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Research article

Global dynamics of a compartmental model for the spread of Nipah virus

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ABSTRACT

Nipah virus, which originated in South-East Asia is a bat-borne virus causing Nipah virus infection in humans. This emerging infectious disease has become one of the most alarming threats to public health due to its periodic outbreaks and extremely high mortality rate. We establish and study a novel SIRS model to describe the dynamics of Nipah virus transmission, considering human-to-human as well as zoonotic transmission from bats and pigs as well as loss of immunity. We determine the basic reproduction number which can be obtained as the maximum of three threshold parameters corresponding to various ways of disease transmission and determining in which of the three species the disease becomes endemic. By constructing appropriate Lyapunov functions, we completely describe the global dynamics of our model depending on these threshold parameters. Numerical simulations are shown to support our theoretical results and assess the effect of various intervention measures.

1. Introduction

Nipah virus (NiV) is a zoonotic virus meaning that it is transmitted between species from animals to humans. The virus is a member of the family *Paramyxoviridae* and the genus *Henipavirus*, causing outbreaks of fatal disease in humans [1].

The virus was first identified when a cluster of patients associated with pig farming in Peninsular Malaysia came down with acute febrile encephalitis that was associated with high mortality in late September 1998. NiV was identified as the etiological agent responsible for the outbreak by early March 1999 when it was isolated from the cerebrospinal fluid of an encephalitic patient of Sungai Nipah village, from which the name of the virus and the disease come from. More than 265 encephalitis cases, including 105 deaths, were reported in Malaysia, and 11 cases of encephalitis or respiratory illness with one death were reported in Singapore by mid-June 1999 [2,3]. After the first detection of NiV in Bangladesh in 2001, a sporadical outbreak of NiV was seen near West Bengal, a state of India bordering Bangladesh. But in May 2018, another epidemic suddenly broke out in Kerala, the southern part of India lying very far away from the nearest border of Bangladesh, and an outbreak happened in the following season [4,5]. A number of countries including Cambodia, Ghana, Indonesia, Madagascar, the Philippines, and Thailand may be at risk for infection according to WHO [6].

The disease has influenza-like symptoms including fever, headache, muscle pain, vomiting, and pain in the throat. In critical cases inflammation of the brain and uncontrolled electrical activity take place in the brain, progressing to coma within 24 to 48 hours [7].

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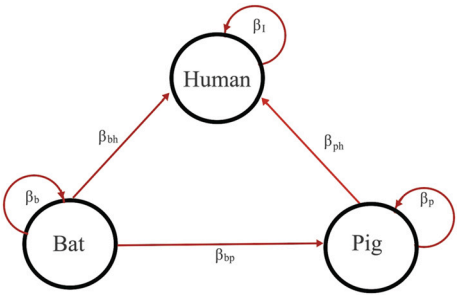


Fig. 1. Flow chart of NiV transition. Red arrows indicate NiV transition among humans, bats, and pigs.

The animal host reservoir for NiV is the fruit bat also known as the flying fox, belonging to the *Pteropus* genus in the *Pteropodidae* family [8]. Different routes of human transmission include direct transmission from fruit bats, indirect transmission from fruit bats via other animal species and human-to-human transmission [9–12]. Fruit partially eaten by bats may be dropped or thrown into pigsties infecting pigs by consuming the contaminated fruit [13]. Pig-to-human transmission mostly results from close contact with sick pigs or their contaminated tissues [14,6]. Fruit bats frequently feed on shaved bark which is shaved to collect date sap and often contaminate the sap with saliva, urine, and excreta. Investigations of NiV outbreaks in Bangladesh have pointed out that consumption of fresh date palm sap is the primary route and fermented alcoholic drink (toddy, tari, or palm wine) is the secondary route of bat-to-human transmission [15]. Human-to-human transmission was reported in the Malaysian outbreaks in March 1999, especially in families of affected index cases and more than 300 health care workers in the three hospitals that looked after 80% of encephalitis patients [16,17].

In South-East Asia, NiV infection has become an alarming threat due to high mortality, periodicity, and the unsatisfactory effect of antiviral drugs and treatment depending on symptomatic patients of the disease [18,19]. Moreover, WHO has included Nipah virus in its blueprint list including ten diseases and pathogens to be prioritized for R&D [20].

Pathological and epidemiological studies of the Nipah virus disease were perceived, but very few mathematical models are available for it which are presented as follows. [21] proposed a simple SIR model with optimal control. [18] studied an optimal control problem model for a similar model, however, with vital dynamics included where creating awareness and health care are considered as controls. [19] formulated and analyzed an SEIR based on a mathematical model incorporating the quarantine of infectious individuals influenced by the availability of isolation centers and surveillance coverage. They assumed birth and death rate are not equal. Among the several possible control parameters, they considered the number of quarantined individuals and the enhanced personal hygiene as a result of the public enlightenment program. A two-layered compartmental model for humans and bats was proposed by [7]. They found that the number of NiV-affected individuals can be reduced by using control on them and bats. A mathematical model of seven compartments including virus dynamics, flying foxes, and humans was proposed by [22] with the assumption that there is no cure for this disease. [23] proposed a model incorporating the role of the deceased who died in Nipah fever without considering the bat population. [24] studied a coupled pig-human Nipah virus disease model concentrating on the optimal control of some adjustable parameters. In [25], the authors considered a model including bats, humans, and an intermediate host. Most recently, Evirgen et al. [26] proposed an SIRD model with Caputo fractional derivative, considering transmission from dead bodies. In [27], a fractional order Nipah virus using the Caputo derivative was studied considering the role of flying foxes and free virus, and an optimal control problem was also studied. Similarly, Baleanu et al. [28] considered a fractional order model including the impact of unsafe contact with an infectious corpse as a possible way of transmission.

It is clear from the above list that in spite of the threat it poses, up to now very little modeling work has been done on Nipah fever transmission. It is also important to note that most of the Nipah models did not consider transmission from bats and pigs, which, however, play a crucial role in the spread of the disease. Moreover, several of the above works did not concentrate on the dynamics of the proposed models but rather considered optimal control problems.

To describe the spread of Nipah fever in a more realistic way, in this paper, we propose a compartmental model considering all possible ways of transmission of NiV among animals and humans: we consider transmission from bats, pigs, and human-to-human transmission (see Fig. 1). In Section 2, we introduce our compartmental model. In Section 3, we calculate the basic reproduction number and determine some basic properties of the model, and in Section 4 we study the local and global dynamics of the model. In Section 5, we perform numerical simulations: we fit the model to data from the 1998–99 outbreak in Malaysia and we assess the effects of changing various disease-related parameters. The paper is closed by a short discussion of the results in Section 6.

2. Model formulation

As mentioned in the introduction, our aim is to include disease transmission among three species. More precisely, we develop a compartmental model considering transmission from bats to humans, bats to pigs, bats to bats, pigs to humans, pigs to pigs, and from humans to humans. That is, we do not consider transmission from humans to any of the two animal species and pig-to-bat transmission either as these ways of transmission have a negligible probability (see Fig. 1).

In this work, populations of all three species are divided into susceptibles, infected, and recovered, furthermore, we also include the possibility of immunity loss, hence, we consider a system consisting of three SIRS models, coupled by intraspecies transmission.

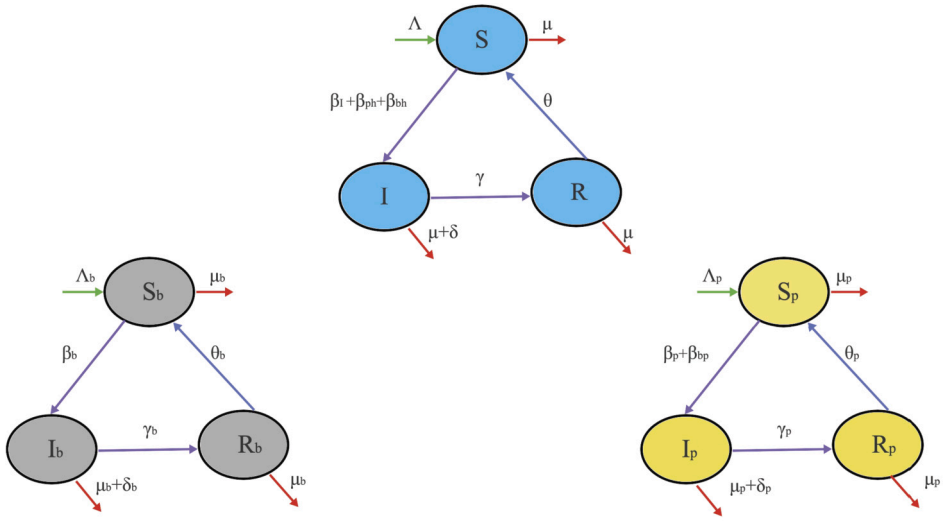


Fig. 2. Transmission diagram. Blue arrows indicate the transition from one compartment to another, and green arrows and red arrows indicate new entry and outflow for humans, bats, and pigs respectively. Light blue, gray, and yellow colored ellipses depict compartments for humans, bats, and pigs, respectively.

