

# Threshold Dynamics for an Epidemic Model with Acute and Chronic Stages

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**Abstract:** In this paper, we formulate a mathematical model of non-autonomous ordinary differential equations describing the dynamics of an epidemic disease with acute and chronic stages. The basic reproduction number  $R_0$  is obtained. It is shown that the disease-free equilibrium is globally asymptotically stable and the disease eventually disappears if  $R_0 < 1$ , and there exists at least one positive periodic solution and the disease is uniformly persistent if  $R_0 > 1$ . Numerical simulations are provided to illustrate analytical results.

**Keywords:** basic reproductive number; periodic solution; global asymptotic stability; uniform persistence

**AMS subject classifications:** 34C12, 34C25, 92D30.

## 1 Introduction

The hepatitis C virus (HCV) was identified in the year 1989. HCV is a small, enveloped, single strand RNA virus that also infects liver cells. The virus is mainly transmitted through transfusion of contaminated blood or blood products. HCV affects an estimated 170 million people worldwide[1]. A large proportion of hepatitis C patients become chronically infected.

Mathematical modelling has been proved to be valuable in understanding the dynamics of HCV infection and many excellent results have been obtained in [2–6]. Martcheva and Castillo-Chavez [4] considered a hepatitis C model with chronic infectious stage in varying population. Yuan and Zhang [5] have extended the model of [4] by modelling of the latent period. Recently, Cai and Li[6] investigated the dynamic behavior of an SEI model with acute and chronic stages based on the reference [5].

In recent years, researchers[7–13] have taken into account oscillations in incidence rates. Much work has been done in analyzing seasonal periodic outbreaks of these infectious diseases considering seasonal variation in the contact rate. However, there are only numerical results and few analysis on periodic solutions. Very little analysis of diseases with chronic stage and periodic contact has been performed. In the current work, we consider the epidemic model with acute and chronic stages. We study the dynamical behavior of the model with periodic transmission rate.

The paper is structured as follows. In Section 2, we present an epidemic model with acute and chronic stages in order to simulate the dynamics of Hepatitis C transmission and define the basic reproduction number  $R_0$ . In Section 3, we obtain the global properties of the proposed model. There is a unique disease-free equilibrium and the disease always dies out if  $R_0 < 1$ ; while the disease uniformly persists in the population and there is at least one positive periodic solution if  $R_0 > 1$ . Numerical simulation are provided to validate analytical results in section 4. In the final section, we give the brief conclusions.

## 2 Model formulation

In our model, we divide the population in researched area into four classes:  $S$ —susceptible,  $I$ —infected with acute stage,  $V$ —infected with chronic stage,  $R$ —recovered.

The basic demographic assumption is:

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- $\Lambda$  is the recruitment rate of susceptible individuals into the population by birth or by immigration and the death rate is  $\mu$ .
- Only the acute and chronic stages are differentiated. Patients with either acute or chronic infections are capable of transmitting the disease. Once a person contacts with a infectious individual he must be infected.  $\beta_1(t)$  and  $\beta_2(t)$  are the transmission rate coefficient of the acute infective and the chronic infective, respectively.
- $k$  is the rate of progression to chronic stage from the acute stage.
- $\alpha_1$  and  $\alpha_2$  are the disease-induced death rate of the acute infective and the chronic infective, respectively.
- $\gamma_1$  and  $\gamma_2$  are the recovery rate of the acute stage and the chronic state.
- We assume that  $\beta_i(t)(i = 1, 2)$  is periodic positive continuous functions in  $t$  with period  $\omega$  for some  $\omega > 0$ , other parameters are positive constant.

Under the above assumptions, we construct the following differential equations model:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \beta_1(t)SI - \beta_2(t)SV - \mu S, \\ \frac{dI}{dt} = \beta_1(t)SI + \beta_2(t)SV - (\mu + k + \alpha_1 + \gamma_1)I, \\ \frac{dV}{dt} = kI - (\mu + \alpha_2 + \gamma_2)V, \\ \frac{dR}{dt} = \gamma_1I + \gamma_2V - \mu R, \\ N = S + I + V + R, \end{cases} \tag{1}$$

with initial condition  $(S(0), I(0), V(0), R(0)) = (S_0, I_0, V_0, R_0) \in \mathbb{R}_+^4$ .

It is obvious that any solution of system (1) with nonnegative initial values is unique and nonnegative.

