4.1. We use the method of Smith et al. [12] for persistence.

Define a persistence function ρ for $u = (T_1, i_1(\cdot), T_2, i_2(\cdot), V) \in X$ by

$$\rho(u) = J_1[i_1] + J_2[i_2] + V.$$

Since $\{ u \in X \,|\, \rho(x) = 0 \}$ is not forward invariant in general, put X_0 by

$$X_0 = \{ u \in X \,|\, \rho(S_t(u)) = 0, \ \text{for each } t \geq 0 \}.$$

Theorem 3.1. *The disease free equilibrium (DFE) is globally asymptotically stable in X_0, and the attractor of the semiflow $\{ S_t \}_{t\geq 0}$ restricted to X_0 consists of DFE.*

Proof. For $u \in X_0$, put $S_t(u) = (T_1(t), i_1(t,\cdot), T_2(t), i_2(t,\cdot), V(t))$. The equation of T_j is

$$\frac{\mathrm{d}T_j}{\mathrm{d}t} = f_j(T_j),$$

then $T_j(t) \to \overline{T}_j$. On the other hand, since $V(t) = 0$ and $J_j(t) = J_j[i_j(t,\cdot)] = 0$ for each $t \geq 0$ in (2.4), it holds

$$\int_0^\infty i_j(t,a)\,\mathrm{d}a = \int_t^\infty \frac{\sigma_j(a)}{\sigma_j(a-t)} i_{j0}(a-t)\,\mathrm{d}a, \leq e^{-m_j t} \int_0^\infty i_{j0}(a)\,\mathrm{d}a \leq e^{-m_j t} \|i_{j0}\|_1.$$

Then $i_j(t,\cdot)$ tends to 0 in L^1 topology.

Lemma 3.2. *We assume $\rho(u) > 0$. Then $V(t) > 0$ for some $t > 0$.*

Proof. We note that $T_j(t) > 0$ for each $t \in \mathbb{R}$. We assume $\rho(u) > 0$. If $V > 0$, $V(t) > 0$ for each $t > 0$, and there is nothing to prove. We assume $J_j[i_j] = J_j(0) > 0$. Then $J_j(t) > 0$ for some neighborhood of 0. Then by the $V(t)$ equation of (2.6), $V(t) > 0$ for some $t > 0$.

3.2. Uniform weak ρ-persistence

We show that DFE is uniformly weakly ρ-repelling by contradiction.

Lemma 3.3. *If we take sufficiently small $\varepsilon > 0$, then for a solution $u(t)$ with initial value $(T_1^0, i_1^0, T_2^0, i_2^0, V^0)$ such that*

$$\overline{T}_1 - \varepsilon < T_1^0 < \overline{T}_1 + \varepsilon, \ \overline{T}_2 - \varepsilon < T_2^0 < \overline{T}_2 + \varepsilon, \ 0 < V^0 < \varepsilon,$$

there exists $t_1 > 0$ such that $u(t_1) = (T_1(t_1), i_1(t_1,\cdot), T_2(t_1), i_2(t_1,\cdot), V(t_1))$ does not satisfy at least one inequality of

$$\overline{T}_1 - \varepsilon < T_1(t_1) < \overline{T}_1 + \varepsilon, \ \overline{T}_2 - \varepsilon < T_2(t_1) < \overline{T}_2 + \varepsilon, \ 0 < V(t_1) < \varepsilon. \tag{3.1}$$

Proof. We assume that (3.1) holds for all $t \geq 0$. Then it holds

$$\begin{aligned} J_j(t) &= \int_0^\infty p_j(a) i_j(t,a)\,\mathrm{d}a \geq \int_0^t p_j(a) i_j(t,a)\,\mathrm{d}a = \int_0^t p_j(a) i_j(t-a,0)\sigma_j(a)\,\mathrm{d}a \\ &= \int_0^t \beta_{j1} p_j(a) T_j(t-a) V(t-a)\sigma_j(a)\,\mathrm{d}a + \int_0^t \beta_{j2} p_j(a)\sigma_j(a) T_j(t-a) J_j(t-a)\,\mathrm{d}a \\ &\geq \int_0^t \beta_{j1}(\overline{T}_j - \varepsilon) p_j(a)\sigma_j(a) V(t-a)\,\mathrm{d}a + \int_0^t \beta_{j2}(\overline{T}_j - \varepsilon) p_j(a)\sigma_j(a) J_j(t-a)\,\mathrm{d}a. \end{aligned} \tag{3.2}$$

On the other hand, it holds

$$\begin{aligned} \frac{\mathrm{d}V}{\mathrm{d}t} &\geq \int_0^t \beta_{11} q_1(a)\sigma_1(a) T_1(t-a) V(t-a)\,\mathrm{d}a + \int_0^t \beta_{12} q_1(a)\sigma_1(a) T_1(t-a) J_1(t-a)\,\mathrm{d}a \\ &\quad + \int_0^t \beta_{21} q_2(a)\sigma_2(a) T_2(t-a) V(t-a)\,\mathrm{d}a + \int_0^t \beta_{22} q_2(a)\sigma_2(a) T_2(t-a) J_2(t-a)\,\mathrm{d}a - cV(t) \\ &\geq \int_0^t \beta_{11} q_1(a)\sigma_1(a)(\overline{T}_1 - \varepsilon) V(t-a)\,\mathrm{d}a + \int_0^t \beta_{12} q_1(a)\sigma_1(a)(\overline{T}_1 - \varepsilon) J_1(t-a)\,\mathrm{d}a \\ &\quad + \int_0^t \beta_{21} q_2(a)\sigma_2(a)(\overline{T}_2 - \varepsilon) V(t-a)\,\mathrm{d}a + \int_0^t \beta_{22} q_2(a)\sigma_2(a)(\overline{T}_2 - \varepsilon) J_2(t-a)\,\mathrm{d}a - cV(t). \end{aligned} \tag{3.3}$$

Note that $J_j(t)$ and $V(t)$ are bounded continuous functions. We assume $\lambda > 0$. Let $\hat{J}_j(\lambda)$, $\hat{V}(\lambda)$, $M_j(\lambda)$ and $N_i(\lambda)$ denote the Laplace transformations of $J_j(t)$, $V(t)$, $p_j(a)\sigma_j(a)$ and $q_j(a)\sigma_j(a)$. We note that the limits $\lim_{\lambda\to+0} M_j(\lambda)$ and $\lim_{\lambda\to+0} N_j(\lambda)$. Let M_j and N_j denote these positive values.

We take Laplace transformations of both sides of (3.2).

