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Research article

A compartmental model for the spread of Nipah virus in a periodic environment

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Abstract: Nipah virus (NiV) is a zoonotic virus that causes outbreaks of fatal disease in humans. Fruit bat, also known as the flying fox, is the animal host reservoir for NiV. It is known to cause illness in pigs, which are considered an intermediate host. In this paper, we propose a model for NiV disease transmission taking into account all human-to-host animal transmission as well as the loss of immunity in those who have recovered. Furthermore, we take into consideration seasonal effects such as varying transmission rate from bats and birth rate of bats. We studied the existence and uniqueness of a disease-free ω-periodic solution and later deals with the basic reproduction number and stability analysis. To support the analytical results we provide numerical examples and assess the effect of parameter changes on disease dynamics, which might help to understand how to avoid a yearly periodic recurrence of the disease.

Keywords: Nipah virus; periodic compartmental model; loss of immunity; periodic solution
Mathematics Subject Classification: 34A99, 92D30

1. Introduction

With about 60% of human infections originating from animals [1], zoonotic diseases pose one of the greatest health threats as shown by the recent outbreaks of severe acute respiratory syndrome coronavirus (SARS-CoV-2), Ebola virus, Middle East respiratory syndrome coronavirus (MERS-CoV). One of the most menacing emerging zoonotic diseases, Nipah virus (NiV) disease is highly infectious and spreads in the community via infected animals, infected people or contaminated food and objects, causing severe neurological and respiratory diseases with high mortality rates in some instances [2]. Nipah virus, whose animal host reservoir is the fruit bat, also known as the flying

fox, causes lethal encephalitis in humans and has recently been reported in Malaysia, Bangladesh, Singapore and India [3–5].

Since the outbreak, very few mathematical models have been available for studies of NiV disease. A basic SIR (susceptible–infected–recovered) model with optimal control was presented by Biswas in [6]. A dynamic model of NiV infections with variable size population and two control strategies was formulated in [7]. Incorporating quarantine of infectious individuals, Mondal et al. [8] analyzed an SEIR (susceptible–exposed–infected–recovered) model where birth and death rates were assumed unequal. Shah et al. [9] presented a two-layered model for humans and bats. Agarwal and Singh [10] presented a mathematical model of seven compartments, including virus dynamics, flying foxes and humans. They considered that this disease has no recovered individuals. Considering no bat population and the role of deceased individuals who died from Nipah fever, Zewdie and Gakkhar [11, 12] concentrated on an optimal control study of some adjustable parameters for a coupled pig-human NiV disease model. In [13], the authors examined a compartmental model that incorporated bats, humans, and an intermediate host. Recently, [14] proposed a numerical model of NiV that focuses on tracking the influence of the fractional order derivative, considering transmission from dead bodies. In [15], the authors developed a mathematical model comprising a nonlinear fractional-order system of differential equations to examine the dynamics and optimal control strategies for NiV using the Caputo derivative. Similarly, Baleanu et al. [16] considered a fractional order model that incorporated the potential transmission pathway of unsafe contact with an infectious corpse. Barua et al. [17] proposed a three-layered model in which bat and pig transmission was also considered.

The above literature review demonstrates that despite the threat posed by NiV disease, so far, little research has been done regarding its transmission. Furthermore, most of the models did not consider all important characteristics of the disease and several studies focused on optimal control problems rather than the dynamics of the proposed models. Another important aspect of transmission, which has not been considered in models for NiV transmission, is the periodicity of the environment. The only location where spillover events can be reliably seen annually is Bangladesh, where seasonal patterns of consuming raw date-palm-sap in the "Nipah belt" correlate with outbreak timing and distribution (November to April) [18]. Data from a six-year multidisciplinary research conducted on bats reveal that one of the causes of outbreaks in Pteropus bats is driven by a gradual loss of immunity, culminating in periods of interepizootic activity that last for several years [19]. Furthermore, the bats' reproduction also shows periodicity as studies reported that the bats' mating season occurs from July to October and mothers give birth to one or two newborns from February to March [20].

Motivated by the above, in the present work we propose a model for Nipah virus disease transmission in a periodic environment in which all possible ways of transmission among humans, the reservoir species of bats and the intermediate host pigs are considered. To our knowledge, this is the first paper considering Nipah virus disease spread taking into consideration the seasonal nature of disease transmission and reproduction. Several studies have been established for the mathematical modeling of epidemics considering a seasonal environment since the generalization of the basic reproduction number for periodic models was first defined by Bacaër and Guernaoui [21] as the spectral radius of an integral operator acting on the space of continuous periodic functions. The proof of the existence and stability of the disease-free ω-periodic solution was first established by Wang and Zhao [22]. The persistence of a class of seasonally forced epidemiological models is investigated by

Rebelo et al. [23]. The methods established in the above papers have since been improved and applied to study the spread of many infectious diseases; see, e.g., [24–32]. However, to the authors' knowledge, no model has studied the spread of an infectious disease considering a transmission chain consisting of three species. Hence, although we follow the general approach established in the above-mentioned studies and applied in many modeling works since then, in the present work we further improve this theory by adjusting the general methods to our three-species system. By doing so, we study the existence and uniqueness of a disease-free ω-periodic solution in Section 3, while Section 4 deals with the basic reproduction number and stability analysis. In Section 5, we provide some numerical examples to support the analytical results and to assess the effect of parameter changes on disease dynamics. In the numerical experiments, we choose the periodic transmission and birth functions (which are kept general in the analytical part of the paper) to correspond to the special seasonal pattern of date palm sap consumption and the bats' breeding behaviour, respectively. The results might help to understand how to avoid a periodic yearly recurrence of the disease. The paper is closed with a short discussion.

2. Model formulation

We develop a compartmental model considering all possible transmissions from animals to humans, animals to animals and from humans to animals, also including periodicity of various parameters due to seasonal patterns in demography and transmission rates.

The total human population $N(t)$ at time t is divided into susceptibles ($S(t)$), exposed ($E(t)$), infected ($I(t)$) and recovered ($R(t)$). Hence,

$$N(t) = S(t) + E(t) + I(t) + R(t).$$

The total population of pigs (intermediate host) $N_p(t)$ at time t is divided into susceptible ($S_p(t)$), exposed ($E_p(t)$), infected ($I_p(t)$) and recovered ($R_p(t)$) individuals, so that

$$N_p(t) = S_p(t) + E_p(t) + I_p(t) + R_p(t).$$

Similarly, the total bat population (animal host reservoir) $N_b(t)$ at time t is divided into susceptible ($S_b(t)$), exposed ($E_b(t)$), infected ($I_b(t)$) and recovered ($R_b(t)$) individuals, such that

$$N_b(t) = S_b(t) + E_b(t) + I_b(t) + R_b(t).$$

We denote the birth and death rates of humans by Π and μ, respectively. There is also a disease-induced death rate, denoted by δ. The force of infection for humans to humans, humans to pigs and humans to bats for NiV transmission is given by $\beta I, \beta_{hp} I$, and $\beta_{hb} I$, respectively. Again, the force of infection for NiV transmission from pigs to humans, pigs to pigs and pigs to bats is expressed here as $\beta_{ph} I_p, \beta_p I_p$ and $\beta_{pb} I_p$. Furthermore, the force of infection for NiV transmission from bats to humans, bats to pigs and bats to bats is expressed here as $\beta_{bh}(t) I_b, \beta_b I_b$ and $\beta_{bp}(t) I_b$. Here, the parameters are the effective contact rate of susceptible individuals who become infected from either humans or animals who became NiV infected. Note that unlike other papers, such as [13, 17], in this work, we also allow transmission from humans to both animal species as well as pig-to-human transmission, although it is hard to find any sources mentioning these ways of transmission (see, e.g.,

under laboratory conditions [33–35]). However, as bat-to-human and bat-to-pig transmission frequently occurs via indirect contact, we presume that (at least) indirect transmission can also happen the other way around, hence, in this model, we decided to allow all possible ways of transmission.

In this context, the average duration of the infectious period is $1/\gamma$ days, so infected individuals are transferred to the recovered compartment at the rate γ and θ is the rate of loss of temporary immunity acquired by recovered individuals, meaning that recovered individuals remain immune for $1/\theta$ days on average. The average length of the incubation period is defined by $1/\nu$. We define all other parameters for pigs and bats and apply the subscripts p and b, respectively, for them. Note that the time-dependent parameters in our model are $\beta_{bh}(t), \beta_{bp}(t)$ and $\Pi_b(t)$.