**Lemma 1** System (1) has a unique and bounded solution with the initial value

$$(S_0, I_0, V_0, R_0) \in X := \mathbb{R}_+^4.$$

Further, the compact set

$$G := \{(S, I, V, R) \in X : S + I + V + R \leq \Lambda/\mu\}$$

is positively invariant set, which attracts all positive orbits in  $X$ .

**Proof.** From (1), the total population  $N(t)$  satisfies the following equation:

$$\frac{dN}{dt} = \Lambda - \alpha_1 I - \alpha_2 V - \mu N \leq \Lambda - \mu N.$$

It is easy to see that the linear differential equation  $\frac{dN}{dt} = \Lambda - \mu N$  has a unique equilibrium  $N_0 = \Lambda/\mu$ , which is globally asymptotically stable. The comparison principle [14, Theorem B.1] implies that  $N(t)$  is ultimately bounded, and hence, the solutions of system (1) exist globally on the interval  $[0, \infty)$ .

And  $\frac{dN}{dt} \leq \Lambda - \mu N \leq 0$ , if  $N(t) \geq \frac{\Lambda}{\mu}$ , which implies that  $G$  is positively invariant with respect to system (1). This proves the lemma. ■

Let  $(\mathbb{R}^n, \mathbb{R}_+^n)$  be the standard ordered  $n$ -dimensional Euclidean space with a norm  $\| \cdot \|$ . For  $u, v \in \mathbb{R}^n$ , we denote  $u \geq v$ , if  $u - v \in \mathbb{R}_+^n$ ;  $u > v$ , if  $u - v \in \mathbb{R}_+^n \setminus \{0\}$ ; and  $u \gg v$ , if  $u - v \in \text{Int}(\mathbb{R}_+^n)$ .

Let  $A(t)$  be a continuous, cooperative, irreducible, and periodic  $n \times n$  matrix function with period  $\omega > 0$ ,  $\Phi_A(t)$  be the fundamental solution matrix of the linear ordinary differential equation

$$\dot{x} = A(t)x.$$

Let  $r(\Phi_A(\omega))$  be the spectral radius of  $\Phi_A(\omega)$ . By Perron-Frobenius theorem,  $r(\Phi_A(\omega))$  is the principle eigenvalue of  $\Phi_A(\omega)$ , in the sense that it is simple and admits an eigenvector  $v^* \gg 0$ . We present the following lemma from [15] for our discussion in the next section.

**Lemma 2** Let  $\rho = \frac{1}{\omega} \ln r(\Phi_A(\omega))$ . Then there exists a positive  $\omega$ -periodic function  $v(t)$  such that  $e^{\rho t}v(t)$  is a solution of  $\dot{x} = A(t)x$ .

It is easy to see that system (1) has exactly one disease-free equilibrium  $P_0(S_0, I_0, V_0, R_0) = (\Lambda/\mu, 0, 0, 0)$ . In what follows, we introduce the basic reproduction number  $R_0$  for system (1) according to the general procedure presented in [16]. We obtain

$$F(t) = \begin{pmatrix} \beta_1(t)S_0 & \beta_2(t)S_0 \\ 0 & 0 \end{pmatrix},$$

and

$$V(t) = \begin{pmatrix} \mu + k + \alpha_1 + \gamma_1 & 0 \\ -k & \mu + \alpha_2 + \gamma_2 \end{pmatrix}.$$

Assume  $Y(t, s), t \geq s$ , is the matrix solution of the linear  $\omega$ -periodic system

$$\frac{dy}{dt} = -V(t)y. \tag{2}$$

That is, for each  $s \in \mathbb{R}$ , the  $2 \times 2$  matrix  $Y(t, s)$  satisfies

$$\frac{d}{dt}Y(t, s) = -V(t)Y(t, s), \quad \forall t \geq s, \quad Y(s, s) = I,$$

where  $I$  is the  $2 \times 2$  identity matrix. Thus, the monodromy matrix  $\Phi_{-V}(t)$  of (2) is equal to  $Y(t, 0), t \geq 0$ .

Let  $C_\omega$  be the ordered Banach space of all  $\omega$ -periodic functions from  $\mathbb{R}$  to  $\mathbb{R}^2$ , which is equipped with the maximum norm  $\|\cdot\|$  and the positive cone  $C_\omega^+ := \{\phi \in C_\omega : \phi(t) \geq 0, \forall t \in \mathbb{R}\}$ . Then we can define a linear operator  $L : C_\omega \rightarrow C_\omega$  by

$$(L\phi)(t) = \int_0^\infty Y(t, t-a)F(t-a)\phi(t-a)da, \quad \forall t \in \mathbb{R}, \quad \phi \in C_\omega. \tag{3}$$

Following [16], we call  $L$  the next infection operator, and define the basic reproduction number as  $R_0 := r(L)$ , the spectral radius of  $L$ .