For $j = 1, 2$, we have

$$\hat{J}_j(\lambda) \geq \beta_{j1} M_j(\lambda)(\overline{T}_j - \varepsilon)\hat{V}(\lambda) + \beta_{j2} M_j(\lambda)(\overline{T}_j - \varepsilon)\hat{J}_j(\lambda). \tag{3.4}$$

First consider the case of $\mathcal{R}_{12} > 1$ or $\mathcal{R}_{22} > 1$. If $\mathcal{R}_{12} = \beta_{12} M_1 \overline{T}_1 > 1$, for sufficiently small $\varepsilon > 0$ it holds

$$\beta_{12} M_1(\overline{T}_1 - \varepsilon) > 1. \tag{3.5}$$

By (3.4), we have

$$\hat{J}_1(\lambda) \geq \beta_{12} M_1(\lambda)(\overline{T}_1 - \varepsilon)\hat{J}_1(\lambda).$$

If the initial value of $V(t)$ is positive, $V(t) > 0$ for each $t > 0$. Then for some $t > 0$, $J_1(t) > 0$, then $\hat{J}_1(\lambda)$ is also positive for $\lambda > 0$. Then it holds

$$1 \geq \beta_{12} M_1(\lambda)(\overline{T}_1 - \varepsilon). \tag{3.6}$$

Then (3.6) contradicts to (3.5). For the case of $\mathcal{R}_{22} > 1$, a contradiction holds using a similar argument.

We consider the case $\mathcal{R}_{12} \leq 1$ and $\mathcal{R}_{22} \leq 1$, and $\mathcal{R}_1 > 1$ or $\mathcal{R}_2 > 1$. We assume that $\mathcal{R}_{12} \leq 1$ and $\mathcal{R}_1 > 1$. The assumption contains the case $\mathcal{R}_{12} = 1$. If $\varepsilon > 0$, then $1 > \beta_{12} M_1(\overline{T}_1 - \varepsilon)$. If we take sufficiently small $\lambda > 0$, it holds

$$1 - \beta_{12} M_1(\lambda)(\overline{T}_1 - \varepsilon) > 0.$$

By (3.4), we have

$$\hat{J}_1(\lambda)\{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)\} \geq \beta_{11}M_1(\lambda)(\overline{T}_1-\varepsilon)\hat{V}(\lambda),$$

and hence we obtain

$$\hat{J}_1(\lambda) \geq \frac{\beta_{11}M_1(\lambda)(\overline{T}_1-\varepsilon)}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}\hat{V}(\lambda). \tag{3.7}$$

We use the following equation obtained by the Laplace transformation of both sides of (3.3):

$$\begin{aligned}\lambda\hat{V}(\lambda)-V(0) \geq &\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)\hat{V}(\lambda)+\beta_{12}N_1(\lambda)(\overline{T}_1-\varepsilon)\hat{J}_1(\lambda)\\ &+\beta_{21}N_2(\lambda)(\overline{T}_2-\varepsilon)\hat{V}(\lambda)+\beta_{22}N_2(\lambda)(\overline{T}_2-\varepsilon)\hat{J}_2(\lambda)-c\hat{V}(\lambda).\end{aligned} \tag{3.8}$$

Thus if we drop the last two nonnegative terms, by (3.7), we have

$$\lambda\hat{V}(\lambda)-V(0) \geq \beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)\hat{V}(\lambda)+\frac{\beta_{11}M_1(\lambda)\beta_{12}N_1(\lambda)(\overline{T}_1-\varepsilon)^2}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}\hat{V}(\lambda)-c\hat{V}(\lambda).$$

Then it holds

$$\left\{\lambda-\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)-\frac{\beta_{11}M_1(\lambda)\beta_{12}N_1(\lambda)(\overline{T}_1-\varepsilon)^2}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}+c\right\}\hat{V}(\lambda) \geq V(0). \tag{3.9}$$

Here the coefficient of $V\hat{(}\lambda)$ is

$$\frac{\lambda-\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)-\lambda\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon))\}+c-c\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}.$$

Since $\mathcal{R}_1 = \mathcal{R}_{11}+\mathcal{R}_{12} > 1$, by taking sufficiently small $\varepsilon > 0$, $\lambda > 0$, we can take the left hand side of (3.9) to be negative. Since the right hand side is positive, a contradiction holds. The case $\mathcal{R}_2 > 1$ is similar.

Last consider the case of $\mathcal{R}_{12} < 1$, $\mathcal{R}_{22} < 1$, $\mathcal{R}_1 \leq 1$ and $\mathcal{R}_2 \leq 1$. We note that $\mathcal{R}_m > 1$, since $R_0 > 1$ is assumed. By taking sufficiently small $\varepsilon > 0$, it holds

$$\beta_{12}M_1(\overline{T}_1-\varepsilon) < 1, \quad \beta_{22}M_2(\overline{T}_2-\varepsilon) < 1.$$

By taking sufficiently small $\lambda > 0$, it holds

$$\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon) < 1, \quad \beta_{22}M_2(\lambda)(\overline{T}_2-\varepsilon) < 1. \tag{3.10}$$

For sufficiently small $\varepsilon > 0$, $\lambda > 0$, by (3.4), it holds

$$\hat{J}_1(\lambda) \geq \frac{\beta_{11}M_1(\lambda)(\overline{T}_1-\varepsilon)}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}\hat{V}(\lambda), \quad \hat{J}_2(\lambda) \geq \frac{\beta_{21}M_2(\lambda)(\overline{T}_2-\varepsilon)}{1-\beta_{22}M_2(\lambda)(\overline{T}_2-\varepsilon)}\hat{V}(\lambda).$$

Substituting these to (3.8),

$$\begin{aligned}\lambda\hat{V}(\lambda)-V(0)\geq&\left\{\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)+\frac{\beta_{12}N_1(\lambda)(\overline{T}_1-\varepsilon)\beta_{11}M_1(\lambda)(\overline{T}_1-\varepsilon))}{1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon)}\right.\\&\left.+\beta_{21}N_2(\lambda)(\overline{T}_2-\varepsilon)+\frac{\beta_{22}N_2(\lambda)(\overline{T}_2-\varepsilon)\beta_{21}M_2(\lambda)(\overline{T}_2-\varepsilon)}{1-\beta_{22}M_2(\lambda)(\overline{T}_2-\varepsilon)}-c\right\}\hat{V}(\lambda)\\=&c\left\{\frac{\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)}{c(1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon))}+\frac{\beta_{21}N_2(\lambda)(\overline{T}_2-\varepsilon)}{c(1-\beta_{22}M_2(\lambda)(\overline{T}_2-\varepsilon))}-1\right\}\hat{V}(\lambda).\end{aligned}$$

Then it holds

$$\left[\lambda-c\left\{\frac{\beta_{11}N_1(\lambda)(\overline{T}_1-\varepsilon)}{c(1-\beta_{12}M_1(\lambda)(\overline{T}_1-\varepsilon))}+\frac{\beta_{21}N_2(\lambda)(\overline{T}_2-\varepsilon)}{c(1-\beta_{22}M_2(\lambda)(\overline{T}_2-\varepsilon))}-1\right\}\right]\hat{V}(\lambda)\geq V(0).$$

Since $\mathcal{R}_m>1$, the coefficient of $\hat{V}(\lambda)$ tends to $-c(\mathcal{R}_m-1)<0$ as $\varepsilon\to+0$ and $\lambda\to+0$. Hence the coefficient is negative for sufficiently small $\lambda>0$ and $\varepsilon>0$. A contradiction occurs because $\hat{V}(\lambda)>0$ and $V(0)\geq 0$.