The transmission diagram of our model is shown in Figure 1. A complete description of the model parameters is summarized in Table 1. With the above notations, our model takes the following form:

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \beta S I - \beta_{ph} S I_p - \beta_{bh}(t) S I_b - \mu S + \theta R,\\
\frac{dE}{dt} &= \beta S I + \beta_{ph} S I_p + \beta_{bh}(t) S I_b - \nu E - \mu E,\\
\frac{dI}{dt} &= \nu E - (\mu + \delta + \gamma) I,\\
\frac{dR}{dt} &= \gamma I - (\mu + \theta) R,
\end{aligned} \tag{2.1a}$$

$$\begin{aligned}
\frac{dS_p}{dt} &= \Pi_p - \beta_p S_p I_p - \beta_{hp} S_p I - \beta_{bp}(t) S_p I_b - \mu_p S_p + \theta_p R_p,\\
\frac{dE_p}{dt} &= \beta_p S_p I_p + \beta_{hp} S_p I + \beta_{bp}(t) S_p I_b - \nu_p E_p - \mu_p E_p,\\
\frac{dI_p}{dt} &= \nu_p E_p - (\mu_p + \delta_p + \gamma_p) I_p,\\
\frac{dR_p}{dt} &= \gamma_p I_p - (\mu_p + \theta_p) R_p,
\end{aligned} \tag{2.1b}$$

$$\begin{aligned}
\frac{dS_b}{dt} &= \Pi_b(t) - \beta_b S_b I_b - \beta_{hb} S_b I - \beta_{pb} S_b I_p - \mu_b S_b + \theta_b R_b,\\
\frac{dE_b}{dt} &= \beta_b S_b I_b + \beta_{hb} S_b I + \beta_{pb} S_b I_p - \nu_b E_b - \mu_b E_b,\\
\frac{dI_b}{dt} &= \nu_b E_b - (\mu_b + \delta_b + \gamma_b) I_b,\\
\frac{dR_b}{dt} &= \gamma_b I_b - (\mu_b + \theta_b) R_b.
\end{aligned} \tag{2.1c}$$

The following initial conditions are associated with system (2.1), define $\phi = (S(0), E(0), I(0), R(0), S_p(0), E_p(0), I_p(0), R_p(0), S_b(0), E_b(0), I_b, R_b(0))$ where $S(0) > 0$, $E(0) \geq 0$, $I(0) \geq 0$, $R(0) \geq 0$, $S_p(0) > 0$, $E_p(0) \geq 0$, $I_p(0) \geq 0$, $R_p(0) \geq 0$, $S_b(0) > 0$, $E_b(0) \geq 0$, $I_b(0) \geq 0$, and $R_b(0) \geq 0$.

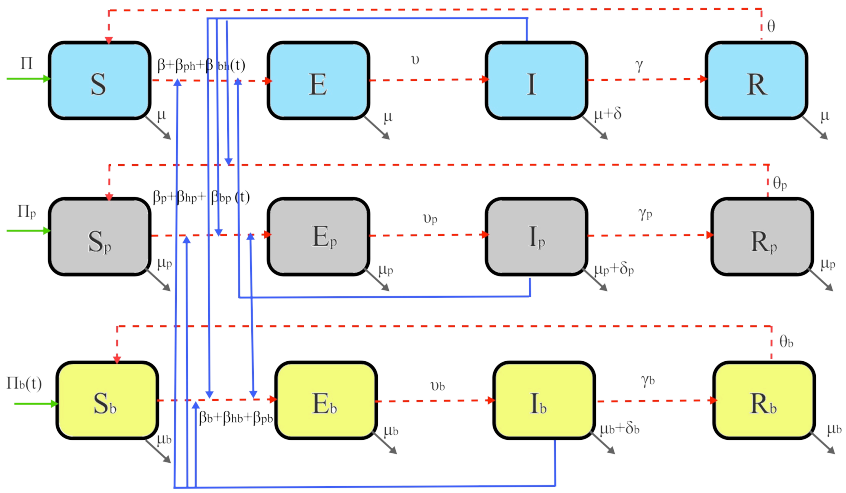


Figure 1. Transmission diagram. Red dashed arrows indicate the transition from one compartment to another. Green arrows and gray indicate new entry and exit for death, respectively. The blue arrow represents virus transmission. Light blue, gray, and yellow colored boxes depict compartments for humans, bats and pigs, respectively.

Table 1. Description of parameters of model (2.1).

Parameters	**Description**
Π	Recruitment rate for humans
$\Pi_b(t), \Pi_p$	Recruitment rate for bats and pigs
μ	Natural death rate of humans
μ_b, μ_p	Natural death rate of bats and pigs
δ	Disease-induced death rate for humans
δ_p, δ_b	Disease-induced death rate for pigs and bats
γ	Recovery rate for humans
γ_p, γ_b	Recovery rate for pigs and bats
β	Human-to-human transmission rate
β_{hp}	Human-to-pig transmission rate
β_{hb}	Human-to-bat transmission rate
β_p	Pig-to-pig transmission rate
β_{ph}	Pig-to-human transmission rate
β_{pb}	Pig-to-bat transmission rate
β_b	Bat-to-bat transmission rate
$\beta_{bh}(t)$	Bat-to-human transmission rate
$\beta_{bp}(t)$	Bat-to-pig transmission rate
$1/\nu$	Average incubation time for humans
$1/\nu_p, 1/\nu_b$	Average incubation time for pigs and bats
$1/\theta$	Average length of immunity for humans
$1/\theta_p, 1/\theta_b$	Average length of immunity for pigs and bats

3. The disease-free periodic solution

3.1. Existence and uniqueness of the disease-free ω-periodic solution

In this section, we will study the existence and uniqueness of the disease-free periodic solution of system (2.1). For this let us consider the subsystem (2.1a) in case of no disease transmission for humans. For the susceptible human population, we have the linear differential equation:

$$S'(t) = \Pi - \mu S(t). \tag{3.1}$$

Clearly, $S(t)$ is bounded and Eq (3.1) has a unique, globally asymptotically stable equilibrium $S^* = \Pi/\mu$. Similarly one can prove that the pig subsystem (2.1b) has a unique, globally asymptotically stable equilibrium $S_p^* = \Pi_p/\mu_p$ and $S_p(t)$ is bounded. Now let us consider the subsystem (2.1c) for bats. To find the disease-free periodic solution of this subsystem, we consider the equation for susceptible bats in case of no disease transmission in the form

$$S_b'(t) = \Pi_b(t) - \mu_b S_b(t), \tag{3.2}$$

with initial condition

$$S_b(0) = S_{b0} := \frac{e^{-\mu_b\omega}\int_0^\omega e^{\mu_b\xi}\Pi_b(\xi)d\xi}{1 - e^{-\mu_b\omega}}.$$

For this initial value problem, we have

$$S_b^*(t) = e^{-\mu_b t}\left(S_{b0} + \int_0^t e^{\mu_b\xi}\Pi_b(\xi)\,d\xi\right) > 0, \tag{3.3}$$

which is globally attractive in $\mathbb{R}_+$. Thus, the system (2.1) has a unique disease-free periodic solution

$$E^* = (S^*, 0, 0, 0, S_p^*, 0, 0, 0, S_b^*(t), 0, 0, 0), \tag{3.4}$$

where $S^* = \Pi/\mu$, $S_p^* = \Pi_p/\mu_p$, and $S_b^*(t)$ is defined in (3.3). To introduce the following result, we set $h^L = \sup_{t\in[0,\omega)} h(t)$ for a continuous positive ω-periodic function $h(t)$.

Lemma 1. *There exists* $N_b^* = \frac{\Pi_b^L}{\mu_b} > 0$ *such that each solution in* $\mathbb{R}_+^{12}$ *of* (2.1) *eventually enters*

$$G_{N^*} = \{(S, E, I, R, S_p, E_p, I_p, R_p, S_b, E_b, I_b, R_b) \in \mathbb{R}_+^{12} : N_h \le N_h^*,\ N_p \le N_p^*,\ N_b \le N_b^*\},$$

and for each $N_b(t) \ge N_b^*$, G_{N^*} *is positively invariant for system* (2.1).