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

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

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

$$N_p(t) = S_p(t) + I_p(t) + R_p(t),$$

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

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

We denote the birth and death rates of humans by Λ and μ, respectively. There is also a disease-induced death rate, denoted by δ. Rates of human-to-human, pig-to-human and bat-to-human transmission are denoted by β_I, β_{ph} and β_{bh}, respectively. The rate of transmission among bats is denoted by β_b, while that of transmission among pigs by β_p. Transmission from bats to pigs is given by β_{bp}.

Infected humans are transferred to the recovered compartment at the rate γ (i.e. the average duration of the infectious period is $1/\gamma$ days) 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. We define all other parameters for pigs and bats in an analogous way, for these parameters, we introduce the subscripts p and b, respectively. The transmission diagram of our model is shown in Fig. 2. A complete description of the model parameters is summarized in Table 1.

The system of differential equations established considering the above assumptions takes the form

$$\begin{aligned}
S'(t) &= \Lambda - \beta_I S(t)I(t) - \beta_{ph}S(t)I_p(t) - \beta_{bh}S(t)I_b(t) - \mu S(t) + \theta R(t),\\
I'(t) &= \beta_I S(t)I(t) + \beta_{ph}S(t)I_p(t) + \beta_{bh}S(t)I_b(t) - (\mu+\delta+\gamma)I(t), \qquad (1a)\\
R'(t) &= \gamma I(t) - (\mu+\theta)R(t),\\
S_p'(t) &= \Lambda_p - \beta_p S_p(t)I_p(t) - \beta_{bp}S_p(t)I_b(t) - \mu_p S_p(t) + \theta_p R_p(t),\\
I_p'(t) &= \beta_p S_p(t)I_p(t) + \beta_{bp}S_p(t)I_b(t) - (\mu_p+\delta_p+\gamma_p)I_p(t), \qquad (1b)\\
R_p'(t) &= \gamma_p I_p(t) - (\mu_p+\theta_p)R_p(t),\\
S_b'(t) &= \Lambda_b - \beta_b S_b(t)I_b(t) - \mu_b S_b(t) + \theta_b R_b(t),\\
I_b'(t) &= \beta_b S_b(t)I_b(t) - (\mu_b+\delta_b+\gamma_b)I_b(t), \qquad (1c)\\
R_b'(t) &= \gamma_b I_b(t) - (\mu_b+\theta_b)R_b(t),
\end{aligned}$$

with nonnegative initial conditions.

Table 1
Description of parameters of model (1).

Parameters	Description
Λ	Recruitment rate for humans
Λ_p, Λ_b	Recruitment rate for pigs, bats respectively
μ	Natural death rate of humans
μ_p, μ_b	Natural death rate of pigs, bats
δ	Disease-induced death rate for humans
δ_p, δ_b	Disease-induced death rate for pigs and bats respectively
γ	Recovery rate for humans
γ_p, γ_b	Recovery rate for pigs and bats respectively
β_I	Transmission rate from infected to susceptible humans
β_p	Transmission rate from infected to susceptible pigs
β_b	Transmission rate from infected to susceptible bats
β_{ph}	Pig-to-human transmission rate
β_{bh}	Bat-to-human transmission rate
β_{bp}	Bat-to-pig transmission rate
$1/\theta$	Average length of immunity for humans
$1/\theta_p, 1/\theta_b$	Average length of immunity for pigs and bats respectively

It is important to note that due to the asymmetric transmission possibilities among the three species, subsystem (1c) can be decoupled from the rest of the equations of (1), furthermore, the subsystem consisting of equations (1b) and (1c) can also be decoupled from the human equations.

3. Basic properties

3.1. Nonnegativity and boundedness

For system (1) it is necessary to prove that all the state variables are nonnegative and all the solutions of the system with positive initial conditions have a positive invariant solution. Thus we start with the following lemma.

Lemma 1. *All solutions of model* (1) *started from nonnegative initial conditions will remain nonnegative for all forward time and will eventually approach the forward invariant set* $\Gamma = \{S, I, R, S_p, I_p, R_p, S_b, I_b, R_b \in \mathbb{R}^3_+ \times \mathbb{R}^3_+ \times \mathbb{R}^3_+ : 0 < N \le \Lambda/\mu, 0 < N_p \le \Lambda_p/\mu_p, 0 < N_b \le \Lambda_b/\mu_b\}$.

Proof. It can easily be proved that all existing solutions starting from nonnegative initial conditions remain nonnegative for all time $t > 0$. For the total human population $N(t)$ we have

$$N'(t) = S'(t) + I'(t) + R'(t) = \Lambda - \mu N(t) - \delta I(t).$$

Clearly,

$$N'(t) \le \Lambda - \mu N(t).$$

If the initial value of the total population $N(0) = N_0$, then it follows that

$$N(t) \le \frac{\Lambda}{\mu} - \left(\frac{\Lambda}{\mu} - N_0\right) e^{-\mu t}.$$

So $N(t) \le \frac{\Lambda}{\mu}$ as $t > 0$. Applying a similar argumentation as above, we can prove that $N_p(t) \le \Lambda_p/\mu_p$ and $N_b(t) \le \Lambda_b/\mu_b$. Hence the region is positively invariant and it attracts all solutions of the equations of the system. □

3.2. Derivation of the basic reproduction number

To calculate the basic reproduction number $\mathcal{R}_0$ of (1), we follow the general approach established in [29,30]. For model (1) the infectious states are I, I_b and I_p. We can create the transmission vector $\mathcal{F}$ representing the new infections and the transition vector $\mathcal{V}$ which denotes the outflow from the infectious compartments in (1) are given by

$$\mathcal{F} = \begin{bmatrix} \beta_I SI + \beta_{ph} SI_p + \beta_{bh} SI_b \\ \beta_p S_p I_p + \beta_{bp} S_p I_b \\ \beta_b S_b I_b \end{bmatrix}, \qquad \mathcal{V} = \begin{bmatrix} (\mu + \delta + \gamma) I \\ (\mu_p + \delta_p + \gamma_p) I_p \\ (\mu_b + \delta_b + \gamma_b) I_b \end{bmatrix}.$$

Model (1) has a unique disease-free equilibrium, given by

$$E_0 = (S, I, R, S_p, I_p, R_p, S_b, I_b, R_b) = \left(\frac{\Lambda}{\mu}, 0, 0, \frac{\Lambda_b}{\mu_b}, 0, 0, \frac{\Lambda_p}{\mu_p}, 0, 0\right).$$

Substituting the value the disease-free equilibrium E_0, we compute the Jacobian F from $\mathcal{F}$ given by

$$F = \begin{bmatrix} \frac{\beta_I \Lambda}{\mu} & \frac{\beta_{ph}\Lambda}{\mu} & \frac{\beta_{bh}\Lambda}{\mu} \\ 0 & \frac{\beta_p \Lambda_p}{\mu_p} & \frac{\beta_{bp}\Lambda_p}{\mu_p} \\ 0 & 0 & \frac{\beta_b \Lambda_b}{\mu_b} \end{bmatrix}$$

and the Jacobian V from $\mathcal{V}$ given by

$$V = \begin{bmatrix} \gamma + \delta + \mu & 0 & 0 \\ 0 & \gamma_p + \delta_p + \mu_p & \\ 0 & 0 & \gamma_b + \delta_b + \mu_b \end{bmatrix},$$

from which the next-generation matrix can be calculated as

$$FV^{-1} = \begin{bmatrix} \frac{\beta_I \Lambda}{\mu(\gamma+\delta+\mu)} & \frac{\beta_{ph}\Lambda}{\mu(\gamma_p+\delta_p+\mu_p)} & \frac{\beta_{bh}\Lambda}{\mu(\gamma_b+\delta_b+\mu_b)} \\ 0 & \frac{\beta_p \Lambda_p}{\mu_p(\gamma_p+\delta_p+\mu_p)} & \frac{\beta_{bp}\Lambda_p}{\mu_p(\gamma_b+\delta_b+\mu_b)} \\ 0 & 0 & \frac{\beta_b \Lambda_b}{\mu_b(\gamma_b+\delta_b+\mu_b)} \end{bmatrix}.$$