Lemma 3.4. *If $R_0>1$, the equilibrium DFE is uniformly weakly ρ-repelling in X.*

Proof. Let $u\in X$ satisfy $\rho(u)>0$. It means that pathogens or forces of infection are present. Since $V(t_2)>0$ for some $t_2>0$ by Proposition 3.2, the solution $u(t)$ with $u(0)=u$, if it enters a neighborhood of the DFE, escapes from the neighborhood by Lemma 3.3, provided that the neighborhood is taken sufficiently small. Then the conclusion holds.

Lemma 3.5. *If $R_0>1$, the equilibrium DFE is isolated in X.*

Proof. By Proposition 3.1, DFE is globally asymptotically stable in X_0, that is DFE has an isolated neighborhood in X_0. Moreover, DFE is uniformly weakly ρ-repelling in X by Lemma 3.4. Then DFE is shown to be isolated in X using Lemma 8.18. of Smith and Thieme [12].

Lemma 3.6. *There exists no cycle in X_0 connecting the sets of attractor.*

Proof. It is shown from the fact that DFE is globally asymptotically stable in X_0.

Proposition 3.7. *The semiflow $\{S_t\}_{t\geq 0}$ on X is uniformly weakly ρ-persistent.*

Proof. It follows from Theorem 8.17 in Smith and Thieme [12].

3.3. Uniform ρ-persistence

It is necessary to exclude total solutions $u(t)$ which is $\rho(u(t_0))>0$, $\rho(u(t_1))=0$ and $\rho(u(t_2))>0$ for some $t_0<t_1<t_2$ to get uniformly ρ-persistence from uniformly weakly ρ-persistence by using the method of Section 5 in Smith and Thieme [12].

Let $u(t) = (T_1(t), i_1(t,a), T_2(t), i_2(t,a), V(t))$ a total solution. Then the following equations are satisfied:

$$V(t) = e^{-ct}V(0)$$
$$+ e^{-ct}\int_0^t e^{cs}\left(\int_0^\infty q_1(a)\sigma_1(a)(\beta_{11}T_1(s-a)V(s-a) + \beta_{12}T_1(s-a)J_1(s-a))\,\mathrm{d}a\right.$$
$$\left. + \int_0^\infty q_2(a)\sigma_2(a)(\beta_{21}T_2(s-a)V(s-a) + \beta_{22}T_2(s-a)J_2(s-a))\,\mathrm{d}a\right)\mathrm{d}s, \tag{3.11}$$

$$J_j(t) = \int_0^\infty p_j(a)\sigma_j(a)(\beta_{j1}T_j(t-a)V(t-a) + \beta_{j2}T_j(t-a)J_j(t-a))\,\mathrm{d}a. \quad (j = 1,2) \tag{3.12}$$

Lemma 3.8. *Let $u(t)$ be a total solution. Then if $V(t_1) > 0$, then it holds $V(t) > 0$ for $t > t_1$.*

Proof. By (3.11), if $V(t_1) > 0$ then $V(t) > 0$ for $t > t_1$.

Lemma 3.9. *There exists no total solution such that $\rho(u(r)) > 0$, $\rho(u(t_0)) = 0$, $\rho(u(s)) > 0$ ($r < t_0 < s$).*

Proof. Without loss of generality, we can set $t_0 = 0$. We assume the existence of such a total solution $u(t)$. Since $\rho(u(0)) = 0$ implies $V(0) = 0$, $V(t) = 0$ for $t \leq 0$ by Lemma 3.8. We will show that $J_j(t) = 0$ for $t < 0$ ($j = 1,2$). We note that $q_1(a)$ is continuous, and that $q_1(a_0) > 0$ for some $a_0 > 0$. Suppose $J_1(t_1) > 0$ for some $t_1 < 0$, then the integrand $q_1(a)\sigma_1(a)\beta_{11}T_1(s-a)J_1(s-a)$ is positive at $s = a_0 + t_1$. Then it holds

$$e^{-ct}\int_0^t e^{cs}\left(\int_0^\infty q_1(a)(\sigma_1(a)\beta_{11}T_1(s-a)J_1(s-a)\,\mathrm{d}a\right)\mathrm{d}s > 0.$$

Since the other integrands are nonnegative, $V(t_1) > 0$. Thus $V(t) > 0$ for $t > t_1$. By Lemma 3.8, it contradicts to $V(t) = 0$ for $t \leq 0$. Then for $t < 0$, $J_j(t) = 0$ ($j = 1,2$). By shifting time, we consider the total solution as the solution with initial value at $t = t_2 < 0$. Since initial value of $V(t)$ and $J_j(t)$ are zero, $T_j(t)$ and $V(t) = 0$, $J_j(t) = 0$ is a solution. By the uniqueness of the integral equation, $V(t) = 0$, $J_j(t) = 0$ for $t \geq t_2$. Then there exists no total solution such that $\rho(u(r)) > 0, \rho(u(0)) = 0, \rho(u(s)) > 0$.

From the proof above, we also obtain the following.

Corollary 3.10. *Let $u(t)$ be a total solution. Then $V(t)$ element of $u(t)$ is always positive or always 0. If $V(t) = 0$ identically, $J_j(t)$ is also identically 0.*

Lemma 3.11. *The semiflow $\{S(t)\}_{t\geq 0}$ on X is uniform ρ-persistence.*

Proof. We verify that two conditions (H0), (H1) in Chapter 5 of Smith and Thieme [12] are satisfied. (H0) follows from the existence of compact attractor in Section 2. The condition (H1) follows from Lemma 3.9. Then semiflow $\{S(t)\}_{t\geq 0}$ is uniform ρ-persistence by Theorem 5.2 in [12].

Proposition 3.12. *(Theorem 5.7 in Smith and Thieme [12]) If the semiflow $\{S_t\}$ is uniformly ρ-persistent, a compact attractor $\mathcal{A}$ is decomposed as $\mathcal{A} = \mathcal{A}_0 \cup \mathcal{A}_1 \cup C$ with invariant sets $\mathcal{A}_0$, $\mathcal{A}_1$ and C. $\mathcal{A}_0$ and $\mathcal{A}_1$ are compact, and they satisfy (a), (b) and (c) in [12].*

The set $\mathcal{A}_1$ is called the persistence attractor. We note that the persistence attractor $\mathcal{A}_1$ is a union of total trajectories.