Proof. It can be easily seen from (2.1) that for the bat subsystem (2.1c), we have

$$N_b'(t) = \Pi_b(t) - \mu_b N_b(t) - \delta_b I_b(t) \le \Pi_b^L - \mu_b N_b(t) \le 0, \text{ if } N_b(t) \ge N_b^*,$$

which implies that G_{N^*} is positively invariant when $N_b(t) \ge N_b^*$, and over time, every forward orbit eventually enters into G_{N^*}. □

4. Basic reproduction number and stability analysis

4.1. Basic reproduction number

In this section, we will follow the technique introduced in [22] to study the local stability properties of the disease-free periodic solution depending on the basic reproduction number. First, we can calculate the disease-free periodic solution E^* defined in (3.4) of system (2.1) for appropriate parameter values. To introduce the basic reproduction number $\mathcal{R}_0$ for system (2.1) we calculate

$$\mathcal{F}(t,\mathcal{X}(t)) = \begin{bmatrix} \beta S I + \beta_{ph} S I_p + \beta_{bh}(t) S I_b \\ 0 \\ \beta_p S_b I_p + \beta_{hp} S_p I + \beta_{bp}(t) S_p I_b \\ 0 \\ \beta_b S_b I_b + \beta_{hb} S_b I + \beta_{pb} S_b I_p \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix},$$

and

$$\mathcal{V}^-(t,\mathcal{X}(t)) = \begin{bmatrix} (\nu+\mu)E \\ (\mu+\delta+\gamma)I \\ (\nu_p+\mu_p)E_p \\ (\mu_p+\delta_p+\gamma_p)I_p \\ (\nu_b+\mu_b)E_b \\ (\mu_b+\delta_b+\gamma_b)I_b \\ \beta S I + \beta_{ph} S I_p + \beta_{bh}(t) S I_b + \mu S \\ (\mu+\theta)R \\ \beta_p S_p I_p + \beta_{hp} S_p I + \beta_{bp}(t) S_p I_b + \mu_p S_p \\ (\mu_p+\theta_p)R_p \\ \beta_b S_b I_b + \beta_{hb} S_b I + \beta_{pb} S_b I_p + \mu_b S_b \\ (\mu_b+\theta_b)R_b \end{bmatrix}, \qquad \mathcal{V}^+(t,\mathcal{X}(t)) = \begin{bmatrix} 0 \\ \nu E \\ 0 \\ \nu_p E_p \\ 0 \\ \nu_b E_b \\ \Pi + \theta R \\ \gamma I \\ \Pi_p + \theta_p R_p \\ \gamma_p I_p \\ \Pi_b(t) + \theta_b R_b \\ \gamma_b I_b \end{bmatrix},$$

where $\mathcal{X} = (E, I, E_p, I_p, E_b, I_b, S, R, S_p, R_p, S_b, R_b)^T$. Here E, I, E_p, I_p, E_b, I_b are the infected compartments and S, R, S_p, R_p, S_b, R_b are the uninfected compartments. Now, let us check conditions (A1)–(A5) from [22, p. 701]. System (2.1) can be written as

$$\mathcal{X}'(t) = \mathcal{F}(t,\mathcal{X}(t)) - \mathcal{V}(t,\mathcal{X}(t)) = f(t,\mathcal{X}(t)), \tag{4.1}$$

where $\mathcal{V}(t,\mathcal{X}(t)) = \mathcal{V}^-(t,\mathcal{X}(t)) - \mathcal{V}^+(t,\mathcal{X}(t))$. It can be easily seen that conditions (A1)–(A5) hold. We also introduce here the function $f(t,\mathcal{X}(t)) = \mathcal{F}(t,\mathcal{X}(t)) - \mathcal{V}(t,\mathcal{X}(t))$ and the matrix

$M = (\frac{\partial f_i(t,\mathcal{X}^*(t))}{\partial \mathcal{X}_j})_{7\le i,j\le 12}$, where $f_i(t, \mathcal{X}(t))$ stands for the i-th coordinate of $f(t, \mathcal{X}(t))$ and $\mathcal{X}_i$ is the i-th entry of $\mathcal{X}$. The matrix M has the form

$$M = \begin{bmatrix} -\mu & \theta & 0 & 0 & 0 & 0 \\ 0 & -\mu-\theta & 0 & 0 & 0 & 0 \\ 0 & 0 & -\mu_p & \theta_p & 0 & 0 \\ 0 & 0 & 0 & -\mu_p-\theta_p & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_b & \theta_b \\ 0 & 0 & 0 & 0 & 0 & -\mu_b-\theta_b \end{bmatrix}. \tag{4.2}$$

We denote by $\Phi_M(t)$ the monodromy matrix of $z' = Mz$. We apply the usual notation $\rho(\Phi_M(t))$ for the spectral radius of $\Phi_M(\omega)$. We obtain that $\rho(\Phi_M(t)) < 1$, from which it follows that $\mathcal{X}^*(t)$ is a linearly asymptotically stable solution in $\mathcal{X} = (0, 0, 0, 0, 0, 0, 0, 0, 0, S, S_p, S_b) \in \mathbb{R}^{12}_+$, the disease-free subspace. Hence, condition $(A6)$ is also fulfilled.

We introduce the matrix functions $F(t) = (\frac{\partial \mathcal{F}_i(t,\mathcal{X}^*(t))}{\partial \mathcal{X}_j})_{1\le i,j\le 6}$ and $V(t) = (\frac{\partial \mathcal{V}_i(t,\mathcal{X}^*(t))}{\partial \mathcal{X}_j})_{1\le i,j\le 6}$ (here again, a lower index i corresponds to the i-th coordinate). The two vector functions can be calculated as

$$F(t) = \begin{bmatrix} 0 & \beta S^* & 0 & \beta_{ph} S^* & 0 & \beta_{bh}(t) S^* \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_{hp} S_p^* & 0 & \beta_p S_p^* & 0 & \beta_{bp}(t) S_p^* \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_{hb} S_b^*(t) & 0 & \beta_{pb} S_b^*(t) & 0 & \beta_b S_b^*(t) \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

and

$$V(t) = \begin{bmatrix} \mu+\nu & 0 & 0 & 0 & 0 & 0 \\ -\nu & \gamma+\delta+\mu & 0 & 0 & 0 & 0 \\ 0 & 0 & \mu_p+\nu_p & 0 & 0 & 0 \\ 0 & 0 & -\nu_p & \gamma_P+\delta_p+\mu_p & 0 & 0 \\ 0 & 0 & 0 & 0 & \mu_b+\nu_b & 0 \\ 0 & 0 & 0 & 0 & -\nu_b & \gamma_b+\delta_b+\mu_b \end{bmatrix}.$$

Note that $F(t)$ is a non-negative matrix function, while $-V(t)$ is cooperative. Suppose $X(t, s)$, $t \ge s$, is the evolution operator of the linear system

$$\frac{dx(t)}{dt} = -V(t)x(t).$$

Thus, for $s \in \mathbb{R}$, $X(t, s)$ satisfies the equation

$$\frac{dX(t,s)}{dt} = -V(t)X(t,s), \quad \forall t \ge s, X(s,s) = I,$$

where I denotes the 6×6 identity matrix.

Denote by $\psi(s)$ the distribution of infected individuals, ω-periodic in s. Then, $F(s)\psi(s)$ provides the rate of new cases due to those infected whose infection occurred at time s. For $t \ge s$, the term

$X(t,s)F(s)\psi(s)$ is the distribution of those infected who became infected at time s and who continue to be infectious at time t. Therefore,

$$g(t) := \int_{-\infty}^{t} X(t,s)F(s)\psi(s)ds = \int_{0}^{\infty} X(t,t-a)F(t-a)\psi(t-a)da,$$

gives the distribution of cumulative new infections at time t generated by all infected individuals $\psi(s)$ who were introduced at any time $s \le t$.

Denote by C_ω the ordered Banach space of ω-periodic functions from $\mathbb{R}$ to $\mathbb{R}^6$, provided with the usual maximum norm $\|\cdot\|_\infty$ and define the positive cone

$$C_\omega^+ := \{\psi \in C_\omega : \psi(t) \ge 0, \forall t \in \mathbb{R}\}.$$

The linear next infection operator $L\colon C_\omega \to C_\omega$ is introduced as

$$(L\psi)(t) = \int_{0}^{\infty} X(t,t-a)F(t-a)\psi(t-a)da, \quad \forall t \in \mathbb{R}, \psi \in C_\omega.$$

The basic reproduction number of (2.1) is defined as $\mathcal{R}_0 := \rho(L)$ [22].