The eigenvalues of the next generation matrix are $\frac{\beta_I \Lambda}{\mu(\gamma+\delta+\mu)}, \frac{\beta_p \Lambda_p}{\mu_p(\gamma_p+\delta_p+\mu_p)}, \frac{\beta_b \Lambda_b}{\mu_b(\gamma_b+\delta_b+\mu_b)}$. According to [29,30], the basic reproduction number $\mathcal{R}_0$ is the spectral radius of FV^{-1}, hence in our model the basic reproduction number is given by

$$\mathcal{R}_0 = \max\left\{\mathcal{R}_0^1, \mathcal{R}_0^2, \mathcal{R}_0^3\right\},$$

where

$$\mathcal{R}_0^1 = \frac{\beta_I \Lambda}{\mu(\gamma+\delta+\mu)}, \qquad \mathcal{R}_0^2 = \frac{\beta_p \Lambda_p}{\mu_p(\gamma_p+\delta_p+\mu_p)}, \quad \text{and} \quad \mathcal{R}_0^3 = \frac{\beta_b \Lambda_b}{\mu_b(\gamma_b+\delta_b+\mu_b)}.$$

3.3. Existence of endemic equilibria

In this subsection, we will determine the existence of endemic equilibria depending on the parameter values. Due to the asymmetric nature of transmission among the three species, we may have various equilibria corresponding to scenarios where Nipah virus infection is only endemic among the human population, where the disease is endemic in humans and pigs, or where the infection is endemic in all three species.

Lemma 2. *The human-only endemic equilibrium* $\hat{E} := \left(\hat{S}, \hat{I}, \hat{R}, \hat{S}_p, 0, \hat{R}_p, \hat{S}_b, 0, \hat{R}_b,\right)$ *exists if and only if* $\mathcal{R}_0^1 > 1$.

Proof. Let us assume that the disease is not endemic among pigs and bats. In this case, by omitting the terms corresponding to infection from animals to humans we get the system

$$\begin{aligned} S'(t) &= \Lambda - \beta_I S(t) I(t) - \mu S(t) + \theta R(t), \\ I'(t) &= \beta_I S(t) I(t) - (\mu + \delta + \gamma) I(t), \\ R'(t) &= \gamma I(t) - (\mu + \theta) R(t), \end{aligned} \tag{2a}$$

$$\begin{aligned} S_p'(t) &= \Lambda_p - \mu_p S_p(t) + \theta_p R_p(t), \\ R_p'(t) &= -(\mu_p + \theta_p) R_p(t), \end{aligned} \tag{2b}$$

$$\begin{aligned} S_b'(t) &= \Lambda_b - \mu_b S_b(t) + \theta_b R_b(t), \\ R_b'(t) &= -(\mu_b + \theta_b) R_b(t). \end{aligned} \tag{2c}$$

The reduced system (2) has the equilibrium $\left(\hat{S}, \hat{I}, \hat{R}, \hat{S}_p, 0, \hat{R}_p, \hat{S}_b, 0, \hat{R}_b\right)$ where

$$\begin{aligned} \hat{S} &= \tfrac{(\gamma+\delta+\mu)}{\beta_I}, \\ \hat{I} &= \tfrac{(\theta+\mu)(\beta_I\Lambda-\mu(\gamma+\delta+\mu))}{\beta_I(\delta\theta+\gamma\mu+\delta\mu+\theta\mu+\mu^2)} = \tfrac{\mu(\theta+\mu)(\gamma+\delta+\mu)(\mathcal{R}_0^1-1))}{\beta_I(\delta\theta+\gamma\mu+\delta\mu+\theta\mu+\mu^2)}, \\ \hat{R} &= \tfrac{\gamma(\beta_I\Lambda-\mu(\gamma+\delta+\mu))}{\beta_I(\delta\theta+\gamma\mu+\delta\mu+\theta\mu+\mu^2)} = \tfrac{\gamma\mu(\gamma+\delta+\mu)(\mathcal{R}_0^1-1))}{\beta_I(\delta\theta+\gamma\mu+\delta\mu+\theta\mu+\mu^2)}, \\ \hat{S}_p &= \tfrac{\Lambda_p}{\mu_p}, \quad \hat{R}_p = 0, \quad \hat{S}_b = \tfrac{\Lambda_b}{\mu_b}, \quad \hat{R}_b = 0, \end{aligned}$$

from which it can clearly be seen that this equilibrium exists if and only if $\mathcal{R}_0^1 > 1$. □

Lemma 3. *The human- and pig-endemic equilibrium* $\tilde{E} := \left(\tilde{S}, \tilde{I}, \tilde{R}, \tilde{S}_p, \tilde{I}_p, \tilde{R}_p, \tilde{S}_b, 0, \tilde{R}_b\right)$ *exists if* $\mathcal{R}_0^2 > 1$.

Proof. This case corresponds to the situation when the disease is not endemic among bats, it only affects humans and pigs, hence, in this case, we can omit the terms corresponding to infection from bats from the right-hand sides of model (1) to obtain

$$\begin{aligned} S'(t) &= \Lambda - \beta_I S(t)I(t) - \beta_{ph} S(t)I_p(t) - \mu S(t) + \theta R(t),\\ I'(t) &= \beta_I S(t)I(t) + \beta_{ph} S(t)I_p(t) - (\mu + \delta + \gamma)I(t), \qquad (3a)\\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t), \end{aligned}$$

$$\begin{aligned} S_p'(t) &= \Lambda_p - \beta_p S_p(t)I_p(t) - \mu_p S_p(t) + \theta_p R_p(t),\\ I_p'(t) &= \beta_p S_p(t)I_p(t) - (\mu_p + \delta_p + \gamma_p)I_p(t), \qquad (3b)\\ R_p'(t) &= \gamma_p I_p(t) - (\mu_p + \theta_p)R_p(t), \end{aligned}$$

$$\begin{aligned} S_b'(t) &= \Lambda_b - \mu_b S_b(t) + \theta_b R_b(t),\\ R_b'(t) &= -(\mu_b + \theta_b)R_b(t). \qquad (3c) \end{aligned}$$

We let the right-hand side of all eight equations equal to zero. From the subsystem (3c) for bats, we again obtain $(\tilde{S}_b, \tilde{R}_b) = (\frac{\Lambda_b}{\mu_b}, 0)$. From the subsystem (3b) for pigs, we get

$$\begin{aligned} \tilde{S}_p &= \tfrac{(\gamma_p+\delta_p+\mu_p)}{\beta_p},\\ \tilde{I}_p &= \tfrac{(\theta_p+\mu_p)(\beta_p\Lambda_p-\mu_p(\gamma_p+\delta_p+\mu_p))}{\beta_p(\delta_p\theta_p+\gamma_p\mu_p+\delta_p\mu_p+\theta_p\mu_p+\mu_p^2)},\\ \tilde{R}_p &= \tfrac{\gamma_p(\beta_p\Lambda_p-\mu_p(\gamma_p+\delta_p+\mu_p))}{\beta_p(\delta_p\theta_p+\gamma_p\mu_p+\delta_p\mu_p+\theta_p\mu_p+\mu_p^2)}, \end{aligned}$$

which can be written as

$$\begin{aligned} \tilde{S}_p &= \tfrac{(\gamma_p+\delta_p+\mu_p)}{\beta_p},\\ \tilde{I}_p &= \tfrac{\mu_p(\theta_p+\mu_p)(\gamma_p+\delta_p+\mu_p)(\mathcal{R}_0^2-1)}{\beta_p(\delta_p\theta_p+\gamma_p\mu_p+\delta_p\mu_p+\theta_p\mu_p+\mu_p^2)},\\ \tilde{R}_p &= \tfrac{\gamma_p\mu_p(\gamma_p+\delta_p+\mu_p)(\mathcal{R}_0^2-1)}{\beta_p(\delta_p\theta_p+\gamma_p\mu_p+\delta_p\mu_p+\theta_p\mu_p+\mu_p^2)}. \end{aligned}$$

