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Research article

Analysis and Bayesian estimation of a model for Chikungunya dynamics with relapse: An outbreak in Acapulco, Mexico

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Abstract: Chikungunya is a vector-borne viral disease transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. It does not have any specific treatment, and there is no vaccine. Recent epidemiological data have indicated that a relapse of the infection can occur within three months of the initial infection; however, until now, mathematical models for the spread of the disease have not considered this factor. We propose a mathematical model for the transmission of the Chikungunya virus that considers relapse. We calculated the basic reproductive number (R_0) of the disease by using the next-generation operator method. We proved the existence of a forward bifurcation. We determined the existence and the global stability of the equilibrium points by using the Lyapunov function method. We fitted the model to data from an outbreak in 2015 in Acapulco, Mexico to estimate the model parameters and R_0 with the Bayesian approach via a Hamiltonian Monte Carlo method. In the local sensitivity analysis, we found that the fraction of infected individuals who become asymptomatic has a strong impact on the basic reproductive number and makes some control measures insufficient. The impact of the fraction of infected individuals who become asymptomatic should be considered in Chikungunya control strategies.

Keywords: Chikungunya virus outbreaks; bifurcation analysis; direct Lyapunov method; Bayesian estimation; local sensitivity analysis

1. Introduction

Chikungunya fever is a viral disease caused by an arboviral alphavirus transmitted to humans by *Aedes* mosquitoes, mainly *Aedes aegypti* and *Aedes albopictus* mosquitoes. These vectors are widely distributed in the Americas. In 1952, this virus was first isolated and described in humans in Tanzania; it was identified in the Americas in 2013, and in Mexico one year later [1].

Once an infected mosquito bites a person, the disease has an incubation period between 3 and 7 days. The symptoms are severe joint pain (arthralgia) and high fever (above 39°C); they also include occasional nausea, myalgia (muscle pain), vomiting and rash [2]. This joint pain is usually debilitating, affecting the quality of life of the patient, but the persistence of the symptoms has not been thoroughly studied.

In 2008, Dumont et al. proposed a host-vector model that considers the aquatic phase of the mosquito for Chikungunya disease; they also studied the local and global stability of the equilibrium points, fitted the model to epidemiological data from four cities in France and estimated the basic reproductive numbers of the outbreak [3]. Subsequently, Dumont et al developed a model that incorporates a combination of the early use of massive fumigation and mechanical control (such as the destruction of breeding sites) and concluded that it can be effective in stopping or containing the spread of Chikungunya infections with minimal environmental impact [4]. In 2012, Ruiz-Moreno et al. developed a climate-based stochastic model of mosquito population dynamics with an epidemiological model to identify temporal windows that carry epidemic risk they found that, in places with a marked seasonal variation in temperature, there was also an epidemic risk season that coincided with the period of the year in which mosquito populations survive and grow [5]. In 2019, González-Parra et al. analyzed an SEIRC-SEI model with intrinsic and extrinsic incubation periods for the dynamics of the transmission of Chikungunya that considers a constant human population and vectors. They studied the global stability of the disease-free and endemic equilibriums by using the second method of Lyapunov and they used bootstrapping and Markov chain Monte Carlo techniques to estimate some model parameters and the basic reproductive number for an outbreak in Colombia [6]. Abboubakar et al. included density-dependent rates and some control mechanisms in existing Chikungunya models. Their model presents a backward bifurcation, and the least squares method was used to estimate the basic reproductive number of an outbreak that occurred in Chad and Cameroon [7].

The phenomenon of relapse has been reported for Chikungunya infections [8–12]. Relapse is defined as the reappearance of arthralgia due to virus' persistence in the cells of the musculoskeletal tissue after a symptom-free period of at least one week [8], or after one month [12]. A cohort study based on data from a laboratory-based surveillance system in France was performed; the initial infection was confirmed via an antibody or polymerase chain reaction (PCR) testing. In this study, relapses of arthralgia were reported in 72% of patients; the mean number of relapses was four and the mean time between two relapses was 8 weeks [8]. On the other hand, a cross-sectional study of Acapulco in southern Mexico in December 2015 was performed; 66% of the population (3531 out of 5870 people) self-reported that they had been infected; 31.1% of those who suffered from Chikungunya (1098 out of 3531 people) reported at least one relapse at least 1 month after they recovered from the disease, 13% reported exactly one relapse, 12% reported two relapses, 4% reported three relapses and just 2% reported more than four relapses [12].

The relapse phenomenon has not been incorporated into the host-vector models for Chikungunya

infections in the mathematical epidemiology literature. For this reason, the objectives of our study were to incorporate relapses into the standard model for Chikungunya, and to study the effect of the relapse rate on Chikungunya outbreaks. Finally, using the data collected in [12] that consisted of self-reported Chikungunya cases per month in Acapulco, Mexico, we have estimated several model parameters and the basic reproductive number of the infection.