To be able to provide a numerical approximation of the value of $\mathcal{R}_0$, following [22], let $W(t,\lambda)$ be a fundamental matrix of the linear ω-periodic equation

$$\frac{dw}{dt} = \left(-V(t) + \frac{F(t)}{\lambda}\right)w, \quad \forall t \in \mathbb{R},$$

with parameter $\lambda \in (0,\infty)$. Furthermore, without loss of generality, we assume that $W(0,\lambda)$ is the identity matrix I. Now, at this point, it is important to recall that $W(\omega,\lambda)$ is the monodromy matrix of the aforementioned linear ω-periodic system.

Theorem 2 ([22, Theorem 2.1])**.** *The following statements are valid.*

(i) *If $\rho(W(\omega,\lambda)) = 1$ has a positive solution λ_0, then λ_0 is a eigenvalue of operator L, and hence $\mathcal{R}_0 > 0$.*

(ii) *If $\mathcal{R}_0 > 0$, then $\lambda_0 = \mathcal{R}_0$ is a unique solution of $\rho(W(\omega,\lambda)) = 1$.*

(iii) *$\mathcal{R}_0 = 0$ if and only if $\rho(W(\omega,\lambda)) < 1$ for all $\lambda > 0$.*

4.2. Local asymptotic stability of the disease-free periodic solution

Based on the results in the previous subsection, we can formulate a theorem concerning the local stability properties of the disease-free periodic solution E^* of model (2.1). Before we state the main result of this subsection, we recall Theorem 2.2 from [22].

Theorem 3 ([22, Theorem 2.2])**.** *The following statements are valid.*

(i) *$\mathcal{R}_0 = 1$ if and only if $\rho(\Phi_{F-V}(\omega)) = 1$;*

(ii) *$\mathcal{R}_0 > 1$ if and only if $\rho(\Phi_{F-V}(\omega)) > 1$;*

(iii) *$\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(\omega)) < 1$.*

Theorem 4. *The disease-free periodic solution E^* of* (2.1) *is locally asymptotically stable if $\mathcal{R}_0 < 1$, and it is unstable if $\mathcal{R}_0 > 1$.*

Proof. The Jacobian of (2.1) calculated at E^* is

$$J(t) = \begin{bmatrix} F(t) - V(t) & 0 \\ A(t) & M \end{bmatrix},$$

with M defined in (4.2) and $A(t)$ given by

$$A(t) = \begin{bmatrix} 0 & -\beta S^* & 0 & -\beta_{ph} S^* & 0 & -\beta_{bh}(t) S^* \\ 0 & \gamma & 0 & 0 & 0 & 0 \\ 0 & -\beta_{hp} S_p^* & 0 & -\beta_p S_p^* & 0 & -\beta_{bp}(t) S_p^* \\ 0 & 0 & 0 & \gamma_p & 0 & 0 \\ 0 & -\beta_{hb} S_b^*(t) & 0 & -\beta_{pb} S_b^*(t) & 0 & -\beta_b S_b^*(t) \\ 0 & 0 & 0 & 0 & 0 & \gamma_b \end{bmatrix}.$$

By [36], E^* is a locally asymptotically stable periodic solution if $\rho(\Phi_M(\omega)) < 1$ as well as $\rho(\Phi_{F-V}(\omega)) < 1$ hold. From condition (A6), we have $\rho(\Phi_M(\omega)) < 1$. It then follows that the stability of E^* is determined by $\rho(\Phi_{F-V}(\omega))$. Hence, E^* is locally asymptotically stable if $\rho(\Phi_{F-V}(\omega)) < 1$, and unstable if $\rho(\Phi_{F-V}(\omega)) > 1$. By using Theorem 3, we complete the proof. □

4.3. Global stability of the disease-free solution

We will show the global asymptotic stability of the disease-free periodic solution E^* for $\mathcal{R}_0 < 1$. We will need the following results.

Lemma 5 ([37, Lemma 2.1])**.** *Let $\mu = \frac{1}{\omega} \ln \rho(\Phi_{A(\cdot)}(\omega))$. Then there exists a positive, ω-periodic function $v(t)$ such that $e^{\mu t} v(t)$ is a positive solution of $x' = A(t)x$.*

Theorem 6. *The disease-free periodic solution E^* of* (2.1) *is globally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. From Theorem 3, we know that if $\mathcal{R}_0 < 1$, then E^* is locally asymptotically stable. Therefore, it is only left to show that for $\mathcal{R}_0 < 1$, E^* is globally attractive, which, together with local asymptotic stability, implies global asymptotic stability. Because $I(t) \geq 0$, $I_p(t) \geq 0$ and $I_b(t) \geq 0$ from Lemma 1, it can be shown that

$$\begin{aligned} N_h'(t) &= \Pi - \mu N_h(t) - \delta I(t) \leq \Pi - \mu N_h(t), \\ N_p'(t) &= \Pi_p - \mu_p N_p(t) - \delta_p I_p(t) \leq \Pi_p - \mu N_p(t), \end{aligned}$$

which implies that

$$\limsup_{t\to\infty} N_h(t) \leq \frac{\Pi}{\mu} = S^*, \quad \text{and} \quad \limsup_{t\to\infty} N_p(t) \leq \frac{\Pi_p}{\mu_p} = S_p^*.$$

Therefore, there exists a $T > 0$ such that $S(t) \leq N_h(t) \leq S^* + \epsilon$, and $S_p(t) \leq N_p(t) \leq S_p^* + \epsilon$, and from Lemma 1, $S_b(t) \leq N_b(t) \leq S_b^*(t) + \epsilon$, for an arbitrary positive ϵ if $t > T$.

Using these estimations for system (2.1), we get

$$\begin{aligned}
\frac{dE}{dt} &\leq (\beta I + \beta_{ph} I_p + \beta_{bh}(t) I_b)(S^* + \epsilon) - \nu E - \mu E,\\
\frac{dI}{dt} &= \nu E - (\mu + \delta + \gamma) I,\\
\frac{dR}{dt} &= \gamma I - (\mu + \theta) R,\\
\frac{dE_p}{dt} &\leq (\beta_p I_p + \beta_{hp} I + \beta_{bp}(t) I_b)(S_p^* + \epsilon) - \nu_p E_p - \mu_p E_p,\\
\frac{dI_p}{dt} &= \nu_p E_p - (\mu_p + \delta_p + \gamma_p) I_p,\\
\frac{dR_p}{dt} &= \gamma_p I_p - (\mu_p + \theta_p) R_p,\\
\frac{dE_b}{dt} &\leq (\beta_b I_b + \beta_{hb} I + \beta_{pb} I_p)(S_b^*(t) + \epsilon) - \nu_b E_b - \mu_b E_b,\\
\frac{dI_b}{dt} &= \nu_b E_b - (\mu_b + \delta_b + \gamma_b) I_b,\\
\frac{dR_b}{dt} &= \gamma_b I_b - (\mu_b + \theta_b) R_b,
\end{aligned} \tag{4.3}$$

for $t > T$. Let $M_\epsilon(t)$ be the matrix function

$$\begin{bmatrix}
-\mu - \nu & \beta(S^* + \epsilon) & 0 & \beta_{ph}(S^* + \epsilon) & 0 & \beta_{bh}(t)(S^* + \epsilon)\\
\nu & -\gamma - \delta - \mu & 0 & 0 & 0 & 0\\
0 & \beta_{hp}(S_p^* + \epsilon) & -\mu_p - \nu_p & \beta_p(S_p^* + \epsilon) & 0 & \beta_{bp}(t)(S_p^* + \epsilon)\\
0 & 0 & \nu_p & -\gamma_P - \delta_p - \mu_p & 0 & 0\\
0 & \beta_{hb}(S_b^*(t) + \epsilon) & 0 & \beta_{pb}(S_b^*(t) + \epsilon) & -\mu_b - \nu_b & \beta_b(S_b^*(t) + \epsilon)\\
0 & 0 & 0 & 0 & \nu_b & -\gamma_b - \delta_b - \mu_b
\end{bmatrix},$$

and let us consider the auxiliary equation

$$\frac{dU(t)}{dt} = M_\epsilon(t) U(t), \tag{4.4}$$

where $U(t) = (E(t), I(t), E_p(t), I_p(t), E_b(t), I_b(t))$. From Theorem 3, we have $\mathcal{R}_0 < 1$ if and only if $\rho(\Phi_{F-V}(\omega)) < 1$. It is clear that $\lim_{\epsilon \to 0} \Phi_{M_\epsilon}(\omega) = \Phi_{F-V}(\omega)$. As $\rho(\Phi_{F-V}(\omega))$ is continuous, $\epsilon > 0$ can be chosen small enough such that $\rho(\phi_{M_\epsilon}(\omega)) < 1$ holds. Now following Lemma 5, we see that there exists a positive ω-periodic function $p(t)$ such that $p(t)e^{\xi t}$ is a solution of (4.4) and $\xi = \frac{1}{\omega} \ln \rho(\Phi_{M_\epsilon}(\omega)) < 0$. For arbitrary $h(0) \in \mathbb{R}^6_+$, we can find k^* such that $h(0) \leq k^* p(0)$ where $h(t) = (E(t), I(t), E_p(t), I_p(t), E_b(t), I_b(t))^T$. Now applying the comparison principle [38, Theorem B.1], we get $h(t) \leq p(t)e^{\xi t}$ for all $t > 0$, from which we get

$$\lim_{t \to \infty} (E(t), I(t), E_p(t), I_p(t), E_b(t), I_b(t))^T = (0, 0, 0, 0, 0, 0)^T.$$