This implies that $\tilde{I}_p, \tilde{R}_p$ are positive if and only if $\mathcal{R}_0^2 > 1$. Then substituting $\tilde{I}_p$ into the place of $I_p(t)$ in the human equations (3a) we obtain

$$\begin{aligned} S'(t) &= \Lambda - \beta_I S(t)I(t) - \beta_{ph} S(t)\tilde{I}_p - \mu S(t) + \theta R(t),\\ I'(t) &= \beta_I S(t)I(t) + \beta_{ph} S(t)\tilde{I}_p - (\mu + \delta + \gamma)I(t), \qquad (4)\\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t). \end{aligned}$$

To obtain equilibria of the latter system (4), we need to solve the algebraic system of equations

$$\begin{aligned} 0 &= \Lambda - \beta_I SI - \beta_{ph} S\tilde{I}_p - \mu S + \theta R,\\ 0 &= \beta_I SI + \beta_{ph} S\tilde{I}_p - (\mu + \delta + \gamma)I, \qquad (5)\\ 0 &= \gamma I - (\mu + \theta)R. \end{aligned}$$

Solving for R in terms of I from the third equation of (5) and replacing into the first equation, we get

$$S = \frac{I\gamma\theta + \Lambda(\theta + \mu)}{(\beta_I I + \beta_{ph}\tilde{I}_p + \mu)(\theta + \mu)}. \qquad (6)$$

Using (6), the second equation of (5) can be written as

$$I^2\beta_I(\gamma\mu + (\delta + \mu)(\theta + \mu)) + I(\beta_{ph}\tilde{I}_p\gamma\mu + (\delta + \mu)(\theta + \mu) + \mu(\gamma + \delta + \mu)(\theta + \mu)(1 - \mathcal{R}_0^1)) - \beta_{ph}\tilde{I}_p\Lambda(\theta + \mu) = 0,$$

a quadratic equation of I. Since the discriminant of this equation is positive and the product of the constant term and that of the leading coefficient is negative, the equation has a unique real positive solution. Hence, a unique equilibrium $\tilde{E}$ with endemicity in humans and pigs exists. □

Lemma 4. *The endemic equilibrium* $E^* := \left(S^*, I^*, R^*, S_p^*, I_p^*, R_p^*, S_b^*, I_b^*, R_b^*\right)$ *with the disease being endemic in all three species exists if and only if* $\mathcal{R}_0^3 > 1$ *and* $\mathcal{R}_0^2 > 1$.

Proof. In this case, we assume that NiV transmission to humans occurs from both animal species. To calculate the endemic equilibrium, we set the right-hand side of all equations to zero. From the subsystem (1c) for bats we get

$$S_b^* = \frac{(\gamma_b + \delta_b + \mu_b)}{\beta_b},$$

$$I_b^* = \frac{(\theta_b + \mu_b)(\beta_b\Lambda_b - \mu_b(\gamma_b + \delta_b + \mu_b))}{\beta_b(\delta_b\theta_b + \gamma_b\mu_b + \delta_b\mu_b + \theta_b\mu_b + \mu_b^2)} = \frac{\mu_b(\theta_b + \mu_b)(\gamma_b + \delta_b + \mu_b)(\mathcal{R}_0^3 - 1)}{\beta_b(\delta_b\theta_b + \gamma_b\mu_b + \delta_b\mu_b + \theta_b\mu_b + \mu_b^2)},$$

$$R_b^* = \frac{\gamma_b(\beta_b\Lambda_b - \mu_b(\gamma_b + \delta_b + \mu_b))}{\beta_b(\delta_b\theta_b + \gamma_b\mu_b + \delta_b\mu_b + \theta_b\mu_b + \mu_b^2)} = \frac{\gamma_b\mu_b(\gamma_b + \delta_b + \mu_b)(\mathcal{R}_0^3 - 1)}{\beta_b(\delta_b\theta_b + \gamma_b\mu_b + \delta_b\mu_b + \theta_b\mu_b + \mu_b^2)}.$$

We may substitute the value of I_b^* into the subsystem (1b) for pigs. Similarly, as before, the pig subsystem has a unique fixed point. Substituting the value of I_p^* into the first three equations, we get the following subsystem (7) for humans:

$$\begin{aligned} S'(t) &= \Lambda - \beta_I S(t)I(t) - \beta_{ph}S(t)I_p^* - \beta_{bh}S(t)I_b^* - \mu S(t) + \theta R(t),\\ I'(t) &= \beta_I S(t)I(t) + \beta_{ph}S(t)I_p^* + \beta_{bh}S(t)I_b^* - (\mu + \delta + \gamma)I(t),\\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t). \end{aligned} \tag{7}$$

Similarly, as in the proof of the previous lemma, we can see that the endemic equilibrium exists if $\mathcal{R}_0^3 > 1$ and $\mathcal{R}_0^2 > 1$. □

4. Stability analysis

4.1. Local stability of the equilibria

Theorem 5. *The disease-free equilibrium* $E_0\left(\frac{\Lambda}{\mu}, 0, 0, \frac{\Lambda_p}{\mu_p}, 0, 0, \frac{\Lambda_b}{\mu_b}, 0, 0\right)$ *is locally asymptotically stable if* $\mathcal{R}_0^1 < 1, \mathcal{R}_0^2 < 1, \mathcal{R}_0^3 < 1$, *while* E_0 *is unstable if any one of the inequalities is altered.*

Proof. The Jacobian of system (1) evaluated at the disease-free equilibrium takes the form

$$\mathcal{J}(E_0) = \begin{bmatrix} -\mu & -\frac{\beta_I\Lambda}{\mu} & \theta & 0 & -\frac{\beta_{ph}\Lambda}{\mu} & 0 & 0 & -\frac{\beta_{bh}\Lambda}{\mu} & 0\\ 0 & j_{22} & 0 & 0 & \frac{\beta_{ph}\Lambda}{\mu} & 0 & 0 & \frac{\beta_{bh}\Lambda}{\mu} & 0\\ 0 & \gamma & -\theta-\mu & 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & -\mu_p & -\frac{\beta_p\Lambda_p}{\mu_p} & \theta_p & 0 & -\frac{\beta_{bp}\Lambda_p}{\mu_p} & 0\\ 0 & 0 & 0 & 0 & j_{55} & 0 & 0 & \frac{\beta_{bp}\Lambda_p}{\mu_p} & 0\\ 0 & 0 & 0 & 0 & \gamma_p & -\theta_p-\mu_p & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu_b & -\frac{\beta_b\Lambda_b}{\mu_b} & \theta_b\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & j_{88} & 0\\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \gamma_b & -\theta_b-\mu_b \end{bmatrix},$$

while the eigenvalues of $\mathcal{J}(E_0)$ are $-\mu, \theta-\mu, j_{22} = \frac{\beta_I\Lambda - \mu(\gamma+\delta+\mu)}{\mu}, -\mu_p, -\theta_p-\mu_p, j_{55} = \frac{\beta_p\Lambda_p - \mu_p(\gamma_p+\delta_p+\mu_p)}{\mu_p}, -\mu_b, -\theta_b-\mu_b, j_{88} = \frac{\beta_b\Lambda_b - \mu_b(\gamma_b+\delta_b+\mu_b)}{\mu_b}$.

So the disease-free equilibrium is locally asymptotically stable if $\frac{\beta_I\Lambda - \mu(\gamma+\delta+\mu)}{\mu} = (\gamma+\delta+\mu)(\mathcal{R}_0^1 - 1) < 0$, $\frac{\beta_p\Lambda_p - \mu_p(\gamma_p+\delta_p+\mu_p)}{\mu_p} = (\gamma_p + \delta_p + \mu_p)(\mathcal{R}_0^2 - 1) < 0$ and $\frac{\beta_b\Lambda_b - \mu_b(\gamma_b+\delta_b+\mu_b)}{\mu_b} = (\gamma_b + \delta_b + \mu_b)(\mathcal{R}_0^3 - 1) < 0$, hence, the disease-free equilibrium is locally asymptotically stable if $\mathcal{R}_0^1 < 1$, $\mathcal{R}_0^2 < 1$ and $\mathcal{R}_0^3 < 1$. If any of these three is altered then that eigenvalue will be positive meaning that the disease-free equilibrium is unstable. This completes our proof. □

4.2. Global stability of the equilibria

First, by applying the fluctuation lemma (see for example [31]), we show that the disease-free equilibrium is globally asymptotically stable if the basic reproduction number is less than 1. For a bounded function f on $\mathbb{R}_+$, we introduce the notations

$$f^\infty = \limsup_{t\to\infty} f(t) \quad \text{and} \quad f_\infty = \liminf_{t\to\infty} f(t).$$

Theorem 6. *The disease-free equilibrium* $E_0\left(\frac{\Lambda}{\mu}, 0, 0, \frac{\Lambda_p}{\mu_p}, 0, 0, \frac{\Lambda_b}{\mu_b}, 0, 0\right)$ *is globally asymptotically stable* $\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}_+^9\}$ *if* $\mathcal{R}_0 < 1$.