In the present paper we address a Chikungunya model with relapse. We have made the following contributions:

- We extended the standard host-vector model of Chikungunya to incorporate the relapse phenomenon.
- The global stability of the disease-free equilibrium and the endemic equilibrium has been analyzed using the method of Lyapunov functions.
- We performed Bayesian estimates of the model parameters and the basic reproductive number of a Chikungunya outbreak in Acapulco, Mexico.
- Local sensitivity analysis was performed to measure the relative change of basic reproductive number for each parameter.

This paper is organized as follows: In Section 2, we will propose a Chikungunya model with relapse. In Section 3, we will compute the equilibria and basic reproductive number, and we will analyze the bifurcation that occurs at the disease-free equilibrium point as well as the global stability of the disease-free and endemic equilibrium points. In Section 4, we will fit the model to data from an outbreak in 2015 in Acapulco, Mexico to estimate model parameters and the basic reproductive number (R_0) with the Bayesian approach by using the Hamiltonian Monte Carlo method. In Section 5, we will present the results of a local sensitivity analysis to describe the impact of the parameters on the R_0 value. Finally, Section 6 contains the concluding remarks.

2. Mathematical model

Let N_h and N_v be the total number of humans (hosts) and the total number of mosquitoes (vectors), respectively. Both populations are divided into mutually exclusive compartments that are dependent on each individual's epidemiological state. Humans are classified into four compartments:

1. *Susceptible humans (S_h):* We assume that all humans are born susceptible to the virus; then, the population in this compartment increases according to a constant rate μ_h and decreases due to natural death at the same rate. Additionally, the size of the susceptible population decreases when a susceptible human becomes an infected human after an infected mosquito bite ($\frac{\beta_h b}{N_h} S_h I_v$); thus, the number of new infections depends on the number of susceptible humans who are bitten by a mosquito per time unit b and the probability of an effective transmission from a vector to a human β_h. Consequently, the dynamics of the compartment of susceptible humans are given by the following equation:
$$S_h' = \mu_h N_h - \frac{\beta_h b}{N_h} S_h I_v - \mu_h S_h.$$
2. *Infected humans (I_h):* The number of infected humans increases when a mosquito bite effectively transmits the virus to a susceptible human according to the mechanism described above, and also when symptoms return after a symptom-free period, that is, the relapse period $1/\delta_h$. The number

of individuals in this compartment decreases when the symptomatology disappears (recovery rate γ) and due to natural death (μ_h). The number of infected humans is determined by the following equation:

$$I_h' = \frac{\beta_h b}{N_h} S_h I_v - (\mu_h + \gamma) I_h + \delta_h A_h.$$

3. *Asymptomatic humans (A_h):* A fraction p of infected individuals are assumed to undergo an asymptomatic period since a significant percentage of patients have relapsed after the initial infection. The number of asymptomatic humans increases at a rate $p\gamma$ and decreases due to natural death (μ_h) and when symptoms occur again at a rate δ_h. The reappearance of symptoms is due to the persistence of the virus in musculoskeletal tissue cells after a symptom-free period ($1/\delta_h$). This mechanism is suggested in [12]. As a result, the dynamics of the asymptomatic humans are described by

$$A_h' = p\gamma I_h - (\mu_h + \delta_h) A_h.$$

4. *Recovered humans* (R_h): A fraction $(1 - p)$ of infected individuals are assumed to undergo a full recovery with permanent immunity. The number of recovered humans increases at a rate $(1 - p)\gamma$ and decreases due to natural death (μ_h). This translates into the following equation:

$$R_h' = (1 - p)\gamma I_h - \mu_h R_h.$$

Mosquitoes are classified into two compartments:

1. *Susceptible vectors (S_v):* Because vertical transmission has not been reported, we assume that all mosquitoes are born without the virus. Additionally, we assume that the birth and death rates are the same (μ_v), and that consequently, the vector population is constant ($S_v + I_v = N_v$). As a susceptible mosquito can become infected only if it comes into contact with an individual who has the virus, it is supposed to become infected after biting an infected or asymptomatic human, because hosts in the second compartment still have a viral load in the cells of the musculoskeletal tissue. Therefore, analogous to transmission in humans, the rate of infection in vectors depends on the bites b and the transmission probability from humans to vectors β_v; under the hypothesis that there is less transmission by the asymptomatic humans than by infected humans, we introduce the non-negative parameter κ to moderate the fraction of transmission from asymptomatic humans to vectors. These assumptions give rise to the following equation:

$$S_v' = \mu_v N_v - \frac{\beta_v b}{N_h} S_v I_h - \frac{\kappa \beta_v b}{N_h} S_v A_h - \mu_v S_v.$$