One directly obtains $N_h(t) \to N_h^*$, $N_p(t) \to N_p^*$, and $N_b(t) \to N_b^*$ as $t \to \infty$. Let $\epsilon > 0$, we can choose $t_\epsilon > 0$ such that $I(t) \leqslant \epsilon$, $I_p(t) \leqslant \epsilon$ and $I_b(t) \leqslant \epsilon$ for all $t \geqslant t_\epsilon$. Then, from the equations for $R'(t)$, $R_p'(t)$

and $R_b'(t)$ of (2.1) we get

$$\begin{aligned} R'(t) &\leqslant \gamma\epsilon - (\mu + \theta)R(t), \\ R_p'(t) &\leqslant \gamma_p\epsilon - (\mu_p + \theta_p)R_p(t), \\ R_b'(t) &\leqslant \gamma_b\epsilon - (\mu_b + \theta_b)R_b(t), \end{aligned}$$

for large enough t, hence $R(t) \to 0$, $R_p(t) \to 0$ and $R_b(t) \to 0$ as $t \to +\infty$.

Thus, the equations for $S'(t)$, $S_p'(t)$ and $S_b'(t)$ in system (2.1) provide that

$$\lim_{t\to\infty} S(t) = S^*, \qquad \lim_{t\to\infty} S_p(t) = S_p^*, \qquad \lim_{t\to\infty}(S_b(t) - S_b^*(t)) = 0.$$

The proof is complete. □

4.3.1. Existence of positive periodic solutions for $\mathcal{R}_0 > 1$

To show the existence of positive periodic solutions, we first introduce the notations

$$\begin{aligned} X &:= \left\{(S, E, I, R, S_p, E_p, I_p, R_p, S_b, E_b, I_b, R_b) \in \mathbb{R}_+^{12}\right\}, \\ X_0 &:= \left\{(S, E, I, R, S_p, E_p, I_p, R_p, S_b, E_b, I_b, R_b) \in X : E > 0, I > 0, E_p > 0, I_p > 0, E_b > 0, I_b > 0\right\}, \end{aligned}$$

and

$$\partial X_0 := X \backslash X_0 = \left\{(S, E, I, R, S_p, E_p, I_p, R_p, S_b, E_b, I_b, R_b) \in X : EIE_pI_pE_bI_b = 0\right\}.$$

Let us define the Poincaré map $\mathcal{P}\colon \mathbb{R}_+^{12} \to \mathbb{R}_+^{12}$ corresponding to (2.1) as

$$\mathcal{P}(x^0) = u(\omega, x^0), \quad x^0 \in \mathbb{R}_+^{12},$$

where $u(t, x^0)$ is the single solution of (2.1) started with initial condition $x^0 \in \mathbb{R}_+^{12}$. Then,

$$\mathcal{P}^m(x^0) = u(m\omega, x^0), \quad \text{for all } m \geq 0.$$

Proposition 7. *The set X_0 and ∂X_0 are both positively invariant w.r.t. the flow defined in* (2.1).

Proof. Let us consider the initial condition $\phi \in X_0$. By solving (2.1) for all $t > 0$, we get that

$$\begin{aligned} S(t) &= e^{\int_0^t(-\mu - a_1(s))ds}\left(S(0) + \int_0^t e^{\int_0^\xi(\mu + a_1(s))ds}(\Pi + \theta R(\xi))\, d\xi\right) > 0, \\ E(t) &= e^{-(\mu+\nu)t}\left(E(0) + \int_0^t e^{(\mu+\nu)s} a_1(s)S(s)ds\right) > 0, \\ I(t) &= e^{-(\gamma+\delta+\mu)t}\left(I(0) + \nu\int_0^t e^{(\gamma+\delta+\mu)s}E(s)ds\right) > 0, \\ R(t) &= e^{-(\theta+\mu)t}\left(R(0) + \gamma\int_0^t e^{(\theta+\mu)s}I(s)ds\right) > 0, \\ S_p(t) &= e^{\int_0^t(-\mu_p - a_2(s))ds}\left(S_p(0) + \int_0^t e^{\int_0^\xi(\mu_p + a_2(s))ds}(\Pi_p + \theta_p R_p(\xi))\, d\xi\right) > 0, \end{aligned}$$

$$
\begin{aligned}
E_p(t) &= e^{-(\mu_p+\nu_p)t}\left(E_p(0)+\int_0^t e^{(\mu_p+\nu_p)s}a_2(s)S_p(s)ds\right)>0,\\
I_p(t) &= e^{-(\gamma_p+\delta_p+\mu_p)t}\left(I_p(0)+\nu_p\int_0^t e^{(\gamma_p+\delta_p+\mu_p)s}E_p(s)ds\right)>0,\\
R_p(t) &= e^{-(\theta_p+\mu_p)t}\left(R_p(0)+\gamma_p\int_0^t e^{(\theta_p+\mu_p)s}I_p(s)ds\right)>0,\\
S_b(t) &= e^{\int_0^t(-\mu_b-a_3(s))ds}\left(S_b(0)+\int_0^t e^{\int_0^\xi(\mu_b+a_3(s))ds}(\Pi_b(t)+\theta_bR_b(\xi))\,d\xi\right)>0,\\
E_b(t) &= e^{-(\mu_b+\nu_b)t}\left(E_b(0)+\int_0^t e^{(\mu_b+\nu_b)s}a_3(s)S_b(s)ds\right)>0,\\
I_b(t) &= e^{-(\gamma_b+\delta_b+\mu_b)t}\left(I_b(0)+\nu_b\int_0^t e^{(\gamma_b+\delta_b+\mu_b)s}E_b(s)ds\right)>0,\\
R_b(t) &= e^{-(\theta_b+\mu_b)t}\left(R_b(0)+\gamma_b\int_0^t e^{(\theta_b+\mu_b)s}I_b(s)ds\right)>0,
\end{aligned}
$$

where

$$
\begin{aligned}
a_1(t) &= \beta I(t)+\beta_{ph}I_p(t)+\beta_{bh}(t)I_b(t),\\
a_2(t) &= \beta_pI_p(t)+\beta_{hp}I(t)+\beta_{bp}(t)I_b(t),\\
a_3(t) &= \beta_bI_b(t)+\beta_{hb}I(t)+\beta_{pb}I_p(t).
\end{aligned}
$$

Thus X_0 is a positively invariant set. Since X is positively invariant and ∂X_0 is relatively closed in X, then it is clear that ∂X_0 is positively invariant. □

Lemma 8. *If $\mathcal{R}_0 > 1$, then there exists a $\sigma > 0$ such that for any $x^0 \in X_0$, with $\|x^0 - E^*\| < \sigma$ we have*

$$\limsup_{m\to\infty} d(\mathcal{P}^m(x^0), E^*) \geq \sigma.$$

Proof. By Theorem 3 we have $\rho(\Phi_{F-V}(\omega)) > 1$ if $\mathcal{R}_0 > 1$. Then we can choose an $\eta > 0$ such that $\rho(\Phi_{F-V-M_\eta}(\omega)) > 1$ where the matrix function $M_\eta(t)$ is defined as

$$
M_\eta(t) = \begin{bmatrix}
0 & \beta\eta & 0 & \beta_{ph}\eta & 0 & \beta_{bh}(t)\eta\\
0 & 0 & 0 & 0 & 0 & 0\\
0 & \beta_{hp}\eta & 0 & \beta_p\eta & 0 & \beta_{bp}(t)\eta\\
0 & 0 & 0 & 0 & 0 & 0\\
0 & \beta_{hb}\eta & 0 & \beta_{pb}\eta & 0 & \beta_b\eta\\
0 & 0 & 0 & 0 & 0 & 0
\end{bmatrix}.
$$