It is easy to verify that system (1) satisfies assumptions (A1)-(A7) in [16]. Thus, we have the following result, which will be used in the proof of our main result in section 3.

**Lemma 3** ([16, Theorem 2.2]) *The following statements are valid:*

- (i)  $R_0 = 1$  if and only if  $r(\Phi_{F-V}(\omega)) = 1$ .
- (ii)  $R_0 > 1$  if and only if  $r(\Phi_{F-V}(\omega)) > 1$ .
- (iii)  $R_0 < 1$  if and only if  $r(\Phi_{F-V}(\omega)) < 1$ .

Thus, the disease-free equilibrium  $P_0$  is locally asymptotically stable if  $R_0 < 1$ , and unstable if  $R_0 > 1$ .

### 3 Threshold dynamics

In this section, we will use the method developed in [16] to analyze the threshold dynamics of system (1).

**Theorem 4** *If the basic reproduction number  $R_0 < 1$ , then the unique disease-free equilibrium  $P_0(\Lambda/\mu, 0, 0, 0)$  is globally asymptotically stable and if  $R_0 > 1$ , it is unstable.*

**Proof.** From Lemma 3, we know that if  $R_0 < 1$ , then  $P_0$  is locally asymptotically stable and if  $R_0 > 1$ ,  $P_0$  is unstable. We now prove the global attractivity of  $P_0$  for  $R_0 < 1$ .

Assume that  $R_0 < 1$ , again from Lemma 3, we have  $r(\Phi_{F-V}(\omega)) < 1$ . From (1), we know that

$$\begin{cases} \frac{dI}{dt} \leq \beta_1(t)S_0I + \beta_2(t)S_0V - (\mu + k + \alpha_1 + \gamma_1)I, \\ \frac{dV}{dt} = kI - (\mu + \alpha_2 + \gamma_2)V, \end{cases} \tag{4}$$

for  $t \geq 0$ . Consider the following auxiliary system

$$\begin{cases} \frac{d\bar{I}}{dt} = \beta_1(t)S_0\bar{I} + \beta_2(t)S_0\bar{V} - (\mu + k + \alpha_1 + \gamma_1)\bar{I}, \\ \frac{d\bar{V}}{dt} = k\bar{I} - (\mu + \alpha_2 + \gamma_2)\bar{V}, \end{cases} \tag{5}$$

By Lemma 2 and the standard comparison principle, there exists a positive,  $\omega$ -periodic function  $\bar{h}(t)$  such that  $J(t) \leq e^{\theta t}\bar{h}(t)$  where  $\theta = \frac{1}{\omega} \ln r(\Phi_{F-V}(\omega)) < 0$  and  $J(t) = (I(t), V(t))^T$ . Therefore, we get  $I(t) \rightarrow 0$  and  $V(t) \rightarrow 0$  as  $t \rightarrow +\infty$ . By the theory of asymptotic autonomous systems [17, Theorem 1.2], it then follows that  $S(t) \rightarrow S_0$  and  $R(t) \rightarrow 0$  as  $t \rightarrow +\infty$ . Therefore, the disease-free equilibrium  $P_0(\Lambda/\mu, 0, 0, 0)$  is globally asymptotically stable. This completes the proof. ■

**Theorem 5** *If the basic reproduction number  $R_0 > 1$ , then the disease is uniformly persistent, i.e., there exists a  $\delta > 0$  such that any solution  $(S(t), I(t), V(t), R(t))$  of system (1) with initial value  $(S^0, I^0, V^0, R^0) \in \{(S, I, E, R) \in X : I > 0, V > 0, \}$  satisfies*

$$\liminf_{t \rightarrow +\infty} I(t) \geq \delta, \text{ and } \liminf_{t \rightarrow +\infty} V(t) \geq \delta,$$

and system (1) admits at least one positive periodic solution.