2. *Infected vectors* (I_v): The number of infected mosquitoes increases according to the transmission mechanism described above and it decreases when infected mosquitoes die, since a mosquito never recovers and its life expectancy is not modified. Therefore, the number of infected mosquitoes is subject to the following equation:

$$I_v' = \frac{\beta_v b}{N_h} S_v I_h + \frac{\kappa \beta_v b}{N_h} S_v A_h - \mu_v I_v.$$

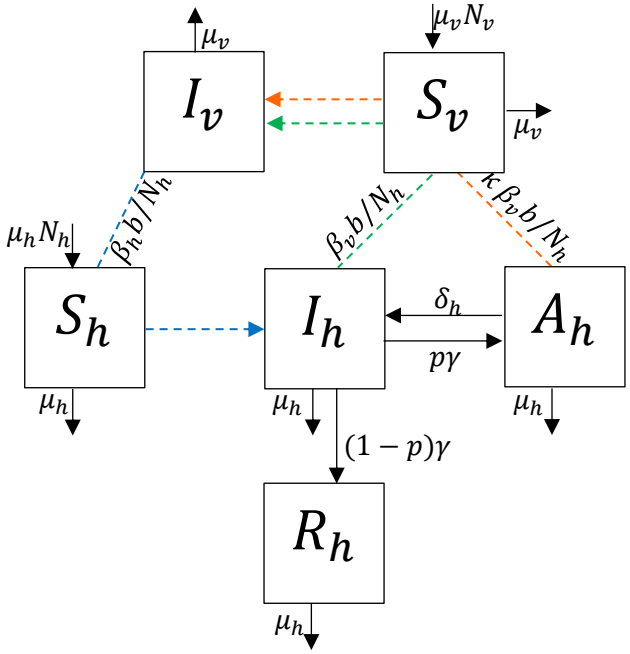

Figure 1. Schematic diagram of Chikungunya transmission model with relapse.

In summary, the dynamics between the hosts and vectors that determine the spread of Chikungunya (see Figure 1), including relapse, translate into the following system of ordinary differential equations:

$$\begin{aligned}
S_h' &= \mu_h N_h - \tfrac{\beta_h b}{N_h} S_h I_v - \mu_h S_h,\\
I_h' &= \tfrac{\beta_h b}{N_h} S_h I_v - (\mu_h + \gamma) I_h + \delta_h A_h,\\
A_h' &= p\gamma I_h - (\mu_h + \delta_h) A_h,\\
R_h' &= (1-p)\gamma I_h - \mu_h R_h,\\
S_v' &= \mu_v N_v - \tfrac{\beta_v b}{N_h} S_v I_h - \tfrac{\kappa\beta_v b}{N_h} S_v A_h - \mu_v S_v,\\
I_v' &= \tfrac{\beta_v b}{N_h} S_v I_h + \tfrac{\kappa\beta_v b}{N_h} S_v A_h - \mu_v I_v.
\end{aligned} \tag{2.1}$$

Here, both total populations are considered constant, so $N_h = S_h + I_h + A_h + R_h$ y $N_v = S_v + I_v$.

Under these conditions, system (2.1) can be written as follows:

$$\begin{aligned} S_h' &= \mu_h N_h - \tfrac{\beta_h b}{N_h} S_h I_v - \mu_h S_h, \\ I_h' &= \tfrac{\beta_h b}{N_h} S_h I_v - (\mu_h + \gamma) I_h + \delta_h A_h, \\ A_h' &= p\gamma I_h - (\mu_h + \delta_h) A_h, \\ I_v' &= \tfrac{\beta_v b}{N_h} (N_v - I_v)(I_h + \kappa A_h) - \mu_v I_v. \end{aligned} \tag{2.2}$$

3. Equilibria, basic reproductive number, bifurcation analysis, and global stability properties

We analyze the model given in (2.2) in the following epidemiologically feasible region:

$$\Delta = \left\{ (S_h, I_h, A_h, I_v) \in \mathbb{R}_+^4 : S_h + I_h + A_h \le N_h, I_v \le N_v \right\}.$$

System (2.2) contains two epidemiologically feasible equilibrium points in the non-negative orthant $\mathbb{R}_+^4$ according to direct calculation: the disease-free equilibrium $P_0 = (N_h, 0, 0, 0)$ and a unique endemic equilibrium $P^* = (S_h^*, I_h^*, A_h^*, I_v^*)$, with