Lemma 3.13. *The V-element and T_j-elements ($j = 1, 2$) of $\mathcal{A}_1$ have positive minimum values.*

Proof. Since persistence attractor is a compact set, V-element and T_j-elements have minimum values. Since T_j can not be 0, the minimum value is positive. We assume that the minimum value of V is zero, and denote by u such element in the phase space. Let $u(t)$ be a total solution with $u(0) = u$. By Corollary 3.10, it holds $\rho(u(t)) = 0$ for each $t \in \mathbb{R}$, then $u \in X_0$. It contradicts to $u \in \mathcal{A}_1$.

We denote by $\tilde{T}_j$ and $\tilde{V}$ the minimum values of T_j, V in $\mathcal{A}_1$ respectively.

Lemma 3.14. *Let $(T_1^*, i_i^*(\cdot), T_2^*, i_2^*(\cdot), V^*)$ be an interior equilibrium. We assume that a total solution $u(t)$ is contained in the persistence attractor $\mathcal{A}_1$. Then there exist M and M' such that $0 < M \le i_j(t,a)/i_j^*(a) \le M'$ for $t \in \mathbb{R}$, $a \in \mathbb{R}_+$.*

Proof. Let $u(t) \in \mathcal{A}_1$, and $i_j(t,a)$ be an element of $u(t)$. Then it holds

$$\begin{aligned}\frac{i_j(t,a)}{i_j^*(a)} =& \frac{i_j(t-a,0)}{i_j^*(0)} = \frac{\beta_{j1}V(t-a)T_j(t-a) + \beta_{j2}T_j(t-a)J_j(t-a)}{\beta_{j1}V^*T_j^* + \beta_{j2}T_j^* + J_j[i_j]} \\ \ge& \frac{\beta_{j1}V(t-a)T_j(t-a)}{\beta_{j1}V^*T_j^* + \beta_{j2}T_j^* + J_j[i_j]} \ge \frac{\beta_{j1}\tilde{V}\tilde{T}_j}{\beta_{j1}V^*T_j^* + \beta_{j2}T_j^* + J_j[i_j]},\end{aligned}$$

where $\tilde{V}$ and $\tilde{T}_j$ are minimum values. We note that

$$J_j[i_j] = \int_0^\infty p(a)i_j^*(a)\,\mathrm{d}a$$

is also a positive value. Then we can take such M. The existence of M' follows from that $u(t)$ is contained in the compact set $\mathcal{A}_1$.

Remark 3.1. *It is not necessary to assume that $i_j(t,a)$ is differentiable with respect to t for the use of Lemma 9.18 in Smith and Thieme [12],*

4. Global stability

4.1. Lyapunov functional for the case $R_0 > 1$

For $R_0 > 1$, we construct a Lyapunov functional, which is defined in $\mathcal{A}_1$, for the system (2.1). By Proposition 2.8, there exists an interior equilibrium. In Section 4.1, we fix one interior equilibrium $u^* = x(T_1^*, i_1^*(\cdot), T_2^*, i_2^*(\cdot), V^*)$. By the V-equation, it holds

$$\int_0^\infty q_1(a)i_1^*(a)\,\mathrm{d}a + \int_0^\infty q_2(a)i_2^*(a)\,\mathrm{d}a - cV^* = 0.$$

Then if we define c_1, c_2 by

$$c_1 = \frac{\int_0^\infty q_1(a)i_1^*(a)\,\mathrm{d}a}{V^*}, \quad c_2 = \frac{\int_0^\infty q_2(a)i_2^*(a)\,\mathrm{d}a}{V^*},$$

then it holds $c_1V^* + c_2V^* = cV^*$, $c = c_1 + c_2$, $c_1 > 0$, $c_2 > 0$. Moreover it holds

$$\int_0^\infty q_1(a)i_1^*(a)\,\mathrm{d}a - c_1V^* = 0, \quad \int_0^\infty q_2(a)i_2^*(a)\,\mathrm{d}a - c_2V^* = 0. \tag{4.1}$$

As in Kajiwara et al. [3], we rewrite the equation of V as

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \left(\int_0^\infty q_1(a)i_1(t,a)\,\mathrm{d}a - c_1V\right) + \left(\int_0^\infty q_2(a)i_2(t,a)\,\mathrm{d}a - c_2V\right).$$

Put, for $j = 1$ or 2,

$$A_j = \int_0^\infty \frac{\beta_{j1}T_j^* q_j(b)\sigma_j(b)}{c_j}\,\mathrm{d}b, \quad B_j = \int_0^\infty \beta_{j2}T_j^* p_j(b)\sigma_j(b)\,\mathrm{d}b.$$

By the boundary condition of (2.1), it holds

$$i_j^*(0) = \beta_{j1}T_j^*V^* + \beta_{j2}T_j^*\int_0^\infty p_j(a)i_j^*(a)\,\mathrm{d}a. \tag{4.2}$$

By substituting

$$i_j^*(a) = i_j^*(0)\sigma_j(a), \quad V^* = (1/c_j)\int_0^\infty q_j(a)i_j^*(a)\,\mathrm{d}a \tag{4.3}$$

obtained from (4.1), we get $A_j + B_j = 1$. Put

$$\psi_1^j(a) = \int_a^\infty \frac{\beta_{j1}T_j^* q_j(b)}{c_j}\sigma_j(b)\sigma_j(a)^{-1}\,\mathrm{d}b, \quad \psi_2^j(a) = \int_a^\infty \beta_{j2}T_j^* p_j(b)\sigma_j(b)\sigma_j(a)^{-1}\,\mathrm{d}b.$$

We note that $\psi_1^j(a)$ and $\psi_2^j(a)$ are integrable on $(0,\infty)$ by the assumption (2.3). It holds $\psi_1^j(0) = A_j$, $\psi_2^j(0) = B_j$. Define functionals W_1^j, $W_{2,1}^j$, and $W_{2,2}^j$ on the persistence attractor $\mathcal{A}_1$ by

$$\begin{aligned} W_1^j(T_j) =& T_j - T_j^* - T_j^*\log\frac{T_j}{T_j^*}, \\ W_{2,1}^j(i_j(\cdot)) =& \int_0^\infty \psi_1^j(a)\left(i_j(a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(a)}{i_j^*(a)}\right)\mathrm{d}a, & (4.4) \\ W_{2,2}^j(i_j(\cdot)) =& \int_0^\infty \psi_2^j(a)\left(i_j(a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(a)}{i_j^*(a)}\right)\mathrm{d}a. & (4.5) \end{aligned}$$