**Proof.**

Define

$$X_0 := \{(S, I, V, R) \in X : I > 0, V > 0\}, \quad \partial X_0 := X \setminus X_0.$$

Let  $P: X \rightarrow X$  be the Poincaré map associated with system (1), i.e.,

$$P(x^0) = u(\omega, x^0), \quad \forall x^0 \in X,$$

where  $u(t, x^0)$  is the unique solution of system (1) with  $u(0, x^0) = x^0$ . It is easy to see that

$$P^m(S^0, I^0, V^0, R^0) = u(m\omega, (S^0, I^0, V^0, R^0)), \quad \forall m \geq 0.$$

We now prove that  $P$  is uniformly persistent with respect to  $(X_0, \partial X_0)$ . It is easy to show that  $X$  and  $X_0$  are positively invariant,  $\partial X_0$  is a relatively closed set in  $X$ , and  $P$  is point dissipative from Lemma 1.

Set

$$M_\partial := \{(S^0, I^0, V^0, R^0) \in \partial X_0 : P^m(S^0, I^0, V^0, R^0) \in \partial X_0, \forall m \geq 0\}.$$

We now show that

$$M_\partial = \{(S, 0, 0, R) \in X : S \geq 0, R \geq 0\}. \tag{6}$$

In fact, it is obvious that

$$\{(S, 0, 0, R) \in X : S \geq 0, R \geq 0\} \subseteq M_\partial. \tag{7}$$

For any  $(S^0, I^0, V^0, R^0) \in \partial X_0 \setminus \{(S, 0, 0, R) : S \geq 0, R \geq 0\}$ , if  $I^0 = 0, V^0 > 0$ , it is clear that  $S(t) > 0$  for all  $t > 0$ , from the third equation of (1), we have

$$V(t) = [V^0 + \int_0^t kI(t)e^{(\mu+\alpha_2+\gamma_2)t} dt] \times e^{-(\mu+\alpha_2+\gamma_2)t} > 0,$$

for any  $t > 0$ .

For the case  $V^0 = 0, I^0 > 0$ , then  $S(t) > 0$  for any  $t > 0, \frac{dV}{dt}(0) = kI^0 > 0$ . Therefore,  $(S(t), I(t), V(t), R(t)) \notin X_0$  for  $t > 0$  sufficiently small. That is to say, for any  $(S^0, I^0, V^0, R^0) \notin \{(S, 0, 0, R) \in X : S \geq 0, R \geq 0\}, (S^0, I^0, V^0, R^0) \notin M_\partial$ . This implies that

$$M_\partial \subseteq \{(S, 0, 0, R) \in X : S \geq 0, R \geq 0\}.$$

Clearly, there is exactly one fixed point  $P_0 = (\Lambda/\mu, 0, 0, 0)$  of  $P$  in  $M_\partial$ . If  $(S, I, V, R)$  is a solution from  $M_\partial$ , then from (1), it follows that  $\lim_{t \rightarrow \infty} (S(t), I(t), V(t), R(t)) = P_0$ .

Next, we prove that  $P$  is uniformly persistent with respect to  $(X_0, \partial X)$ . In the case where  $R_0 > 1$ , we have the following claims:

**Claim:** There exists a  $\sigma^* > 0$ , such that for any  $(S^0, I^0, V^0, R^0) \in X_0$  with  $\|(S^0, I^0, V^0, R^0) - P_0\| \leq \sigma^*$ , we have

$$\limsup_{m \rightarrow \infty} d(P^m(S^0, I^0, V^0, R^0), P_0) \geq \sigma^*. \tag{8}$$

Suppose, by contradiction, that

$$\limsup_{m \rightarrow \infty} d(P^m(S^0, I^0, V^0, R^0), P_0) < \sigma^*$$

for some  $(S^0, I^0, V^0, R^0) \in X_0$ . Without loss of generality, we assume that  $d(P^m(S^0, I^0, V^0, R^0), P_0) < \sigma^*$ , for all  $m \geq 0$ . It follows that

$$\|u(t, P^m(S^0, I^0, V^0, R^0)) - u(t, P_0)\| < \sigma, \forall m \geq 0, \forall t \in [0, \omega].$$

For any  $t \geq 0$ , let  $t = m\omega + t'$ , where  $t' \in [0, \omega)$ , and  $m$  is the largest integer less than or equal to  $\frac{t}{\omega}$ . Therefore, we have

$$\begin{aligned} & \|u(t, (S^0, I^0, V^0, R^0)) - u(t, P_0)\| \\ &= \|u(t', P^m(S^0, I^0, V^0, R^0)) - u(t', P_0)\| < \sigma, \forall t \geq 0. \end{aligned}$$