$$\begin{aligned} S_h^* &= \frac{N_h(N_h N_v^{-1}\mu_h \hat{R}_0 + \beta_h b)}{\hat{R}_0(N_h N_v^{-1}\mu_h + \beta_h b)}, \\ I_h^* &= \left(\frac{\mu_h N_h(\mu_h + \delta_h)\beta_h b}{(\mu_h + \gamma)(\mu_h + \delta_h) - \delta_h p\gamma} \right) \left(\frac{\hat{R}_0 - 1}{\hat{R}_0(N_h N_v^{-1}\mu_h + \beta_h b)} \right), \\ A_h^* &= \left(\frac{\mu_h N_h \beta_h b p\gamma}{(\mu_h + \gamma)(\mu_h + \delta_h) - \delta_h p\gamma} \right) \left(\frac{\hat{R}_0 - 1}{\hat{R}_0(N_h N_v^{-1}\mu_h + \beta_h b)} \right), \\ I_v^* &= \frac{\mu_h N_h(\hat{R}_0 - 1)}{N_h N_v^{-1}\mu_h \hat{R}_0 + \beta_h b}, \end{aligned} \tag{3.1}$$

where

$$\hat{R}_0 = \frac{\beta_h \beta_v b^2 N_v(\kappa p\gamma + \mu_h + \delta_h)}{N_h \mu_v[(\mu_h + \gamma)(\mu_h + \delta_h) - \delta_h p\gamma]}. \tag{3.2}$$

For the computation of the basic reproductive number, we use the next-generation operator method introduced in [13]. The notation is as follows: F is a non-negative matrix of the new transmission terms, and V is an M-matrix of the transition terms for individuals between compartments. For system (2.2), the matrices F and V are, respectively,

$$F = \begin{pmatrix} 0 & 0 & \beta_h b \\ 0 & 0 & 0 \\ \frac{\beta_v b N_v}{N_h} & \frac{\kappa\beta_v b N_v}{N_h} & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \mu_h + \gamma & -\delta_h & 0 \\ -p\gamma & \mu_h + \delta_h & 0 \\ 0 & 0 & \mu_v \end{pmatrix}.$$

It follows that the basic reproductive number, denoted by $R_0 = \rho(FV^{-1})$, where ρ is the spectral radius, is given by

$$R_0 = \sqrt{\hat{R}_0}. \tag{3.3}$$

In the following subsections, without loss of generality, we present the bifurcation and global stability results in terms of the threshold quantity $\hat{R}_0$.

3.1. Forward bifurcation

It is easy to prove that the disease-free equilibrium P_0 is non-hyperbolic when $\hat{R}_0 = 1$ since one of its eigenvalues vanishes; consequently, in this case, a bifurcation could occur. This subsection shows that this is indeed the case. For this purpose, Theorem 4.1 of [14] will be used.

First, the abbreviated set of equations in (2.2) is rewritten in the following form:

$$\begin{aligned}
\frac{dx_1}{dt} &= \mu_h N_h - \frac{\beta_h b}{N_h} x_1 x_4 - \mu_h x_1, \\
\frac{dx_2}{dt} &= \frac{\beta_h b}{N_h} x_1 x_4 - (\mu_h + \gamma)\, x_2 + \delta_h x_3, \\
\frac{dx_3}{dt} &= p\gamma x_2 - (\mu_h + \delta_h)\, x_3, \\
\frac{dx_4}{dt} &= \frac{\beta_v b}{N_h} (N_v - x_4)\, (x_2 + \kappa x_3) - \mu_v x_4,
\end{aligned} \tag{3.4}$$

to which the following new variables have been introduced:

$$x_1 \equiv S_h, \quad x_2 \equiv I_h, \quad x_3 \equiv A_h, \quad x_4 \equiv I_v.$$

If we assume that $\beta_v = \xi\beta_h$ and $\phi \equiv \beta_h b$ is the bifurcation parameter, system (3.4) can take the following form:

$$\begin{aligned}
\frac{dx_1}{dt} &= \mu_h N_h - \frac{\phi}{N_h} x_1 x_4 - \mu_h x_1 \equiv f_1, \\
\frac{dx_2}{dt} &= \frac{\phi}{N_h} x_1 x_4 - \alpha_1 x_2 + \delta_h x_3 \equiv f_2, \\
\frac{dx_3}{dt} &= p\gamma x_2 - \alpha_2 x_3 \equiv f_3, \\
\frac{dx_4}{dt} &= \frac{\xi\phi}{N_h} (N_v - x_4)\, (x_2 + \kappa x_3) - \mu_v x_4 \equiv f_4,
\end{aligned} \tag{3.5}$$

where we have made the following identifications:

$$\alpha_1 \equiv \mu_h + \gamma \quad \text{and} \quad \alpha_2 \equiv \mu_h + \delta_h, \tag{3.6}$$

and the components of the vector field of (3.5) have been denoted by f_i, with $i = 1, ..., 4$. When $\hat{R}_0 = 1$, we write $\phi = \phi^*$, which, according to (3.2), satisfies the following relationship:

$$1 = \frac{\xi\, (\phi^*)^2\, N_v\, (\kappa p\gamma + \mu_h + \delta_h)}{N_h \mu_v \left[(\mu_h + \gamma)\, (\mu_h + \delta_h) - \delta_h p\gamma \right]}. \tag{3.7}$$

The Jacobian matrix of system (3.5), evaluated at the equilibrium point P_0 when $\phi = \phi^*$, is given as

$$J(P_0) = \begin{pmatrix}
-\mu_h & 0 & 0 & -\phi^* \\
0 & -\alpha_1 & \delta_h & \phi^* \\
0 & p\gamma & -\alpha_2 & 0 \\
0 & \xi\phi^* \frac{N_v}{N_h} & \kappa\xi\phi^* \frac{N_v}{N_h} & -\mu_v
\end{pmatrix}. \tag{3.8}$$

It can easily be shown that this matrix has a zero eigenvalue.