By Proposition 3.14, the right hand sides of (4.4) and (4.5) are well defined. Then

$$W_{2,1}^j(i_j(\cdot)) = \int_0^\infty \psi_1^j(a)\sigma_j(a)\left(i_j(a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(a)}{i_j^*(a)}\right)\sigma_j(a)^{-1}\mathrm{d}a,$$
$$W_{2,2}^j(i_j(\cdot)) = \int_0^\infty \psi_2^j(a)\sigma_j(a)\left(i_j(a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(a)}{i_j^*(a)}\right)\sigma_j(a)^{-1}\mathrm{d}a,$$

and

$$\psi_1^j(a)\sigma_j(a) = \int_a^\infty \frac{\beta_{j1}T_j^* q_j(b)}{c_j}\sigma_j(b)\,\mathrm{d}b, \qquad \psi_2^j(a)\sigma_j(a) = \int_a^\infty \beta_{j2}T_j^* p_j(b)\sigma_j(b)\,\mathrm{d}b.$$

Then it holds

$$\frac{\mathrm{d}}{\mathrm{d}a}(\psi_1^j(a)\sigma_j(a)) = -\frac{\beta_{j1}T_j^* q_j(a)}{c_j}\sigma_j(a), \quad \frac{\mathrm{d}}{\mathrm{d}a}(\psi_2^j(a)\sigma_j(a)) = -\beta_{j2}T_j^* p_j(a)\sigma_j(a).$$

On the other hand, if $u(t)$ is a total solution and $i_j(t,a)$ is an element of $u(t)$,

$$\left(i_j(t,a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(t,a)}{i_j^*(a)}\right)\sigma_j(a)^{-1} = i_j(t-a,0) - i_j^*(0) - i_j^*(0)\log\frac{i_j(t-a,0)}{i_j^*(0)}$$

is a function of $t-a$.

We define a functional $W(u)$ for $u = (T_1, i_1(\cdot), T_2, i_2(\cdot), V) \in \mathcal{A}_1$ as follows:

$$W(u) = V - V^* - V^*\log\frac{V}{V^*} + \sum_{j=1}^{2}\frac{c_j}{\beta_{j1}T_j^*}\left(W_1^j(T_j) + W_{2,1}^j(i_j(\cdot)) + W_{2,2}^j(i_j(\cdot))\right). \tag{4.6}$$

We calculate the derivative of $W(u)$ along solutions in $\mathcal{A}_1$:

$$\begin{aligned}
&\frac{\mathrm{d}W(u(t))}{\mathrm{d}t} &(4.7)\\
&=\sum_{j=1}^{2}\left\{\left(1-\frac{V^*}{V}\right)\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV\right) + \frac{c_j}{\beta_{j1}T_j^*}\left(\frac{\mathrm{d}W_1^j(T_j(t))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,1}^j(i_j(t,\cdot))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,2}^j(i_j(t,\cdot))}{\mathrm{d}t}\right)\right\}\\
&=\sum_{j=1}^{2}\frac{c_j}{\beta_{j1}T_j^*}\left\{\frac{\mathrm{d}W_1^j(T_j(t))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,1}^j(i_j(t,\cdot))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,2}^j(i_j(t,\cdot))}{\mathrm{d}t} + \frac{\beta_{j1}T_j^*}{c_j}\left(1-\frac{V^*}{V}\right)\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV\right)\right\}. &(4.8)
\end{aligned}$$

We calculated each term in (4.8). By (2.1), we have

$$\begin{aligned}
\frac{\mathrm{d}W_1^j(T_j(t))}{\mathrm{d}t} =&\frac{1}{T_j}(T_j - T_j^*)(f_j(T_j) - f_j(T_j^*)) - i_j(t,0) + i_j^*(0) - \beta_{j1}\frac{V^*(T_j^*)^2}{T_j}\\
&+\beta_{j1}VT_j^* - \frac{\beta_{j2}(T_j^*)^2}{T_j}\int_0^\infty p_j(a)i_j^*(a)\,\mathrm{d}a + \beta_{j2}T_j^*\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a,\\
\frac{\mathrm{d}W_{2,1}^j(i_j(t,\cdot))}{\mathrm{d}t} =&A_j\left(i_j(t,0) - i_j^*(0) - i_j^*(0)\log\frac{i_j(t,0)}{i_j^*(0)}\right)\\
&-\int_0^\infty\frac{\beta_{j1}T_j^*q_j(a)}{c_j}\left(i_j(t,a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(t,a)}{i_j^*(a)}\right)\mathrm{d}a.
\end{aligned}$$

Here we use Lemma 9.18 in Smith and Thieme [12]. We can use this Lemma in this case, because the solution $u(t)$ is contained in the persistence attractor. In fact, $i_j(t,\cdot)$ lies in a bounded set in $L^1([0,\infty))$, and we assume that q_j is essentially bounded. Thus the sufficient condition for Fubini's theorem in the proof of Lemma 9.18 holds. Similarly it holds that

$$\begin{aligned}
\frac{\mathrm{d}W_{2,2}^j(i_j(t,\cdot))}{\mathrm{d}t} =&B_j\left(i_j(t,0) - i_j^*(0) - i_j^*(0)\log\frac{i_j(t,0)}{i_j^*(0)}\right)\\
&-\int_0^\infty\beta_{j2}T_j^*p_j(a)\left(i_j(t,a) - i_j^*(a) - i_j^*(a)\log\frac{i_j(t,a)}{i_j^*(a)}\right)\mathrm{d}a,
\end{aligned}$$

$$
\begin{aligned}
&\frac{\beta_{j1}T_j^*}{c_j}\left(1-\frac{V^*}{V}\right)\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV\right)\\
&\qquad =\frac{\beta_{j1}T_j^*}{c_j}\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - \beta_{j1}T_j^*V + \beta_{j1}T_j^*V^* - \frac{\beta_{j1}T_j^*V^*}{c_jV}\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a.
\end{aligned}
$$

If we add these, $i_j(t,0)$-terms and $i_j^*(0)$-terms vanish by $A_j + B_j = 1$.

We gather terms containing β_{j1}. Noting that in (4.2), $i_j^*(0)$ contains both β_{j1} and β_{j2}, we have by (4.3)

$$
\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c_j}\left(-\frac{T_j^*}{T_j} - \log\frac{i_j(t,0)}{i_j^*(0)} + 1 + \log\frac{i_j(t,a)}{i_j^*(a)} + 1 - \frac{V^*i_j(t,a)}{Vi_j^*(a)}\right)\mathrm{d}a. \tag{4.9}
$$

On the other hand, which are obtained by (4.3):

$$
\begin{aligned}
V^* &= \int_0^\infty \frac{q_j(a)i_j^*(a)}{c_j}\,\mathrm{d}a,\\
\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c_j}\mathrm{d}a &= \int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)\sigma_j(a)}{c_j}\mathrm{d}a\cdot i_j^*(0) = A_ji_j^*(0).
\end{aligned}
$$

Using these, it holds

$$
\begin{aligned}
\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c_j}\left(\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)} - 1\right)\mathrm{d}a &= \frac{i_j^*(0)}{i_j(t,0)}\cdot\beta_{j1}T_jV\int_0^\infty \frac{q_j(a)i_j^*(a)}{c_j}\,\mathrm{d}a\cdot\frac{1}{V^*} - A_ji_j^*(0)\\
&= \frac{i_j^*(0)}{i_j(t,0)}\cdot\beta_{j1}T_jV - A_ji_j^*(0),
\end{aligned} \tag{4.10}
$$

which will be used later.