Let us use the notation ϕ for an initial condition of (2.1). The continuous dependence of the solutions on initial values implies that we can find a $\sigma = \sigma(\eta) > 0$ such that for arbitrary $\phi \in X_0$ with $\|\phi - E^*\| \leq \sigma$,

$$\|u(t,\phi) - u(t,E^*)\| \leq \eta, \quad \text{for } 0 \leq t \leq \omega,$$

holds, moreover,

$$\limsup_{m\to\infty} d(\mathcal{P}^m(x^0), E^*) \geq \sigma. \tag{4.5}$$

Indeed, suppose by contradiction that (4.5) is not true, then

$$\limsup_{m\to\infty} d(\mathcal{P}^m(x^0), E^*) < \sigma,$$

hence, it follows from the above that

$$\|u(t, \mathcal{P}^m(\phi)) - u(t, E^*)\| < \eta, \quad \text{for all } m \geq 0, t \in [0, \omega].$$

For an arbitrary $t \geq 0$, let us write t as $t = m\omega + \hat{t}$, where $\hat{t} \in [0, \omega)$ and $m = [\frac{t}{\omega}]$, the integer part of $\frac{t}{\omega}$. We obtain

$$\|u(t, x^0) - u(t, E^*)\| = \|u(\hat{t}, \mathcal{P}^m(x^0)) - u(\hat{t}, E^*)\| < \eta, \quad \text{for all } t \geq 0.$$

From this, we have

$$S(t) \geq S^* - \eta, \quad S_p(t) \geq S_p^* - \eta, \quad \text{and} \quad S_b(t) \geq S_b^*(t) - \eta,$$

and hence for $\|\phi - E^*\| < \sigma$, we get

$$\begin{aligned}
\frac{dE}{dt} &\geq (\beta I + \beta_{ph} I_p + \beta_{bh}(t) I_b)(S^* - \eta) - \nu E - \mu E,\\
\frac{dI}{dt} &= \nu E - (\mu + \delta + \gamma) I,\\
\frac{dR}{dt} &= \gamma I - (\mu + \theta) R,\\
\frac{dE_p}{dt} &\geq (\beta_p I_p + \beta_{hp} I + \beta_{bp}(t) I_b)(S_p^* - \eta) - \nu_p E_p - \mu_p E_p,\\
\frac{dI_p}{dt} &= \nu_p E_p - (\mu_p + \delta_p + \gamma_p) I_p,\\
\frac{dR_p}{dt} &= \gamma_p I_p - (\mu_p + \theta_p) R_p,\\
\frac{dE_b}{dt} &\geq (\beta_b I_b + \beta_{hb} I + \beta_{pb} I_p)(S_b^*(t) - \eta) - \nu_b E_b - \mu_b E_b,\\
\frac{dI_b}{dt} &= \nu_b E_b - (\mu_b + \delta_b + \gamma_b) I_b,\\
\frac{dR_b}{dt} &= \gamma_b I_b - (\mu_b + \theta_b) R_b.
\end{aligned}$$

Introduce now the auxiliary linear system

$$U'(t) = (F(t) - V(t) - M_\eta(t))U(t), \tag{4.6}$$

with $U(t) = (E(t), I(t), E_p(t), I_p(t), E_b(t), I_b(t))$. Now we have $\rho(F(t) - V(t) - M_\eta(t)) > 1$, while from Lemma 5 we know that there exists a positive, ω-periodic function $p_1(t)$ such that $h(t) = e^{\xi t} p_1(t)$ is a solution of (4.6) and $\xi = \frac{1}{\omega} \ln \rho(\Phi_{F-V-M_\eta}(\omega)) > 0$. Let $t = n\omega$ and n be a non-negative integer, we get

$$h(n\omega) = e^{n\omega\xi} p_1(n\omega) \to (\infty, \infty, \infty, \infty, \infty, \infty, \infty, \infty, \infty, \infty)^T.$$

For any $h(0) \in \mathbb{R}^9_+$, we can choose a real number $n_0 > 0$ such that $h(0) \geq n_0 p_1(0)$ where

$$h(t) = (E(t), I(t), R(t), E_p(t), I_p(t), R_p(t), E_b(t), I_b(t), R_b(t))^T.$$

Applying the comparison principle [38, Theorem B.1], we obtain $h(t) \geq p_1(t)e^{\xi t}$ for all $t > 0$, which implies that

$$\lim_{t\to\infty}(E(t), I(t), R(t), E_p(t), I_p(t), R_p(t), E_b(t), I_b(t), R_b(t))^T = (\infty, \infty, \infty, \infty, \infty, \infty, \infty, \infty, \infty)^T.$$

This leads to a contradiction that completes the proof. □

Theorem 9. *Let $\mathcal{R}_0 > 1$. Then system* (2.1) *has at least one positive periodic solution and there exists an $\epsilon_1 > 0$ such that*

$$\liminf_{t\to\infty}(E(t), I(t), R(t), E_p(t), I_p(t), R_p(t), E_b(t), I_b(t), R_b(t))^T \geq (\epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1)^T,$$

for all $\phi \in X_0$.

Proof. First, we prove that the Poincaré map $\mathcal{P}$ is uniformly persistent with respect to $(X_0, \partial X_0)$, from this, applying [39, Theorem 3.1.1], it follows that the solution of (2.1) is uniformly persistent with respect to $(X_0, \partial X_0)$. From Proposition 7, we have that both X and X_0 are positively invariant, and ∂X_0 is relatively closed in X. Furthermore, from Lemma 1 it follows that system (2.1) is point dissipative. Let us introduce

$$M_\partial = \{\phi \in \partial X_0 : \mathcal{P}^m(\phi) \in \partial X_0, \forall m \geq 0\}.$$

To apply the theory developed in [39] (see also [37, Theorem 2.3]), we first show that

$$M_\partial = \{(S, 0, 0, S_p, 0, 0, S_b, 0, 0) : S \geq 0, S_p \geq 0, S_b \geq 0\}. \tag{4.7}$$

Let us note that $M_\partial \supseteq (S, 0, 0, S_p, 0, 0, S_b, 0, 0) : S \geq 0, S_p \geq 0, S_b \geq 0$. It is sufficient to prove that $M_\partial \subset \{(S, 0, 0, S_p, 0, 0, S_b, 0, 0) : S \geq 0, S_p \geq 0, S_b \geq 0\}$, i.e., for arbitrary initial condition $\phi \in \partial X_0, E(n\omega) = 0$ or $I(n\omega) = 0$ or $R(n\omega) = 0$ or $E_p(n\omega) = 0$ or $I_p(n\omega) = 0$ or $R_p(n\omega) = 0$ or $E_b(n\omega) = 0$ or $I_b(n\omega) = 0$ or $R_b(n\omega) = 0$ for all $n \geq 0$.

Assume by contradiction the existence of an integer $n_1 \geq 0$ for which

$$(E(n_1\omega), I(n_1\omega), R(n_1\omega), E_p(n_1\omega), I_p(n_1\omega), R_p(n_1\omega), E_b(n_1\omega), I_b(n_1\omega), R_b(n_1\omega)) > (0, 0, 0, 0, 0, 0, 0, 0, 0).$$

Then, by putting $t = n_1\omega$ into the place of the initial time $t = 0$ in Proposition 7, we get that $S(t) > 0$, $E(t) > 0$, $I(t) > 0$, $R(t) > 0$, $S_p(t) > 0$, $E_p(t) > 0$, $I_p(t) > 0$, $R_p(t) > 0$, $S_b(t) > 0$, $E_b(t) > 0$, $I_b(t) > 0$, and $R_b(t) > 0$. This is in contradiction with the positive invariance of ∂X_0.

By Lemma 8, $\mathcal{P}$ is weakly uniformly persistent w.r.t. $(X_0, \partial X_0)$. Lemma 1 guarantees the existence of a global attractor of $\mathcal{P}$. Then E^* is an isolated invariant set in X and $W^s(E^*) \cap X_0 = \emptyset$. Each solution in M_∂ tends to E^* and it is clearly acyclic in M_∂.