According to the procedure described in [14], the eigenvector corresponding to this zero eigenvalue is

$$w = \frac{1}{\alpha_1 + \alpha_2 + \frac{\xi(\phi^*)^2 N_v(\kappa p\gamma + \alpha_2 - \mu_v)}{N_h \mu_v^2}} \begin{pmatrix} -\frac{\phi^*}{\mu_h} \\ \frac{\phi^* \alpha_2}{\alpha_1\alpha_2 - \delta_h p\gamma} \\ \frac{p\gamma\phi^*}{\alpha_1\alpha_2 - \delta_h p\gamma} \\ 1 \end{pmatrix}, \tag{3.9}$$

while the left eigenvector corresponding to the same eigenvalue of the transpose of the matrix in (3.8) is

$$v = \frac{\alpha_1\alpha_2 - \delta_h p\gamma}{\phi^*} \begin{pmatrix} 0 \\ 1 \\ \frac{1}{p\gamma}\left[\alpha_1 - \frac{\xi(\phi^*)^2 N_v}{\mu_v N_h}\right] \\ \frac{\phi^*}{\mu_v} \end{pmatrix}. \tag{3.10}$$

Both vectors satisfy the condition that $w \cdot v = 1$. The nonzero second partial derivatives of the components f_i are given by

$$\frac{\partial^2 f_2(P_0)}{\partial x_1 \partial x_4} = \frac{\partial^2 f_2(P_0)}{\partial x_4 \partial x_1} = \frac{\phi}{N_h}, \quad \frac{\partial^2 f_4(P_0)}{\partial x_2 \partial x_4} = \frac{\partial^2 f_4(P_0)}{\partial x_4 \partial x_2} = -\frac{\xi\phi}{N_h},$$
$$\frac{\partial^2 f_4(P_0)}{\partial x_3 \partial x_4} = \frac{\partial^2 f_4(P_0)}{\partial x_4 \partial x_3} = -\frac{\kappa\xi\phi}{N_h} \tag{3.11}$$

and

$$\frac{\partial^2 f_2(P_0)}{\partial x_4 \partial \phi} = 1, \quad \frac{\partial^2 f_4(P_0)}{\partial x_2 \partial \phi} = \frac{\xi N_v}{N_h}, \quad \frac{\partial^2 f_4(P_0)}{\partial x_3 \partial \phi} = \frac{\kappa\xi N_v}{N_h}. \tag{3.12}$$

Thus, the quantities a and b as indicated in Theorem 4.1 of [14] and written in terms of the previous derivatives, are, respectively,

$$a = 2v_2 w_1 w_4 \frac{\phi}{N_h} - 2v_4 w_4 (w_2 + \kappa w_3) \frac{\xi\phi}{N_h} \tag{3.13}$$

and

$$b = v_2 w_4 + v_4 (w_2 + \kappa w_3) \frac{\xi N_v}{N_h}, \tag{3.14}$$

where w_1, w_2, w_3 and w_4 are the first, second, third and fourth components of the eigenvector in (3.9); meanwhile, v_2 and v_4 are the first and fourth components of the left eigenvector given in (3.10).

It can be shown that, according to the Routh-Hurwitz stability criterion, to guarantee the local asymptotic stability of P_0 when $\hat{R}_0 < 1$, the following relations must be satisfied:

$$\alpha_1\alpha_2 - \delta_h p\gamma > 0 \tag{3.15}$$

and

$$\alpha_1 + \alpha_2 - \frac{\hat{R}_0(\alpha_1\alpha_2 - \delta_h p\gamma)}{\kappa p\gamma + \alpha_2} > 0. \tag{3.16}$$

Based on relations (3.7), (3.15) and (3.16), it can be shown that $w_1 < 0$, $w_2 > 0$, $w_3 > 0$ and $w_4 > 0$, while $v_1 > 0$, $v_2 > 0$ and $v_4 > 0$. Thus, according to (3.13) and (3.14), we have that $a < 0$ and $b > 0$.

Therefore, since $a < 0$ and $b > 0$, part iv of Theorem 4.1 in [14] must hold. Alternatively, this result can be formulated as follows.