Proof. In the previous subsection, we showed that the disease-free equilibrium E_0 is locally asymptotically stable if the basic reproduction number is less than one, hence it is sufficient to prove that E_0 is globally attractive in the positively invariant and attractive set ϕ.

Let $(S_b(t), I_b(t), R_b(t))$ be a solution of the subsystem (1c). According to the fluctuation lemma there exists a sequence $\{t_n\}$ such that $t_n \to \infty$ we have $R(t_n) \to R^\infty$, and $R'(t_n) \to 0$ as $n \to \infty$. From the equation for recovered bats we have

$$R_b'(t_n) = \gamma_b I_b(t_n) - (\mu_b + \theta_b) R_b(t_n),$$

then letting $n \to \infty$ implies $0 \le \gamma_b I_b^\infty - (\mu_b + \theta_b) R_b^\infty$ and hence $R_b^\infty \le \frac{\gamma_b I_b^\infty}{\mu_b + \theta_b}$. Again by the fluctuation lemma, there exists a sequence $u_n \to \infty$ such that $I_b(u_n) \to I_b^\infty$, and $I_b'(u_n) \to 0$ as $n \to \infty$. From the equation for infected bats, we have

$$I_b'(u_n) = \beta_b S_b(u_n) I_b(u_n) - (\mu_b + \delta_b + \gamma_b) I_b(u_n),$$

which implies $0 \le \frac{\beta_b \Lambda_b}{\mu_b} I_b^\infty - (\mu_b + \delta_b + \gamma_b) I_b^\infty$ using Lemma 1 and hence $0 \le (\mathcal{R}_0^3 - 1) I_b^\infty$. Since $\mathcal{R}_0^3 < 1$, we have $I_b^\infty = 0$. It follows that $R_b^\infty = 0$. Applying once again the fluctuation lemma, there exists a sequence $v_n \to \infty$ such that $S(v_n) \to S_\infty$, and $S'(v_n) \to 0$ as $n \to \infty$. From the equation for susceptible bats, we get

$$S_b'(v_n) = \Lambda_b - \beta_b S_b(v_n) I_b(v_n) - \mu_b S_b(v_n) + \theta_b R_b(v_n).$$

Using that $I_b^\infty = 0$ and $R_b^\infty = 0$ and letting $n \to \infty$ we get $(S_b)_\infty = \frac{\Lambda_b}{\mu_b} \ge S_b^\infty$. It follows that $\lim_{t\to\infty} S_b(t) = \frac{\Lambda_b}{\mu_b}$ if $\mathcal{R}_0^3 < 1$. Hence, for the bats subsystem we have that $\lim_{t\to\infty}(S_b(t), I_b(t), R_b(t)) = \left(\frac{\Lambda_b}{\mu_b}, 0, 0\right)$ holds for all solutions of (1c). Applying these results in subsystem (1b) for pigs and following a similar calculation, we can prove $\lim_{t\to\infty}(S_p(t), I_p(t), R_p(t)) = \left(\frac{\Lambda_p}{\mu_p}, 0, 0\right)$ if $\mathcal{R}_0^2 < 1$. Finally, for the human subsystem (1a) one can prove that $\lim_{t\to\infty}(S(t), I(t), R(t)) = \left(\frac{\Lambda}{\mu}, 0, 0\right)$ if $\mathcal{R}_0^1 < 1$ in an analogous way. Hence, the disease-free equilibrium E_0 is globally asymptotically stable if $\mathcal{R}_0 < 1$. □

Theorem 7. *The human-only endemic equilibrium* $\hat{E} := \left(\hat{S}, \hat{I}, \hat{R}, \hat{S}_p, 0, \hat{R}_p, \hat{S}_b, 0, \hat{R}_b\right)$ *is globally asymptotically stable in* $\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}_+^9\}$ *if* $\mathcal{R}_0^1 > 1$, $\mathcal{R}_0^2 < 1$ *and* $\mathcal{R}_0^3 < 1$.

Proof. In proving the global asymptotic stability of the equilibrium $\hat{E}$, we first take advantage of the fact that if $\mathcal{R}_0^2 < 1$ and $\mathcal{R}_0^3 < 1$ and there is no disease among bats and pigs, then the three species do not affect each other, hence, the subsystems corresponding to each species can be decoupled from the rest of equations. Moreover, the subsystems for bats and pigs can be reduced to the single equations for $S_b'(t)$ and $S_p'(t)$, respectively. That is, we only have to consider the equations

$$S_b'(t) = \Lambda_b - \mu_b S_b(t) \quad \text{and} \quad S_p'(t) = \Lambda_p - \mu_p S_p(t),$$

which clearly have the globally asymptotically stable equilibria $\left(\frac{\Lambda_b}{\mu_b}\right)$ and $\left(\frac{\Lambda_p}{\mu_p}\right)$, respectively. Now, we can turn to the human subsystem consisting of the first three equations of (1), however, without transmission from animals. For the convenience of constructing a Lyapunov function, following [32,33] we consider an equivalent subsystem by letting $N(t) = S(t) + I(t) + R(t)$. Then we can write the subsystem for humans as

$$\begin{aligned} N'(t) &= \Lambda - \mu N(t) - \delta I(t), \\ I'(t) &= \beta_I I(t)(N(t) - I(t) - R(t)) - (\mu + \delta + \gamma) I(t), \\ R'(t) &= \gamma I(t) - (\mu + \theta) R(t), \end{aligned} \tag{8}$$

and the equilibrium for humans $\hat{E} := \left(\hat{S}, \hat{I}, \hat{R}\right)$ for the system (2) gives the boundary equilibrium of (7). Clearly, $\hat{N}, \hat{I}$ and $\hat{R}$ satisfy the equations

$$\begin{aligned} \Lambda - \mu \hat{N} - \delta \hat{I} &= 0, \\ \beta_I \hat{I}(\hat{N} - \hat{I} - \hat{R}) - (\mu + \delta + \gamma)\hat{I} &= 0, \\ \gamma \hat{I} - (\mu + \theta)\hat{R} &= 0. \end{aligned}$$

We define the Lyapunov function $V(t)$ as

$$V(t) = \frac{\beta_I}{2\delta}(N - \hat{N})^2 + \left(I - \hat{I} - \hat{I} \ln \frac{I}{\hat{I}}\right) + \frac{\beta_I}{2\gamma}(R - \hat{R})^2.$$

Thus the derivative of the Lyapunov function can be computed along the solution of the system of equations (7) considering no disease is transmitted from bats and pigs are given by

$$
\begin{aligned}
V'(t) &= \frac{\beta_I}{\delta}(N-\hat{N})N' + \left(1-\frac{\hat{I}}{I}\right)I' + \frac{\beta_I}{\gamma}(R-\hat{R})R' \\
&= \frac{\beta_I}{\delta}(N-\hat{N})(\mu\hat{N}+\delta\hat{I}-\mu N-\delta I) + \left(1-\frac{\hat{I}}{I}\right)(\beta_I I(N-I-R)-\beta_I I(\hat{N}-\hat{I}-\hat{R})) \\
&\quad - \frac{\beta_I}{\gamma}(R-\hat{R})(\gamma I-\gamma\hat{I}+(\mu+\theta)\hat{R}-(\mu+\theta)R) \\
&= \frac{\beta_I}{\delta}(N-\hat{N})\big[-\mu(N-\hat{N})-\delta(I-\hat{I})\big] + \beta_I(I-\hat{I})(N-\hat{N}-I+\hat{I}-R+\hat{R}) + \frac{\beta_I}{\gamma}(R-\hat{R})\big[\gamma(I-\hat{I})-(\mu+\theta)(R-\hat{R})\big] \\
&\leq -\beta_I(N-\hat{N})(I-\hat{I}) + \beta_I(I-\hat{I})(N-\hat{N}) - \beta_I(I-\hat{I})(R-\hat{R}) + \beta_I(R-\hat{R})(I-\hat{I}) \\
&= 0.
\end{aligned}
$$