By [39, Theorem 1.3.1 and Remark 1.3.1], we can deduce that P is uniformly (strongly) persistent w.r.t. $(X_0, \partial X_0)$. Hence, there exists an $\epsilon_1 > 0$ such that

$$\liminf_{t\to\infty}(E(t), I(t), R(t), E_p(t), I_p(t), R_p(t), E_b(t), I_b(t), R_b(t))^T \geq (\epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1)^T,$$

for all $\phi \in X_0$.

By [39, Theorem 1.3.6], $\mathcal{P}$ has a fixed point $\tilde{\phi} \in X_0$, and hence the system (2.1) has at least one periodic solution $u(t, \tilde{\phi})$ with

$$\tilde{\phi} = (\tilde{S}(0), \tilde{E}(0), \tilde{I}(0), \tilde{R}(0), \tilde{S}_p(0), \tilde{E}_p(0), \tilde{I}_p(0), \tilde{R}_p(0)\tilde{S}_b(0), \tilde{E}_b(0), \tilde{I}_b(0), \tilde{R}_b(0)) \in X_0.$$

Now, let us prove that $\tilde{S}(0), \tilde{S}_p(0)$ and $\tilde{S}_b(0)$ are positive. If ($\tilde{S}(0) = 0$, $\tilde{S}_p(0) = 0$, $\tilde{S}_p(0)) = 0$, then we obtain $\tilde{S}(0) > 0$, $\tilde{S}_p(0) > 0$ and $\tilde{S}_b(0) > 0$ for all $t > 0$. However, using the periodicity of the solution, we have $\tilde{S}(0) = \tilde{S}(n\omega) = 0$, $\tilde{S}_p(0) = \tilde{S}_p(n\omega) = 0$ and $\tilde{S}_b(0) = \tilde{S}_b(n\omega) = 0$, which is a contradiction and hence the statement of the theorem is proved. □

5. Numerical simulation

To illustrate our analytical results, we perform some numerical simulations. These simulations will also give us suggestions regarding the changes in model parameters that might lead to a periodic yearly recurrence of Nipah virus disease and how to avoid such a recurrence. The periodic transmission rates are described by functions of the form

$$\beta_x(t) = \tilde{\beta}_x \cdot \begin{cases} \sin(4t/365 * \Pi) + a, & 0 \le t \le 365/4 \quad \text{mod } 365, \\ a, & 365/4 < t < 365 \quad \text{mod } 365, \end{cases}$$

where $x \in \{bp, bh\}$, $\tilde{\beta}_x$ is a baseline value for the transmission rate and a is a positive constant. The form of this periodic transmission function corresponds to the increase of contacts between humans and bats due to date palm consumption in the period between December and February, with its peak value in January. The periodic function describing the birth rate of bats is defined in a similar way, taking into account the breeding season of the bats. We show three examples that correspond to different values of the basic reproduction number. To numerically approximate this value, we follow the method described in [40]. Note that all simulations were performed using *Wolfram Mathematica*.

A thorough analysis employing Latin hypercube sampling in conjunction with the partial rank correlation coefficient (PRCC) approach was done, involving 10,000 Monte Carlo simulations per iteration. The PRCC technique has allowed us to quantify the effect of changing these factors on the model's feedback using a variety of parameter values. As a result, we have developed statistical connections between the eight parameters used as input and the cumulative number of infections up until the end of the specified time period chosen as the output parameter. It is worth mentioning that increasing parameters with positive PRCC values causes the cumulative number of cases to increase, whereas increasing parameters with negative PRCC values causes the cumulative case count to drop. The results, as shown in Figure 2, highlight the variables that have the biggest effects, particularly the rates of transmission from bats to humans (β_{bh}), pigs to humans (β_{ph}) and bats to pigs (β_{bp}). Our experiment suggests that human-to-human transmission has a lesser effect than animal-to-human transmission.

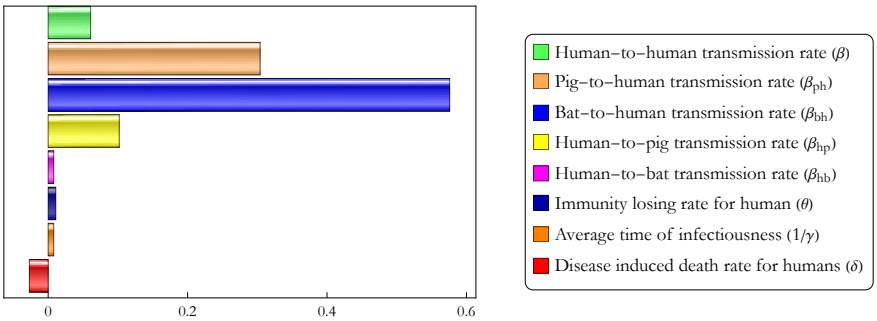
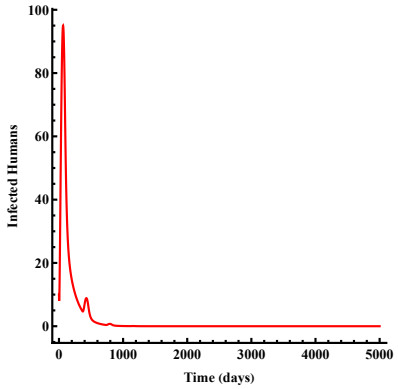


Figure 2. Partial rank correlation coefficients (PRCC).

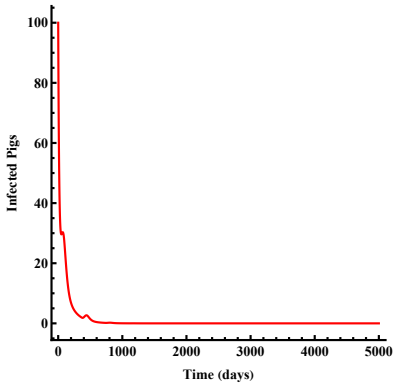
Table 2. Parameters for model (2.1) providing values for extinction and persistence (in units of per day).

Parameter	Extinction (Example 1)	Extinction (Example 2)	Persistence	Source
Π	6.69852	6.69852	6.69852	[41]
Π_p	300.3	300.3	300.3	[42]
$\tilde{\Pi}_b$	0.411	0.411	0.411	Assumed
μ	0.0000379	0.0000379	0.0000379	[41]
μ_p	0.002747	0.002747	0.002747	[43]
μ_b	0.00013699	0.00013699	0.00013699	Assumed
β	2.28×10^{-9}	2.0×10^{-9}	2.0×10^{-9}	[11]
β_{ph}	1.3×10^{-8}	2.0×10^{-8}	2.0×10^{-8}	Assumed
$\tilde{\beta}_{bh}$	1.0×10^{-6}	1.0×10^{-6}	1.04×10^{-6}	Assumed
β_p	6.71×10^{-8}	6.71×10^{-8}	1.32×10^{-6}	Assumed
β_{hp}	7.0×10^{-8}	7.0×10^{-8}	7.0×10^{-8}	Assumed
$\tilde{\beta}_{bp}$	1.0×10^{-7}	1.0×10^{-7}	1.0×10^{-5}	Assumed
β_b	6.71×10^{-6}	6.71×10^{-6}	6.71×10^{-5}	[19]
β_{hb}	7.0×10^{-10}	7.0×10^{-10}	7.0×10^{-10}	Assumed
β_{pb}	7.0×10^{-10}	7.0×10^{-10}	7.0×10^{-10}	Assumed
ν	0.047	0.0476	0.0476	[44]
ν_p	0.066	0.066	0.066	[45]
ν_b	0.066	0.066	0.066	Assumed
θ	0.033	0.0333	0.0333	Assumed
θ_p	0.001	0.001	0.001	Assumed
θ_b	0.00046	0.000456	0.000456	[19]
γ	0.045	0.0177	0.0177	[46]
γ_p	0.049	0.049	0.0499	[45]
γ_b	0.0225	0.0197	0.05	Assumed
δ	0.09	0.02065	0.09	Assumed
δ_p	0.00232	0.000325	0.000265	[47]
δ_b	0.000746	0.000575	0.000501	Assumed

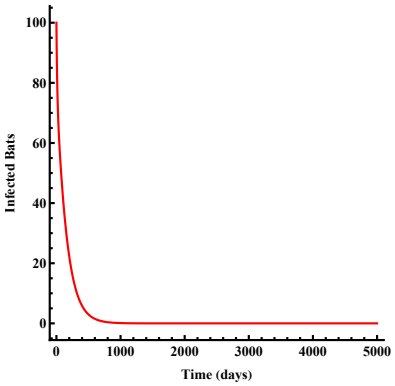
In our first example, the basic reproduction number has the value $\mathcal{R}_0 = 0.86$, i.e., it is significantly smaller than 1. The parameter values corresponding to this example can be found in the first column of Table 2, while the number of infected humans, pigs and bats are plotted in Figure 3. One can see that-just like expected based on our analytical results-the disease will die out in all three species and the population reaches a (globally asymptotically stable) disease-free steady state.