Theorem 3.1. *The disease-free equilibrium point $P_0 = (N_h, 0, 0, 0)$, when $\hat{R}_0 = 1$, presents a forward bifurcation.*

As a consequence of this result, when $\hat{R}_0 > 1$, there is a family of asymptotically stable infected equilibrium points, which we will denote as $P^* = \left(S_h^*, I_h^*, A_h^*, I_v^*\right)$, constituting the upper branch of these types of bifurcations.

3.2. Global stability of the disease-free equilibrium

We obtained some conditions on the global stability of the disease-free equilibrium of system (2.2) by using the method of Lyapunov functions. The usual process to construct a Lyapunov function for a disease-free equilibrium in epidemic or intra-host viral infection models is to introduce the Volterra-type function to the susceptible compartment and linear functions to the other compartments, and to determine the constants to guarantee the negativity of the derivative of the Lyapunov function along trajectories.

Theorem 3.2. *If $\hat{R}_0 \leq 1$, then the disease-free equilibrium $P_0 = (N_h, 0, 0, 0)$ of system (2.2) is globally asymptotically stable in Δ.*

Proof. We construct the following Lyapunov function for system (2.2):

$$V(S_h, I_h, A_h, I_v) = \left(S_h - N_h - N_h \ln \frac{S_h}{N_h}\right) + I_h + \frac{1}{\mu_h + \delta_h}\left(\delta_h + \frac{\beta_h \beta_v b^2}{N_h \mu_v}\kappa N_v\right) A_h + \frac{\beta_h b}{\mu_v} I_v. \tag{3.17}$$

The function $V(t)$ is defined, continuous and positive definite for all $S_h, I_h, A_h, I_v \geq 0$. Additionally, the global minimum $V(S_h, I_h, A_h, I_v) = 0$ occurs at $P_0 = (N_h, 0, 0, 0)$, and, therefore, V is a Lyapunov

function. By calculating its derivative along the solution of (2.2), we obtain

$$\begin{aligned}
\frac{d}{dt}V(S_h, I_h, A_h, A_v) &= \left(1 - \frac{N_h}{S_h}\right)\frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{1}{\mu_h + \delta_h}\left(\delta_h + \frac{\beta_h\beta_v b^2}{N_h\mu_v}\kappa N_v\right)\frac{dA_h}{dt} + \frac{\beta_h b}{\mu_v}\frac{dI_v}{dt} \\
&= \left(\frac{S_h - N_h}{S_h}\right)\left(\mu_h N_h - \frac{\beta_h b}{N_h}S_h I_v - \mu_h S_h\right) \\
&+ \left(\frac{\beta_h b}{N_h}S_h I_v - (\mu_h + \gamma)I_h + \delta_h A_h\right) \\
&+ \frac{1}{\mu_h + \delta_h}\left(\delta_h + \frac{\beta_h\beta_v b^2}{N_h\mu_v}\kappa N_v\right)(p\gamma I_h - (\mu_h + \delta_h)A_h) \\
&+ \frac{\beta_h b}{\mu_v}\left(\frac{\beta_v b}{N_h}(N_v - I_v)(I_h + \kappa A_h) - \mu_v I_v\right) \\
&= -\mu_h\frac{(S_h - N_h)^2}{S_h} \\
&+ \left[\frac{p\gamma}{\mu_h + \delta_h}\left(\delta_h + \frac{\beta_h\beta_v b^2}{N_h\mu_v}\kappa N_v\right) + \frac{\beta_h\beta_v b^2}{N_h\mu_v} - (\mu_h + \gamma)\right]I_h \\
&- \frac{\beta_h\beta_v b^2}{N_h\mu_v}(I_h + \kappa A_h)I_v, \\
&= -\mu_h\frac{(S_h - N_h)^2}{S_h} - \left[\frac{(\mu_h + \gamma)(\mu_h + \delta_h) - \delta_h p\gamma}{\mu_h + \delta_h}\right]\left(1 - \hat{R}_0\right)I_h - \frac{\beta_h\beta_v b^2}{N_h\mu_v}(I_h + \kappa A_h)I_v.
\end{aligned}$$

If $\hat{R}_0 \leq 1$, then $dV/dt \leq 0$. Note that $dV/dt = 0$ if and only if $S_h = N_h$, $I_h = 0$ and $I_v = 0$ or if $\hat{R}_0 = 1$, $S_h = N_h$ and $I_v = 0$. Therefore, the largest compact invariant set in $\{(S_h, I_h, A_h, I_v) : dV/dt = 0\}$ is the singleton $\{P_0\}$. By the classical LaSalle invariance principle (Theorem 5.3 of [15]), P_0 is globally asymptotically stable in Δ if $\hat{R}_0 \leq 1$. □

3.3. Global stability of the endemic equilibrium point

We consider the global asymptotic stability of a unique endemic equilibrium P^* by using linear combinations of Volterra-type functions. The usual process to construct a Lyapunov function for a positive equilibrium in epidemic [16–19] or intra-host viral infection [20] models is to propose the use of the Volterra-type function, and to determine the constants to guarantee the negativity of the derivative of the Lyapunov function along trajectories.