Next we gather terms containing β_{j2}:

$$
\int_0^\infty \beta_{j2}T_j^*p_j(a)i_j^*(a)\left(-\frac{T_j^*}{T_j} - \log\frac{i_j(t,0)}{i_j^*(0)} + 1 + \log\frac{i_j(t,a)}{i_j^*(a)}\right)\mathrm{d}a. \tag{4.11}
$$

We prepare

$$
\int_0^\infty \beta_{j2}T_j^*p_j(a)i_j^*(a)\left(\frac{T_ji_j^*(0)i_j(t,a)}{T_j^*i_j^*(a)i_j(t,0)} - 1\right)\mathrm{d}a = \frac{i_j^*(0)}{i_j(t,0)}\cdot\beta_{j2}T_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}t - B_ji_j^*(0). \tag{4.12}
$$

Adding (4.10) and (4.12), we have

$$
\begin{aligned}
&\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c}\left(\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)} - 1\right)\mathrm{d}a + \int_0^\infty \beta_{j2}T_j^*p_j(a)i_j^*(a)\left(\frac{T_ji_j^*(0)i_j(t,a)}{T_j^*i_j^*(a)i_j(t,0)} - 1\right)\mathrm{d}a\\
&= \frac{i_j^*(0)}{i_j(t,0)}\cdot\beta_{j1}T_jV - A_ji_j^*(0) + \frac{i_j^*(0)}{i_j(t,0)}\cdot\beta_{j2}T_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}t - B_ji_j^*(0)\\
&= \frac{i_j^*(0)}{i_j(t,0)}\left(\beta_{j1}T_jV + \beta_{j2}T_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a\right) - (A_j + B_j)i_j^*(0) = 0.
\end{aligned} \tag{4.13}
$$

Then, by subtracting (4.13) from the sum, we have

$$\begin{aligned}
&\frac{\mathrm{d}W_1^j(u(t))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,1}^j(u(t))}{\mathrm{d}t} + \frac{\mathrm{d}W_{2,2}^j(u(t))}{\mathrm{d}t} + \frac{\beta_{j1}T_j^*}{c_j}\left(1-\frac{V^*}{V}\right)\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV\right)\\
=&\frac{1}{T_j}(T_j - T_j^*)(f_j(T_j) - f_j(T_j^*))\\
&+\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c_j}\left(3-\frac{T_j^*}{T_j}-\frac{V^*i_j(t,a)}{Vi_j^*(a)}-\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)}+\log\frac{i_j(t,a)i_j^*(0)}{i_j^*(a)i_j(t,0)}\right)\mathrm{d}a\\
&+\int_0^\infty \beta_{j2}T_j^*p_j(a)i_j^*(a)\left(2-\frac{T_j^*}{T_j}-\frac{T_ji_j^*(0)i_j(t,a)}{T_j^*i_j^*(a)i_j(t,0)}+\log\frac{i_j^*(0)i_j(t,a)}{i_j^*(a)i_j0,t)}\right)\mathrm{d}a.
\end{aligned}$$

Using these, it holds

$$\begin{aligned}
&\frac{\mathrm{d}W(u(t))}{\mathrm{d}t}\\
=&\sum_{j=1}^2\left[\frac{c_j}{\beta_{j1}T_j^*}\left\{\frac{1}{T_j}(T_j - T_j^*)(f_j(T_j) - f_j(T_j^*))\right.\right.\\
+&\int_0^\infty \frac{\beta_{j1}T_j^*q_j(a)i_j^*(a)}{c_j}\left(3-\frac{T_j^*}{T_j}-\frac{V^*i_j(t,a)}{Vi_j^*(a)}-\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)}+\log\frac{i_j(t,a)i_j^*(0)}{i_j^*(a)i_j(t,0)}\right)\mathrm{d}a\\
+&\left.\left.\int_0^\infty \beta_{j2}T_1^*p_j(a)i_j^*(a)\left(2-\frac{T_j^*}{T_j}-\frac{T_ji_j^*(0)i_j(t,a)}{T_j^*i_j^*(a)i_j(t,0)}+\log\frac{i_j^*(0)i_j(t,a)}{i_j^*(a)i_j(t,0)}\right)\mathrm{d}a\right\}\right].
\end{aligned}\tag{4.14}$$

Then the following theorem holds.

Theorem 4.1. *Let $u(t)$ be a total solution in the persistence attractor $\mathcal{A}_1$. Then the time derivative of $W(u(t))$ is nonpositive. Moreover the maximum invariant subset of the set $\{\, u \in \mathcal{A}_1 \mid \dot{W}(u) = 0 \,\}$ is the singleton set containing the interior equilibrium u^*.*

Proof. By the property of f_j,

$$\frac{1}{T_j}(T_j - T_j^*)(f_j(T_j) - f_j(T_j^*)) \le 0$$

and the left hand side is 0 if and only if $T_j = T_j^*$. It follows

$$\begin{aligned}
3-\frac{T_j^*}{T_j}-\frac{V^*i_j(t,a)}{Vi_j^*(a)}-\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)}+\log\frac{i_j(t,a)i_j^*(0)}{i_j^*(a)i_j(t,0)} &\le 0,\\
2-\frac{T_j^*}{T_j}-\frac{T_ji_j^*(0)i_j(t,a)}{T_j^*i_j^*(a)i_j(t,0)}+\log\frac{i_j^*(0)i_j(t,a)}{i_j^*(a)i_j(t,0)} &\le 0,
\end{aligned}$$

and the left hand sides are zero if and only if each term with minus sign equals 1 by [18].