(a) Extinction of infection in humans.



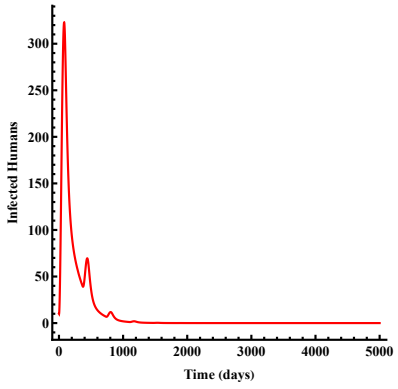
(b) Extinction of infection in pigs.



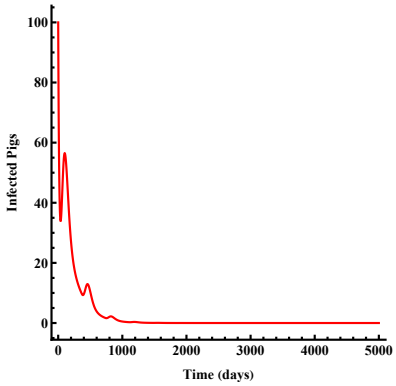
(c) Extinction of infection in bats.

Figure 3. Extinction of NiV when $\mathcal{R}_0 = 0.86 < 1$ with parameter values in Table 2 (Example 1).

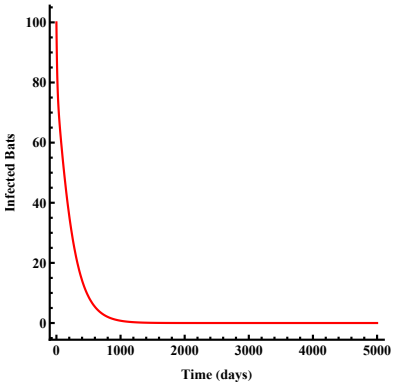
In Example 2, we consider another set of parameters with which the reproduction number is still below 1, however, in this case, the value $\mathcal{R}_0 = 0.985$ is very close to the threshold value. In this case, one can see that again the disease goes extinct in all three species, as expected from the analytical results. The results of the numerical simulations for the three species are shown in Figure 4.



(a) Extinction of infection in humans.



(b) Extinction of infection in pigs.

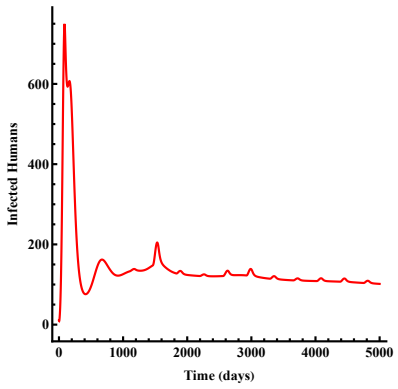


(c) Extinction of infection in bats.

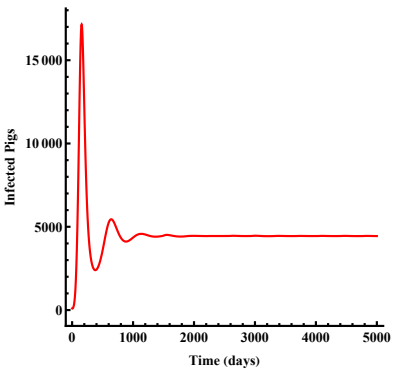
Figure 4. Extinction of the disease for $\mathcal{R}_0 = 0.985 < 1$ with parameter values shown in Table 2 (Example 2).

In our last example, shown in Figure 5, the applied parameter values (shown in the last column of Table 2) result in a basic reproduction number $\mathcal{R}_0 = 3.965$ with a value larger than 1. In this

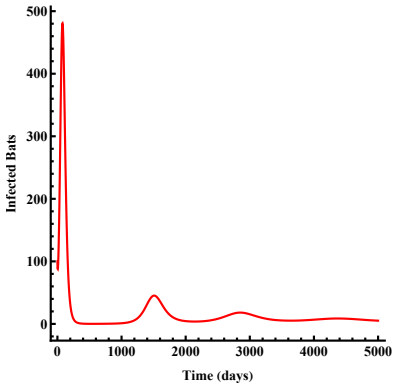
case, we can see that the disease persists and the figures suggest that all solutions tend to an endemic periodic solution corresponding to the annual recurrence of the disease. Comparing the parameter values applied in our last example with those of the two previous cases, one can see that a significant increase in all transmission rates was needed to obtain a situation where the disease remains endemic, along with an increase in the length of the infectious period. On the other hand, the simulations suggest that keeping the transmission rates as low as possible is sufficient to prevent huge seasonal outbreaks of the disease.



(a) Persistence of infection in humans.



(b) Persistence of infection in pigs.



(c) Persistence of infection in bats.

Figure 5. Persistence of NiV when $\mathcal{R}_0 = 3.965 > 1$ with parameter values in Table 2.

6. Discussion and conclusions

In this study, we developed a three-species compartmental model to characterize the spread of the Nipah virus infection among bats, pigs, and humans, taking into account all possible directions of transmission between the three species. To make our model more realistic, we included periodicity in our model considering the periodic birth rate of the reservoir species bats and periodic transmission rates due to the seasonal nature of date palm sap consumption, an important way of disease transmission from bats to humans. We also included the loss of immunity in those who have recovered, as according to studies conducted on bats, one of the factors contributing to outbreaks in Pteropus bats is the gradual loss of immunity over the course of six years. The novelty of our model is that we tried to incorporate several of the key characteristics of the disease, namely, the transmission chain consisting of the reservoir bats, the intermediate host pigs and humans, periodic transmission, long latent period and loss of immunity.

Using the methods established by Wang and Zhao [22] and adapting them to our special model, we calculated the basic reproduction number ($\mathcal{R}_0$) and determined the existence and uniqueness of a disease-free ω-periodic solution. We showed that this solution is globally asymptotically stable if $\mathcal{R}_0$ is less than 1, while it is unstable otherwise. In the latter case, the disease becomes endemic in the three populations, and we also proved the existence of at least one positive periodic solution. To support the analytical findings and evaluate the impact of parameter changes on disease dynamics, we present several numerical examples. For three values of $\mathcal{R}_0$, we performed numerical simulations to highlight our analytical findings with reference to the NiV disease. When $\mathcal{R}_0 < 1$, the simulations in the first two

examples supported the conclusion that the disease has been eradicated in people, pigs, and bats. This is consistent with the mathematical expectations and points to a disease-free solution. With $\mathcal{R}_0 > 1$, however, the simulations showed sustained disease transmission, as in the final example, pointing to an endemic periodic solution that corresponds to periodic recurrence. The simulations showed that higher transmission rates and longer infectious periods were necessary for the disease to remain endemic when comparing the parameter values between the examples. On the other hand, simulations showed that reducing transmission rates could successfully stop significant seasonal disease outbreaks. These examples may assist readers in understanding how to prevent the disease from recurring on an annual basis.

Our work certainly has its limitations. One of the more important is the lack of sufficient data as fortunately, up to now, there have not been any very large-scale Nipah outbreaks in humans. A future better understanding of the characteristics of this disease will contribute to more precise models that might include some additional compartments, i.e., convalescent, infected with relapsed onset or deceased who may contribute to disease transmission. Temperature, humidity and climatic conditions can impact the survival and transmission of the Nipah virus, with higher temperatures and increased rainfall that potentially increase virus dissemination and infection rates. Future research should take these environmental aspects into account to fully comprehend the dynamics of disease. Due to the poor understanding of many disease parameters, the numerical analysis of the model is difficult. Future studies should concentrate on examining an extended system that takes into account other variables and makes use of extensive and well-supported data in order to address this. To improve comprehension, enable more precise predictions, and permit recommendations for disease control and prevention efforts, the model's scope should be expanded and credible data should be included.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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