Note that  $(S(t), I(t), V(t), R(t)) = u(t, (S^0, I^0, V^0, R^0))$ . It then follows that  $\frac{\Lambda}{\mu} - \sigma \leq S(t) \leq \frac{\Lambda}{\mu} + \sigma, 0 \leq I(t) \leq \sigma, 0 \leq V(t) \leq \sigma, 0 \leq R(t) \leq \sigma$ . Thus, from system (1) we obtain

$$\begin{cases} \frac{dI}{dt} \geq \beta_1(t)(\frac{\Lambda}{\mu} - \sigma)I + \beta_2(t)(\frac{\Lambda}{\mu} - \sigma)V - (\mu + k + \alpha_1 + \gamma_1)I, \\ \frac{dV}{dt} = kI - (\mu + \alpha_2 + \gamma_2)V. \end{cases} \tag{9}$$

By Lemma 3, we know that  $r(\Phi_{F-V}(\omega)) > 1$ , then we can choose  $\sigma > 0$  small enough such that  $r(\Phi_{F_\sigma-V}(\omega)) > 1$ , where

$$F_\sigma(t) = \begin{pmatrix} \beta_1(t)(S_0 - \sigma) & \beta_2(t)(S_0 - \sigma) \\ 0 & 0 \end{pmatrix}.$$

Again by Lemma 2 and the standard comparison principle, we know that there exists a positive,  $\omega$ -periodic function  $v_2(t)$  such that  $J(t) \leq v_2(t)e^{p_2 t}$  where  $J(t) = (I(t), V(t))^T$  and  $p_2 = \frac{1}{\omega} \ln r(\Phi_{F_\sigma-V}(\omega)) > 0$ , which implies that  $I(t) \rightarrow \infty$  and  $V(t) \rightarrow \infty$  as  $t \rightarrow \infty$ . This leads to a contradiction.

The above claim implies that  $P_0(\Lambda/\mu, 0, 0, 0)$  is isolated invariant set in  $X$  and  $W^s(P_0) \cap X_0 = \emptyset$ . Note that every orbit in  $M_\partial$  approaches to  $P_0$ , and  $P_0$  is acyclic in  $M_\partial$ . By [18, Theorem 1.3.1], we obtain that  $P$  is uniformly persistent with respect to  $(X_0, \partial X_0)$ . It follows from [18, Theorem 3.1.1], the solutions of system (1) are uniformly persistent with respect to  $(X_0, \partial X_0)$ , that is, there exists a  $\delta > 0$  such that any solution  $(S(t), I(t), V(t), R(t))$  of system (1) with initial value  $(S^0, I^0, I^0, R^0, V(t)) \in X_0$  satisfies  $\liminf_{t \rightarrow +\infty} E(t) \geq \delta$  and  $\liminf_{t \rightarrow +\infty} I(t) \geq \delta$ .

Furthermore, [18, theorem 1.3.6] implies that  $P$  has a fixed point  $(S^*(0), I^*(0), V^*(0), R^*(0)) \in X_0$ . Then  $S^*(0) \geq 0, I^*(0) > 0, V^*(0) > 0$ , and  $R^*(0) \geq 0$ . We further prove that  $S^*(0) > 0$  and  $R^*(0) > 0$ . Suppose not, if  $S^*(0) = 0$ , then we obtain

$$\begin{aligned} S^*(t) &= \exp\left(\int_0^t (\mu + \beta_1(\xi)I(\xi)/N(\xi) + p) d\xi\right) \times \\ &\quad \Lambda \int_0^t \exp\left(\int_0^\xi (\mu + \beta_1(\zeta)I(\zeta)/N(\zeta) + p) d\zeta\right) d\xi > 0, \forall t > 0. \end{aligned}$$

The periodicity of  $S^*(t)$  implies  $S^*(n\omega) = S^*(0) = 0$ , it is a contradiction. Similarly, we can prove that  $R^*(0) > 0$ . Therefore,  $(S^*(t), I^*(t), V^*(t), R^*(t))$  is a positive  $\omega$ -periodic solution of system (1). ■