We denote by μ_j the measure given by $q_j(a)\,\mathrm{d}a$ on $[0,\infty)$. Let $u \in X$ be contained in the maximum invariant subset $\mathcal{M}$ of the set $\{\, u \in \mathcal{A}_1 \mid \dot{W}(u) = 0 \,\}$. Then $\dot{W}(u(t)) = 0$ for each $t \in \mathbb{R}$, where $u(t) = (T_1(t), i_1(t,a), T_2(t), i_2(t,a), V(t))$ is the total solution such that $u(0) = u$. Then, using the measure μ_j, we have

$$3-\frac{T_j^*}{T_j}-\frac{V^*i_j(t,a)}{Vi_j^*(a)}-\frac{T_jVi_j^*(0)}{T_j^*V^*i_j(t,0)}+\log\frac{i_j(t,a)i_j^*(0)}{i_j^*(a)i_j(t,0)} = 0,\ \text{ a.a. } a \in [0,\infty).$$

Then, by $T_j = T_j^*$, it holds

$$\frac{V}{V^*} = \frac{i_j(t,a)}{i_j^*(a)} = \frac{i_j(t,0)}{i_j^*(0)}, \text{ a.a. } a \in [0,\infty).$$

Then for each $t \in \mathbb{R}$

$$i_j(t,a) = \frac{V}{V^*} i_j^*(a), \text{ a.a. } a \in [0,\infty). \tag{4.15}$$

Substitute (4.15) to the equation of V,

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \frac{1}{V^*}\left(\int_0^\infty i_1^*(a)q_1(a)\,\mathrm{d}a + \int_0^\infty i_2^*(a)q_2(a)\,\mathrm{d}a - cV^*\right)V = 0.$$

Then

$$J_j(t) = \int_0^\infty p_j(a) i_j^*(a)\,\mathrm{d}a,$$

is a constant, and we put $J_j^* = J_j(t)$. By the boundary condition,

$$i_j(t,0) = \beta_{j1}T_j(t)V(t) + \beta_{j2}T_j(t)J_j(t) = \beta_{j1}T_j^*V^* + \beta_{j2}T_j^*J_j^*,$$

and hence $i_j(t,0)$ does not depend on t. Then, by the equation that determines the equilibrium $i_j^*(0)$, we have $i_j(t-a,0) = i_j(t,0) = i_j^*(0)$. Then $i_j(t,a) = i_j(t-a,0)\sigma_j(a) = i_j^*(0)\sigma_j(a) = i_j^*(a)$. It follows $\mathcal{M} = \{u^*\}$.

4.2. Lyapunov functional for the case $R_0 \le 1$

Since $R_0 \le 1$, $\mathcal{R}_{12} < 1$ and $\mathcal{R}_{22} < 1$. Then $\mathcal{R}_m$ is well defined, and by [11], it holds that $\mathcal{R}_m \le 1$.

Lemma 4.2. *We can take $c_1 > 0$, $c_2 > 0$, $c_1 + c_2 = c$ with*

$$\frac{\beta_{11}\overline{T}_1N_1}{c_1} + \beta_{12}\overline{T}_1M_1 \le 1, \quad \frac{\beta_{21}\overline{T}_1N_2}{c_2} + \beta_{22}\overline{T}_2N_2 \le 1.$$

Proof. Since $\mathcal{R}_m \le 1$, it holds

$$\frac{(\beta_{11}\overline{T}_1N_1)/c}{1-\beta_{12}\overline{T}_1M_1} + \frac{(\beta_{21}\overline{T}_2N_2)/c}{1-\beta_{22}\overline{T}_2M_2} \le 1,$$

or

$$\frac{\beta_{11}\overline{T}_1N_1}{1-\beta_{12}\overline{T}_1M_1} + \frac{\beta_{21}\overline{T}_2N_2}{1-\beta_{22}\overline{T}_2M_2} \le c.$$

Then it is possible to find c_1 and c_2 with $c_1 > 0$, $c_2 > 0$, $c_1 + c_2 = c$, and

$$\frac{\beta_{11}\overline{T}_1N_1}{1-\beta_{12}\overline{T}_1M_1} \le c_1, \quad \frac{\beta_{21}\overline{T}_2N_2}{1-\beta_{22}\overline{T}_2M_2} \le c_2.$$

That is

$$\frac{\beta_{11}\overline{T}_1N_1}{c_1} + \beta_{12}\overline{T}_1M_1 \le 1, \quad \frac{\beta_{21}\overline{T}_1N_2}{c_2} + \beta_{22}\overline{T}_2M_2 \le 1.$$

We take and fix c_1, c_2 as in Lemma 4.2. For $j = 1$, and 2, put

$$\overline{\psi}_1^j(a) = \int_a^\infty \frac{\beta_{j1}\overline{T}_j q_j(b)}{c_j}\sigma_j(b)\sigma_j(a)^{-1}\,\mathrm{d}b, \quad \overline{\psi}_2^j(a) = \int_a^\infty \beta_{j2}\overline{T}_j p_j(b)\sigma_j(b)\sigma_j(a)^{-1}\,\mathrm{d}b$$
$$\overline{\psi}^j(a) = \overline{\psi}_1^j(a) + \overline{\psi}_2^j(a).$$

Define a functional $\overline{W}(u)$ on the compact attractor $\mathcal{A}$ by

$$\overline{W}(u) = V + \sum_{j=1}^2 \frac{c_j}{\beta_{j1}\overline{T}_j}\left\{T_j - \overline{T}_j + \overline{T}_j \log\frac{T_j}{\overline{T}_j} + \int_0^\infty \overline{\psi}^j(b)i_j(b)\,\mathrm{d}b\right\}.$$

Theorem 4.3. *We assume $R_0 \le 1$. Let $u(t)$ be a total solution contained in the compact attractor $\mathcal{A}$. Then the derivative of $\overline{W}(u(t))$ is less or equal to* 0. *Moreover, the maximum invariant subset contained in the set* $\{\, u \in \mathcal{A} \mid \dot{\overline{W}}(u) = 0 \,\}$ *is the singleton set* $\{\,\mathrm{DFE}\,\}$ *that contains only the disease free equilibrium.*

Proof. It holds

$$\begin{aligned}
&\frac{\mathrm{d}\overline{W}(u(t))}{\mathrm{d}t}\\
=&\frac{\mathrm{d}V}{\mathrm{d}t} + \sum_{j=1}^2 \frac{c_j}{\beta_{j1}\overline{T}_j}\left\{\left(1 - \frac{\overline{T}_j}{T_j}\right)\frac{\mathrm{d}T_j}{\mathrm{d}t} + \frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty \overline{\psi}^j(b)i_j(t,b)\,\mathrm{d}b\right\}\\
=&\sum_{j=1}^2 \int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV + \sum_{j=1}^2 \frac{c_j}{\beta_{j1}\overline{T}_j}\left\{\left(1 - \frac{\overline{T}_j}{T_j}\right)\frac{\mathrm{d}T_j}{\mathrm{d}t} + \frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty \overline{\psi}^j(b)i_j(t,b)\,\mathrm{d}b\right\}\\
=&\sum_{j=1}^2 \frac{c_j}{\beta_{j1}\overline{T}_j}\left\{\left(1 - \frac{\overline{T}_j}{T_j}\right)\frac{\mathrm{d}T_j}{\mathrm{d}t} + \frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty \overline{\psi}^j(b)i_j(t,b)\,\mathrm{d}b + \frac{\beta_{j1}\overline{T}_j}{c_j}\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a - c_jV\right)\right\}.
\end{aligned}$$