Furthermore, the equality $V'(t)=0$ holds only if $N=\hat{N}$, $I=\hat{I}$, and $R=\hat{R}$. Thus, the endemic equilibrium $\hat{E}$, is the only positive invariant set to the system (7) contained entirely in $\Gamma := \{(S(t),I(t),R(t),S_p(t),I_p(t),R_p(t),S_b(t),I_b(t),R_b(t)) \in \mathbb{R}^9_+\}$. Therefore, it follows from the Lyapunov method that, since endemic equilibrium for the equivalent system is stable, hence the positive endemic equilibrium for the original system is globally asymptotically stable if $\mathcal{R}_0^1 > 1$. □

Theorem 8. *The equilibrium* $\tilde{E} := (\tilde{S},\tilde{I},\tilde{R},\tilde{S}_p,\tilde{I}_p,\tilde{R}_p,\tilde{S}_b,0,\tilde{R}_b)$*, where the disease is endemic among humans and pigs, is globally asymptotically stable in* $\Gamma := \{(S(t),I(t),R(t),S_p(t),I_p(t),R_p(t),S_b(t),I_b(t),R_b(t)) \in \mathbb{R}^9_+\}$ *if* $\mathcal{R}_0^2 > 1$ *and* $\mathcal{R}_0^3 < 1$.

Proof. In case $\mathcal{R}_0^3 < 1$, there is no disease among bats, then only pig-to-pig, pig-to-human, and human-to-human infection occur. Without bat-to-pig infection, we can first decouple the equations for the pigs from the remaining equations. Similarly to the previous theorem, by letting $N_p(t) = S_p(t) + I_p(t) + R_p(t)$ we may consider an equivalent system for the pigs given as

$$
\begin{aligned}
N_p'(t) &= \Lambda_p - \mu_p N_p(t) - \delta_p I_p(t), \\
I_p'(t) &= \beta_p I_p(t)(N_p(t) - I_p(t) - R_p(t)) - (\mu_p + \delta_p + \gamma_p) I_p(t), \\
R_p'(t) &= \gamma_p I_p(t) - (\mu_p + \theta_p) R_p(t).
\end{aligned} \tag{9}
$$

We can observe that subsystem (9) has the same structure as system (8). Following the procedure of Theorem 7 we can show that $(\tilde{S}_p,\tilde{I}_p,\tilde{R}_p)$ is a globally asymptotically stable fixed point of (9).

Let us now substitute the limiting value $\tilde{I}_p$ of $I_p(t)$ into the human subsystem to obtain

$$
\begin{aligned}
S'(t) &= \Lambda - \beta_I S(t) I(t) - \beta_{ph}\tilde{I}_p S(t) - \mu S(t) + \theta R(t), \\
I'(t) &= \beta_I S(t) I(t) + \beta_{ph} S(t) I_p(t) + \beta_{bh} S(t) I_b(t) - (\mu + \delta + \gamma) I(t), \\
R'(t) &= \gamma I(t) - (\mu + \theta) R(t).
\end{aligned}
$$

We note that this system is now different from the reduced pig system and from the reduced human subsystem studied in the previous theorem. Namely, a new type of movement appears from the S compartment to the I compartment, which is given as $S(t)$ multiplied by a constant. By introducing again $N(t) = S(t) + I(t) + R(t)$, we get the equivalent system

$$
\begin{aligned}
N'(t) &= \Lambda - \mu N(t) - \delta I(t), \\
I'(t) &= (\beta_I I(t) + \beta_{ph}\tilde{I}_p)(N(t) - I(t) - R(t)) - (\mu + \delta + \gamma) I(t), \\
R'(t) &= \gamma I(t) - (\mu + \theta) R(t).
\end{aligned} \tag{10}
$$

We define the Lyapunov function $W(t)$ as

$$
W(t) = \frac{1}{2\delta}(N-\tilde{N})^2 + \int_{\tilde{I}}^{I} \frac{u-\tilde{I}}{\beta_I u + \beta_{ph}\tilde{I}_p}\, du + \frac{1}{2\gamma}(R-\tilde{R})^2.
$$

The derivative of the Lyapunov function along solutions of system (10) is given by

$$
\begin{aligned}
W'(t) &= \frac{1}{\delta}(N-\tilde{N})N' + \frac{I-\tilde{I}}{\beta_I I + \beta_{ph}\tilde{I}_p} I' + \frac{1}{\gamma}(R-\tilde{R})R' \\
&= \frac{1}{\delta}(N-\tilde{N})(\mu\tilde{N}+\delta\tilde{I}-\mu N-\delta I) + (I-\tilde{I})\left[(N-\tilde{N})-(I-\tilde{I})-(R-\tilde{R})-(\mu+\delta+\gamma)\left(\frac{I}{\beta_I I+\beta_{ph}\tilde{I}_p} - \frac{\tilde{I}}{\beta_I\tilde{I}+\beta_{ph}\tilde{I}_p}\right)\right] \\
&\quad + \frac{1}{\gamma}(R-\tilde{R})(\gamma I - \gamma\tilde{I} + (\mu+\theta)\tilde{R} - (\mu+\theta)R)
\end{aligned}
$$

Table 2
Existence and stability properties of equilibria. E_0 denotes disease-free equilibrium, $\hat{E}$ denotes equilibrium where the disease is only endemic among humans, $\tilde{E}$ denotes equilibrium where the disease is only endemic among humans and pigs, E^* denotes equilibrium where the disease is endemic among humans, pigs, and bats.

Reproduction numbers	E_0	$\hat{E}$	$\tilde{E}$	E^*
$\mathcal{R}_0^1<1, \mathcal{R}_0^2<1, \mathcal{R}_0^3<1$	GAS	-	-	-
$\mathcal{R}_0^1>1, \mathcal{R}_0^2<1, \mathcal{R}_0^3<1$	unstable	GAS	-	-
$\mathcal{R}_0^2>1, \mathcal{R}_0^3<1$	unstable	unstable	GAS	-
$\mathcal{R}_0^3>1$	unstable	unstable	unstable	GAS

$$= \frac{1}{\delta}(N-\tilde{N})\left[-\mu(N-\tilde{N})-\delta(I-\tilde{I})\right]+(I-\tilde{I})(N-\tilde{N})-(I-\tilde{I})^2$$
$$-(I-\tilde{I})(R-\tilde{R})-(I-\tilde{I})\left(\frac{I}{\beta_I I+\beta_{ph}\tilde{I}_p}-\frac{\tilde{I}}{\beta_I \tilde{I}+\beta_{ph}\tilde{I}_p}\right)+\frac{1}{\gamma}(R-\tilde{R})\left[(\gamma(I-\tilde{I})-(\mu+\theta)(R-\tilde{R})\right]$$
$$\leq -(N-\tilde{N})(I-\tilde{I})+(I-\tilde{I})(N-\tilde{N})-(I-\tilde{I})(R-\tilde{R})-(I-\tilde{I})\left(\frac{I}{\beta_I I+\beta_{ph}\tilde{I}_p}-\frac{\tilde{I}}{\beta_I \tilde{I}+\beta_{ph}\tilde{I}_p}\right)+(R-\tilde{R})(I-\tilde{I}).$$

So $W'(t)\leq 0$ since the function $\frac{I}{\beta_I I+\beta_{ph}\tilde{I}_p}$ is continuous and monotonically increasing in I. i.e. $W(t)<0$. Furthermore, the equality $W'(t)=0$ holds only if $N=\tilde{N}, I=\tilde{I}$ and $R=\tilde{R}$. i.e. $W(t)=0$ Thus, the endemic equilibrium $\tilde{E}$ is the only positive invariant set to the system contained entirely in $\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}_+^9\}$. Therefore, it follows from the direct Lyapunov method that, since endemic equilibrium for the equivalent system is stable, hence the endemic equilibrium $\tilde{E}$ of the original system is globally asymptotically stable if $\mathcal{R}_0^2>1$ and $\mathcal{R}_0^3<1$. □

Theorem 9. *The endemic equilibrium* $E^* := \left(S^*, I^*, R^*, S_p^*, I_p^*, R_p^*, S_b^*, I_b^*, R_b^*\right)$ *is globally asymptotically stable if* $\mathcal{R}_0^3>1$.