Theorem 3.3. *If $\hat{R}_0 > 1$, then the endemic equilibrium $P^* = \left(S_h^*, I_h^*, A_h^*, I_v^*\right)$ of system (2.2) is globally asymptotically stable in int(Δ).*

Proof. Define $L : int(\mathbb{R}_+^4) \to \mathbb{R}_+$:

$$\begin{aligned}
L(S_h, I_h, A_h, I_v) &= (I_h^* + \kappa A_h^*)\left(S_h - S_h^* - S_h^*\ln\frac{S_h}{S_h^*}\right) \\
&+ (I_h^* + \kappa A_h^*)\left(I_h - I_h^* - I_h^*\ln\frac{I_h}{I_h^*}\right) \\
&+ \frac{1}{p\gamma I_h^*}\left(\delta_h A_h^*(I_h^* + \kappa A_h^*) + \frac{\kappa\beta_h b}{N_h}S_h^* I_v^* A_h^*\right)\left(A_h - A_h^* - A_h^*\ln\frac{A_h}{A_h^*}\right)
\end{aligned}$$

$$+\frac{\beta_h S_h^* I_v^*}{\beta_v (N_v - I_v^*)}\left(I_v - I_v^* - I_v^* \ln \frac{I_v}{I_v^*}\right).$$

The function $L(t)$ is defined, continuous and positive definite for all $S_h, I_h, A_h, I_v \geq 0$. Additionally, the global minimum $L(S_h, I_h, A_h, I_v) = 0$ occurs at $P^* = (S_h^*, I_h^*, A_h^*, I_v^*)$, and, therefore, L is a Lyapunov function. We calculate the time derivative of $L(t)$:

$$\begin{aligned}
\frac{dL(t)}{dt} &= (I_h^* + \kappa A_h^*)\left(1 - \frac{S_h^*}{S_h}\right)\left[\mu_h N_h - \frac{\beta_h b}{N_h} S_h I_v - \mu_h S_h\right] \\
&+ (I_h^* + \kappa A_h^*)\left(1 - \frac{I_h^*}{I_h}\right)\left[\frac{\beta_h b}{N_h} S_h I_v - (\mu_h + \gamma) I_h + \delta_h A_h\right] \\
&+ \frac{1}{p\gamma I_h^*}\left(\delta_h A_h^* (I_h^* + \kappa A_h^*) + \frac{\kappa \beta_h b}{N_h} S_h^* I_v^* A_h^*\right)\left(1 - \frac{A_h^*}{A_h}\right)[p\gamma I_h - (\mu_h + \delta_h) A_h] \\
&+ \frac{\beta_h S_h^* I_v^*}{\beta_v (N_v - I_v^*)}\left(1 - \frac{I_v^*}{I_v}\right)\left(\frac{\beta_v b}{N_h}(N_v - I_v^*) I_h^* \frac{I_h}{I_h^*} + \kappa \frac{\beta_v b}{N_h}(N_v - I_v^*) A_h^* \frac{A_h}{A_h^*} - \mu_v I_v^* \frac{I_v}{I_v^*}\right) \\
&+ \frac{\beta_h S_h^* I_v^*}{\beta_v (N_v - I_v^*)} \frac{\beta_v b}{N_h} I_v^* \left(2 - \frac{I_v^*}{I_v} - \frac{I_v}{I_v^*}\right)(I_h + \kappa A_h).
\end{aligned}$$

The coordinates S_h^*,I_h^*, A_h^* and I_v^* of the endemic equilibrium (3.1) satisfy the following equations:

$$\begin{aligned}
\mu_h N_h &= \frac{\beta_h b}{N_h} S_h^* I_v^* + \mu_h S_h^*, \\
\mu_h + \gamma &= \frac{\beta_h b}{N_h} S_h^* \frac{I_v^*}{I_h^*} + \delta_h \frac{A_h^*}{I_h^*}, \\
\mu_h + \delta_h &= p\gamma \frac{I_h^*}{A_h^*}, \\
\mu_v I_v^* &= \frac{\beta_v b}{N_h}(N_v - I_v^*)(I_h^* + \kappa A_h^*).
\end{aligned} \tag{3.18}$$