We calculate each term in the summation. Then it holds

$$\begin{aligned}
&\left(1 - \frac{\overline{T}_j}{T_j}\right)\frac{\mathrm{d}T_j}{\mathrm{d}t}\\
=&\left(1 - \frac{\overline{T}_j}{T_j}\right)\left(f_j(T_j) - f_j(\overline{T}_j) - \beta_{j1}T_jV - \beta_{j2}T_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a\right)\\
=&\frac{1}{T_j}(T_j - \overline{T}_j)(f_j(T_j) - f_j(\overline{T}_j)) - \beta_{j1}T_jV - \beta_{j2}T_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a\\
&+ \beta_{j1}\overline{T}_jV + \beta_{j2}\overline{T}_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a\\
=&\frac{1}{T_j}(T_j - \overline{T}_j)(f_j(T_j) - f_j(\overline{T}_j)) - i_j(t,0) + \beta_{j1}\overline{T}_jV + \beta_{j2}\overline{T}_j\int_0^\infty p_j(a)i_j(t,a)\,\mathrm{d}a
\end{aligned}$$

Since $i_j(t,a)\sigma_j(a)^{-1}$ is a function of $t-a$, using Lemma 9.18 in Smith and Thieme [12], we have

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty \overline{\psi}^j(a)i_j(t,a)\,\mathrm{d}a =&\frac{\mathrm{d}}{\mathrm{d}t}\int_0^\infty \overline{\psi}^j(a)\sigma_j(a)i_j(t,a)\sigma_j(a)^{-1}\,\mathrm{d}a\\ =&\overline{\psi}^j(0)i_j(t,0)+\int_0^\infty \frac{\mathrm{d}}{\mathrm{d}a}\left\{\overline{\psi}^j(a)\sigma_j(a)\right\} i_j(t,a)\sigma_j(a)^{-1}\,\mathrm{d}a\\ =&\overline{\psi}^j(0)i_j(t,0)-\int_0^\infty \left(\frac{\beta_{j1}\overline{T}_j}{c_j}q_j(a)+\beta_{j2}\overline{T}_jp_j(a)\right)\sigma_j(a)i_j(t,a)\sigma_j(a)^{-1}\,\mathrm{d}a\\ =&\overline{\psi}^j(0)i_j(t,0)-\int_0^\infty \left(\frac{\beta_{j1}\overline{T}_j}{c_j}q_j(a)+\beta_{j2}\overline{T}_jp_j(a)\right)i_j(t,a)\,\mathrm{d}a.\end{aligned}$$

The calculation for the term related with V is as follows:

$$\frac{\beta_{j1}\overline{T}_j}{c_j}\left(\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a-c_jV\right)=\frac{\beta_{j1}\overline{T}_j}{c_j}\int_0^\infty q_j(a)i_j(t,a)\,\mathrm{d}a-\beta_{j1}\overline{T}_jV.$$

Then it holds

$$\frac{\mathrm{d}\overline{W}(u(t))}{\mathrm{d}t}=\sum_{j=1}^2\frac{c_j}{\beta_{j1}\overline{T}_j}\left\{\frac{1}{T_j}(T_j-\overline{T}_j)(f_j(T_j)-f_j(\overline{T}_j))+(\overline{\psi}^j(0)-1)i_j(t,0)\right\}.$$

By Lemma 4.2, for $j=1,2$, it holds

$$\overline{\psi}^j(0)=\frac{\beta_{j1}\overline{T}_jN_j}{c_j}+\beta_{j2}\overline{T}_jM_j\leq 1,$$

and hence

$$\begin{aligned}&\frac{\mathrm{d}\overline{W}(u(t))}{\mathrm{d}t}\\ =&\sum_{j=1}^2\frac{c_j}{\beta_{j1}\overline{T}_j}\left\{\frac{1}{T_j}(T_j-\overline{T}_j)(f_j(T_j)-f_j(\overline{T}_j))+\left(\frac{\beta_{j1}\overline{T}_jN_j}{c_j}+\beta_{j2}\overline{T}_jM_j-1\right)i_j(t,0)\right\}\leq 0.\end{aligned}$$

Then it holds

$$\frac{\mathrm{d}\overline{W}(u(t))}{\mathrm{d}t}\leq 0.$$

Let $u\in X$ be in the maximum invariant subset $\mathcal{M}$ of $\{\,u\in\mathcal{A}\,|\,\dot{\overline{W}}(u)=0\,\}$. Then for each $t\in\mathbb{R}$, $u(t)\in\mathcal{M}$, where $u(t)=(T_1(t),i_1(t,\cdot),T_2(t),i_2(t,\cdot),V(t))$ is the total solution in $\mathcal{A}$ such that $u(0)=u$. Then $T_j(t)=\overline{T}_j$. By the equation of T_j, it holds $f_j(\overline{T}_j)-\beta_{j1}\overline{T}_jV(t)-\beta_{j2}\overline{T}_jJ(t)=0$, and therefore $\beta_{j1}V(t)+\beta_{j2}J_j(t)=0$. Then $V(t)=0$ and $J_j(t)=0$ for $t\in\mathbb{R}$. By the boundary condition, $i_j(t,a)=i_j(t-a,0)\sigma_j(a)=0$ for $t\in\mathbb{R}$ and $a\in[0,\infty)$. Then the maximum invariant subset of the set $\{\,u\in X\,|\,\dot{\overline{W}}(u)=0\,\}$ is the singleton set {DFE}.

4.3. Conclusions

Theorem 4.4. *If $R_0 > 1$, the unique interior equilibrium exists and is globally asymptotically stable in $X \backslash X_0$. The disease free equilibrium is globally asymptotically stable in X_0. If $R_0 \leq 1$, the disease free equilibrium is globally asymptotically stable in X.*

Proof. We assume $R_0 > 1$. By Proposition 3.1, DFE is globally asymptotically stable in X_0. On the other hand, the alpha-limit set of each total solution in the persistence attractor $\mathcal{A}_1$ consists of an interior equilibrium u^* used in Section 4.1 by Theorem 4.1, because $\mathcal{A}_1$ is compact. Then the persistence attractor $\mathcal{A}_1$ is the singleton set consists of the interior equilibrium u^*. Then by Proposition 2.13, the interior equilibrium u^* is globally asymptotically stable in $X \backslash X_0$, and then the interior equilibrium is unique.

We assume $R_0 \leq 1$. Then the alpha-limit set of each total solution of the compact attractor $\mathcal{A}$ is the singleton set which consists of the DFE by Theorem 4.3. Then also by Proposition 2.13, the DFE is globally asymptotically stable in X.

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Conflict of interest

The authors declare there is no conflict of interest.

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