Proof. Let us now assume that the disease is endemic among bats and pigs, then NiV transmission occurs from both these two species. The subsystem (3c) for bats can be decoupled from the rest of the equations. Similarly to the previous theorems, we consider an equivalent system of (3c) by letting $N_b(t)=S_b(t)+I_b(t)+R_b(t)$. Then we get a system for bats that has the same structure as (8). Following Theorem 7, it can be shown that the endemic equilibrium (S_b^*, I_b^*, R_b^*) is a globally asymptotically stable equilibrium of the subsystem for bats. Substituting I_b^* into the subsystem (3b) for pigs we get a similar subsystem in Theorem 7. Following Theorem 7 we conclude that the endemic equilibrium E^* is globally asymptotically stable if $\mathcal{R}_0^3>1$. □

The results concerning the existence and stability of the equilibria are summarized in Table 2.

5. Numerical simulations

In this section, we perform numerical simulations to validate our model and to assess the efficiency of various possible intervention strategies. It is important to note that due to the low number and relatively small volume of outbreaks so far, available data on parameters and epidemic spread are rather scarce, hence, it is a difficult task to find data or give precise estimations regarding model parameters. It is worth mentioning that all numerical simulations were performed using *Wolfram Mathematica*.

5.1. Fitting to data from the 1998–99 outbreak in Malaysia

We start by fitting our model to real-world data. We have to note that due to the large number of parameters and the uncertainty of several parameter values, we cannot expect to obtain a single parameter set perfectly fitting the epidemic data. Our aim can rather be only to approximate reasonably well the real scenario and obtain parameter ranges such that the real parameter values fall into these ranges with a high probability. As an example, we chose the outbreak in early 1999 in the Malaysian state Negeri Sembilan [34]. In fact, the outbreak in Malaysia started in September 1998 and affected the three states Perak, Negeri Sembilan and Selangor inducing 265 cases of acute encephalitis with 105 deaths. However, as most cases occurred in the spring of 1999 in Negeri Sembilan, we only consider this period of the outbreak. An interesting characteristic of the epidemic was that the Muslim majority was not affected by the disease as it was mainly transmitted to humans by pigs, hence, we restrict our simulations to the Chinese minority [35,36].

We use Latin Hypercube Sampling to create a representative sample of parameter values and start a solution of model (1) with each of these 10,000 parameter sets. Then we use the least squares method to find the parameter values offering the best fit to real data regarding the cumulative number of infected. Fig. 3 shows the best fitting solution plotted along with epidemic data.

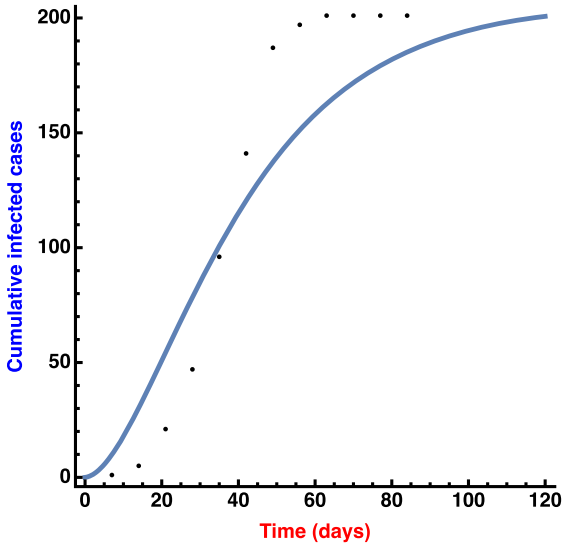


Fig. 3. The best fitting solution plotted with 12 weeks data for Negeri Sembilan state, Malaysia started from February 3, 1999.

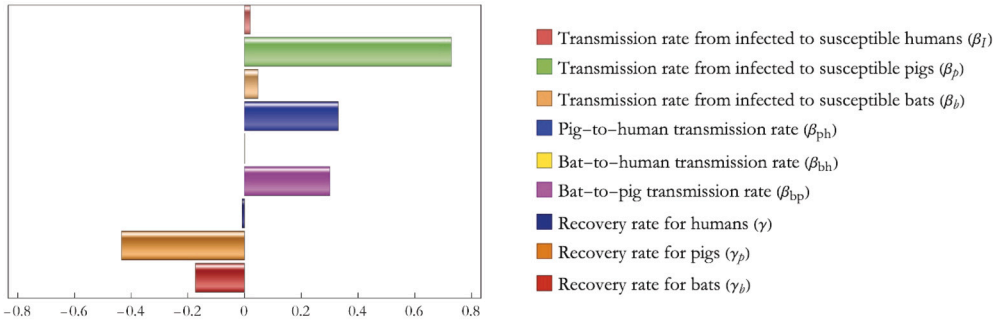


Fig. 4. Partial Rank Correlation Coefficients (PRCC).

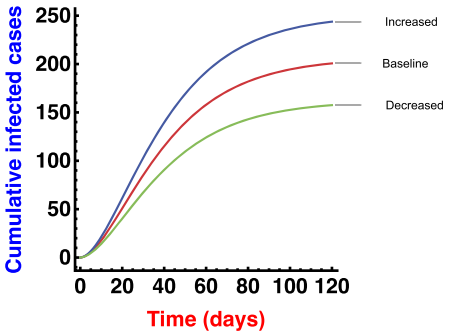
5.2. Sensitivity analysis

We have conducted another analysis using the Latin Hypercube Sampling along with the Partial Rank Correlation Coefficient (PRCC) method with $10,000$ Monte Carlo simulations per run. Using the variation of parameter values, the PRCC method assists us to quantify the effect of changing the various parameter values on the model's feedback, hence, establishing statistical relationships between the input parameters and the outcome value. Note that increasing parameters with positive PRCC values results in the growth of the number of cumulative cases, increasing parameters with negative PRCC will result in a smaller number of cumulative cases. Furthermore, parameters with larger PRCC values are regarded to be most critical for the model.

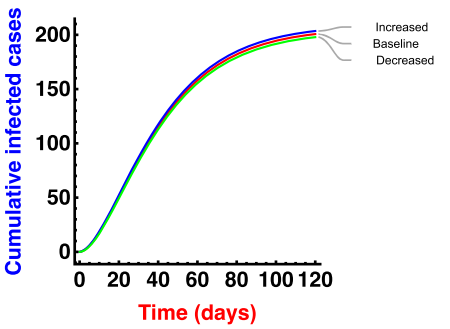
The input parameters considered for our PRCC analysis included all transmission rates $(\beta_I, \beta_p, \beta_b, \beta_{ph}, \beta_{bh}, \beta_{bp})$ and recovery rates $(\gamma, \gamma_p, \gamma_b)$ while the output parameter was chosen as the cumulative number of infected until the end of the time period under consideration in the fitting. The results obtained and shown in Fig. 4 demonstrate that the parameters with the largest effect are transmission from infected pigs to susceptible pigs β_p, pigs-to-humans transmission rate β_{ph}, bats-to-pigs transmission rate β_{bp} and recovery rates for pigs γ_p. Hence, parameters related to the intermediate host of NiV, i.e. pigs are seen to be the most important parameters among those that might be subject to control measures.

5.3. Effect of possible control measures

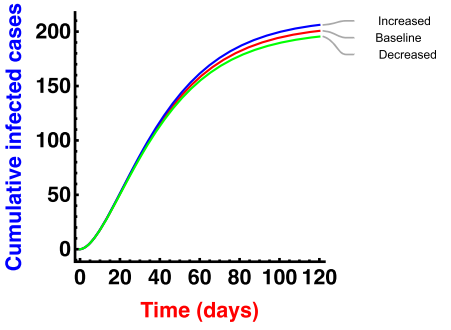
The PRCC analysis described in the previous section indicates us which might be the most efficient tools to reduce the number of infected. In this subsection, we investigate numerically the extent of changes in the number of cases caused by modifying model parameters corresponding to various intervention measures. In Fig. 5 we plot the cumulative number of infected humans for three different values of selected parameters, while the rest of the parameters are the values obtained in the fitting and shown in Table 3. Fig. 5a suggests that decreasing transmission from pigs to humans may contribute significantly to a decrease in the number of human infections. On the other hand, Figs. 5b and 5c suggest that transmission from bats and transmission among humans has a smaller importance than transmission from pigs. Finally, Fig. 5d shows that increasing the pigs' death rate by introducing their culling should also be an efficient tool to prevent further infections among humans.