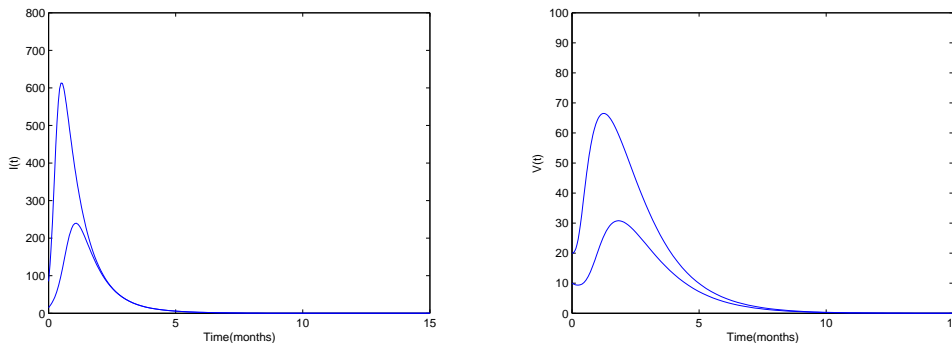


Figure 1: The global asymptotic stability of the disease-free equilibrium  $P_0$  when  $R_0 = 0.8672$ .

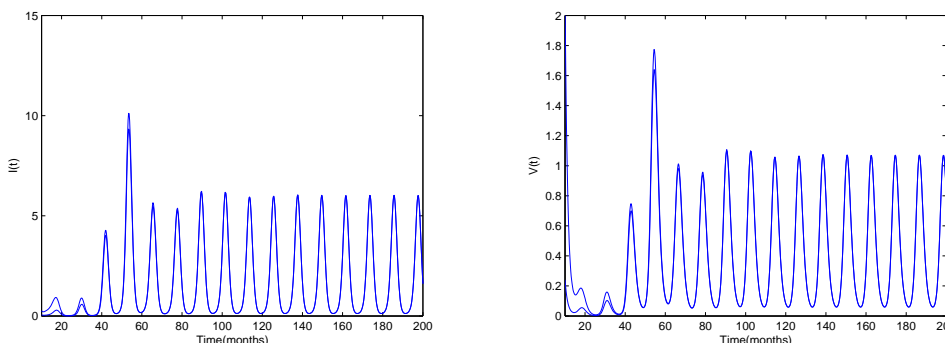


Figure 2: The existence of a periodic solution when  $R_0 = 26.23$ .

### 4 Numerical simulations

From our theoretical results we see that  $R_0$  is a threshold parameter to determine whether or not the disease persists in the population. Our numerical simulations in this section will demonstrate the asymptotical behavior of (1) in different cases.

The model parameters with time unit as 1 month are taken as:  $\Lambda = 10, \mu = 1/12, k = 1/6, \alpha_1 = \alpha_2 = 0.5, \gamma_1 = 0.5, \gamma_2 = 1/6, \beta_1(t) = a_0(1.1 + \sin \frac{\pi t}{6})$  and  $\beta_2(t) = b_0(1.1 + \sin \frac{\pi t}{6})$ .

$a_0$  and  $b_0$  are used in the simulation to demonstrate the asymptotical behavior of the solutions. For the small  $a_0 = 0.008$  and  $b_0 = 0.005$ , numerical simulation gives the basic reproductive number  $R_0 = 0.8672$ . The simulation shows that the disease dies out (see Figure 1). The simulation results are the same as what we got in Theorem 3.1.

For the large  $a_0 = 0.01$  and  $b_0 = 0.008$ , numerical simulation gives the basic reproductive number  $R_0 = 26.23$ , then Theorem 3.2 indicate that system 1 has one positive periodic solution and the disease keeps persistent in the population. Figure 2 confirm this conclusion, and the simulation suggests that in the case where  $R_0 > 1$ , every solution with nontrivial initial data is asymptotic to a periodic solution (see Figure (2)). From the numerical point of view, there exists a unique global attractive positive periodic solution. It is worth studying the uniqueness and stability of positive periodic solution of model (1) in the case where  $R_0 > 1$ . We leave these challenging problems for further investigation.

### 5 Conclusions

In this paper, we have formulated a compartmental epidemic model with acute and chronic stages. The dynamics of the disease transmission are analyzed, and the basic reproductive number  $R_0$  is determined. It is proved that  $R_0$  is the threshold to distinguish the disease extinction or persistence. It shows that the disease-free equilibrium is globally asymptotically stable if  $R_0 < 1$ , while the disease persists if  $R_0 > 1$  and the system has one positive periodic solution.

Numerical simulations have been done. The simulation result illustrate the analytical results. Furthermore, numerical simulations indicate that there may be a unique positive periodic solution which is globally asymptotically stable, which will be another further work.

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