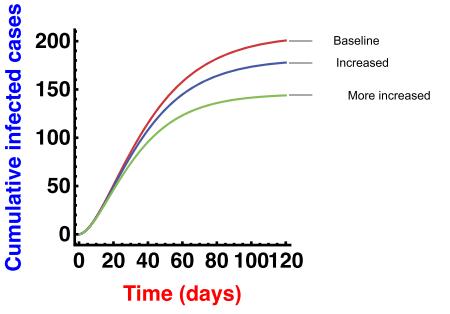
(a) Number of infected cases for various values of β_{ph}. Baseline $= 4.52495 \times 10^{-6}$, Increased $= 5.52495 \times 10^{-6}$, Decreased $= 3.52495 \times 10^{-6}$.



(b) Number of infected cases for various values of β_{bh}. Baseline $= 3.775596 \times 10^{-7}$, Increased $= 5.775596 \times 10^{-7}$, Decreased $= 1.775596 \times 10^{-7}$.



(c) Number of infected cases for various values of β_I. Baseline $= 1.3989714 \times 10^{-8}$, Increased $= 2.3989714 \times 10^{-8}$, Decreased $= 0.3989714 \times 10^{-8}$.



(d) Number of infected cases for various values of μ_p. Baseline $= 0.002747$, Increased $= 0.005556$, More increased $= 0.011111$.

Fig. 5. Cumulative infected cases for various values of disease parameters.

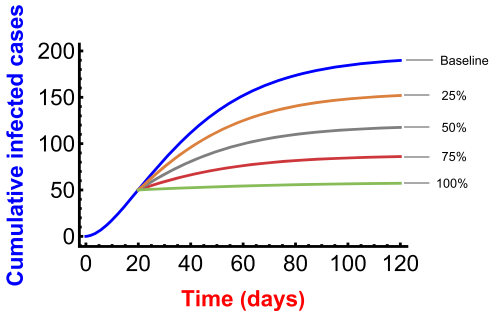
It is important to emphasize, that these results confirming the important role of pigs in disease transmission are not only in accordance with the results of the PRCC analysis but also with observations. Several studies confirm that the primary reason for human Nipah infection during 1998–1999 in Malaysia was the close contact with pigs, especially sick pigs though there might have been secondary exposures by other infected animals, see e.g. [12,37,38]. It is noteworthy that the outbreak in Malaysia was controlled by the culling of more than 1 million pigs in the outbreak area and immediately surrounding areas [39,40].

For this reason, we studied the impact of decreasing the number of pigs by culling at different rates (see Fig. 6). Culling was assumed here to be instantaneous. For this, we have continued our simulation for a given time period (in Fig. 6a 20 days, in Fig. 6b 40 days, in Fig. 6c 60 days from the beginning of the epidemic) and then imposed different rates of culling to see the degree of changes of cumulative infection. Fig. 6 suggests that culling has a notable influence on reducing disease burden. Fig. 6 also shows the importance of timely interventions. The effects of interventions in an early period of the epidemic are much more significant than those of control measures introduced later. E.g., a complete culling of pigs may decrease the number of infected by approximately to its quarter if done after 20 days, to its half if done after 40 days, and to three quarters after 60 days. In the latter case, there is only a small difference in the results obtained by culling different fractions of the pig population, while if the interventions are introduced earlier, higher culling rates provide significantly better results in decreasing the cumulative number of infected.

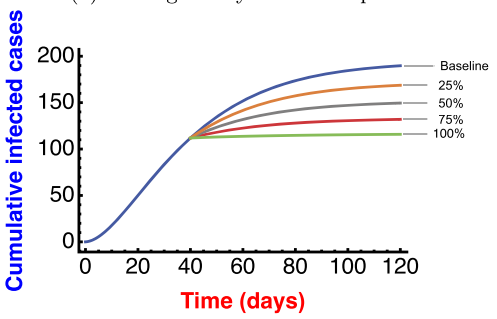
6. Conclusions and limitations

In this work, we established a compartmental model to describe the spread of Nipah virus infection. The main novelties of the model are the inclusion of the role of the reservoir species fruit bats and the intermediate host pigs as well as the loss of immunity of recovered individuals, assuming that intraspecies transmission is only one-directional, from bats to pigs and humans and from pigs to humans. The latter property allowed us to decouple first the equations for bats, then those for pigs, to arrive at a limit equation for humans. Both the limit subsystem for pigs and the one for humans yield us a novel type of model with a linear term describing the movement from susceptibles to infected due to intraspecies transmission.

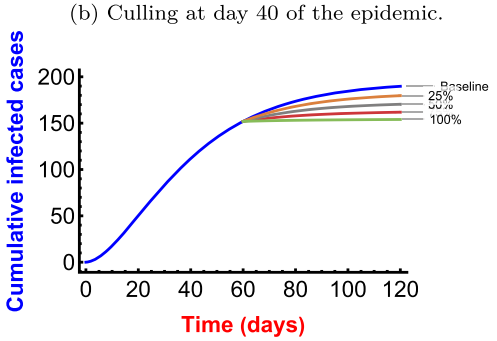
We determined all possible equilibria of the system and calculated three threshold parameters which determine the global dynamics of the system by determining in which of the three species the disease becomes endemic. By providing appropriate Lyapunov functions, we were able to completely describe the global dynamics of our model. We note that the novel structure of the limit systems mentioned in the previous paragraph demanded the construction of a novel Lyapunov function.



(a) Culling at day 20 of the epidemic.



(b) Culling at day 40 of the epidemic.



(c) Culling at day 60 of the epidemic.

Fig. 6. Number of cumulative infected cases for various culling rates of pigs and different time of culling.

We also performed numerical studies to validate our model, to determine the key parameters regarding disease transmission, and to study the effect of possible intervention measures. Our results suggest that the most important parameters are those related to the intermediate host pigs, which is in accordance with observations during the 1998–99 Malaysian outbreak.

Our study certainly has its limitations. For technical reasons, we chose to include only three compartments for each of the three species. A more realistic description of the disease would include an exposed compartment. Temperature, humidity, and climatic conditions may impact Nipah virus survival and transmission. Higher temperatures and increased rainfall can potentially boost virus dissemination, leading to elevated infection rates. Consideration of these environmental parameters might be an element of future studies. The numerical study of the model is made difficult by the limited knowledge regarding various disease parameters. The study of an extended system and its application to more fully known data might be subject of a future work.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Table 3
Parameters for model (1) providing the best fit.

Parameter	Baseline (Range)	Unit	Source
Λ	6.69852	day^{-1}	[41]
Λ_b	0.411	day^{-1}	Assumed
Λ_p	300.3	day^{-1}	[39]
μ	0.0000379	day^{-1}	[41]
μ_b	0.00013699	day^{-1}	Assumed
μ_p	0.002747	day^{-1}	[42]
β_I	$1.39897 \times 10^{-8} (2.0 \times 10^{-9}, 1.0 \times 10^{-7})$	day^{-1}	[23]
β_p	1.20377×10^{-7} $(0.0000000671, 0.000001857)$	day^{-1}	Fitted
β_b	0.0000155344 (0.00000671, 0.00001857)	day^{-1}	[43]
β_{ph}	4.52495×10^{-6} $(2.0 \times 10^{-7}, 2.0 \times 10^{-5})$	day^{-1}	Fitted
β_{bh}	3.7756×10^{-7} $(1.0 \times 10^{-8}, 1.0 \times 10^{-6})$	day^{-1}	Fitted
β_{bp}	1.67739×10^{-6} $(1.0 \times 10^{-7}, 1.0 \times 10^{-5})$	day^{-1}	Fitted
θ	0.00153737 (0.033, 0.001)	day^{-1}	Fitted
θ_p	0.000651486 (0.001, 0.00033)	day^{-1}	Fitted
θ_b	0.000444376 (0.001, 0.00033)	day^{-1}	[43]
γ	0.0225626 (0.015625, 0.03125)	day^{-1}	[1]
γ_p	0.0692084 (0.01, 0.1)	day^{-1}	[6]
γ_b	0.0750248 (0.01, 0.1)	day^{-1}	Fitted
δ	0.0436999 (0.015625, 0.046875)	day^{-1}	[6]
δ_p	0.000374955 (0.0001, 0.001)	day^{-1}	[44]
δ_b	0.000622043 (0.0001, 0.001)	day^{-1}	Fitted

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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