Using the identities given in (3.18), we have

$$\begin{aligned}
\frac{dL(t)}{dt} &= (I_h^* + \kappa A_h^*)\left[\mu_h S_h^*\left(2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*}\right) + \frac{\beta_h b}{N_h} S_h^* I_v^*\left(1 - \frac{S_h^*}{S_h} - \frac{S_h I_v}{S_h^* I_v^*} + \frac{I_v}{I_v^*}\right)\right] \\
&+ (I_h^* + \kappa A_h^*)\left[\frac{\beta_h b}{N_h} S_h^* I_v^*\left(1 + \frac{S_h I_v}{S_h^* I_v^*} - \frac{I_h}{I_h^*} - \frac{I_h^*}{I_h}\frac{S_h I_v}{S_h^* I_v^*}\right) + \delta_h A_h^*\left(1 + \frac{A_h}{A_h^*} - \frac{I_h}{I_h^*} - \frac{A_h}{A_h^*}\frac{I_h^*}{I_h}\right)\right] \\
&+ \frac{1}{p\gamma I_h^*}\left(\delta_h A_h^* (I_h^* + \kappa A_h^*) + \frac{\kappa \beta_h b}{N_h} S_h^* I_v^* A_h^*\right)\left[p\gamma I_h^*\left(1 + \frac{I_h}{I_h^*} - \frac{A_h}{A_h^*} - \frac{A_h^*}{A_h}\frac{I_h}{I_h^*}\right)\right] \\
&+ \frac{\beta_h S_h^* I_v^*}{\beta_v (N_v - I_v^*)}\left[\frac{\beta_v b}{N_h}(N_v - I_v^*) I_h^*\left(1 - \frac{I_v^* I_h}{I_v I_h^*} + \frac{I_h}{I_h^*} - \frac{I_v}{I_v^*}\right) + \kappa \frac{\beta_v b}{N_h}(N_v - I_v^*) A_h^*\left(1 - \frac{I_v^* A_h}{I_v A_h^*} + \frac{A_h}{A_h^*} - \frac{I_v}{I_v^*}\right)\right] \\
&+ \frac{\beta_h S_h^* I_v^*}{\beta_v (N_v - I_v^*)} \frac{\beta_v b}{N_h} I_v^*\left(2 - \frac{I_v^*}{I_v} - \frac{I_v}{I_v^*}\right)(I_h + \kappa A_h).
\end{aligned}$$

After several calculations, we have

$$\begin{aligned}\frac{dL(t)}{dt} &= (I_h^* + \kappa A_h^*)\,\mu_h S_h^*\left(2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*}\right)\\ &+ (I_h^* + \kappa A_h^*)\,\frac{\beta_h b}{N_h} S_h^* I_v^*\left(2 - \frac{S_h^*}{S_h} - \frac{I_h}{I_h^*} - \frac{I_h^* S_h I_v}{I_h S_h^* I_v^*} + \frac{I_v}{I_v^*}\right)\\ &+ \delta_h A_h^*\,(I_h^* + \kappa A_h^*)\left(1 + \frac{A_h}{A_h^*} - \frac{I_h}{I_h^*} - \frac{A_h}{A_h^*}\frac{I_h^*}{I_h}\right)\\ &+ \left(\delta_h A_h^*\,(I_h^* + \kappa A_h^*) + \frac{\kappa\beta_h b}{N_h} S_h^* I_v^* A_h^*\right)\left(1 + \frac{I_h}{I_h^*} - \frac{A_h}{A_h^*} - \frac{A_h^*}{A_h}\frac{I_h}{I_h^*}\right)\\ &+ \frac{b\beta_h S_h^* I_v^* I_h^*}{N_h}\left(1 - \frac{I_v^* I_h}{I_v I_h^*} + \frac{I_h}{I_h^*} - \frac{I_v}{I_v^*}\right)\\ &+ \frac{\kappa b\beta_h S_h^* I_v^* A_h^*}{N_h}\left(1 - \frac{I_v^* A_h}{I_v A_h^*} + \frac{A_h}{A_h^*} - \frac{I_v}{I_v^*}\right)\\ &+ \frac{b\beta_h S_h^* (I_v^*)^2}{(N_v - I_v^*)\,N_h}\left(2 - \frac{I_v^*}{I_v} - \frac{I_v}{I_v^*}\right)(I_h + \kappa A_h).\end{aligned}$$

Therefore,

$$\begin{aligned}\frac{dL(t)}{dt} &= \mu_h S_h^*\,(I_h^* + \kappa A_h^*)\left(2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*}\right) + \frac{b\beta_h S_h^* (I_v^*)^2}{(N_v - I_v^*)\,N_h}\left(2 - \frac{I_v^*}{I_v} - \frac{I_v}{I_v^*}\right)(I_h + \kappa A_h)\\ &+ \frac{b\beta_h S_h^* I_v^* I_h^*}{N_h}\left(3 - \frac{S_h^*}{S_h} - \frac{I_v^* I_h}{I_v I_h^*} - \frac{I_h^* S_h I_v}{I_h S_h^* I_v^*}\right)\\ &+ \delta_h A_h^*\,(I_h^* + \kappa A_h^*)\left(2 - \frac{A_h^* I_h}{A_h I_h^*} - \frac{A_h I_h^*}{A_h^* I_h}\right)\\ &+ \frac{\kappa b\beta_h S_h^* I_v^* A_h^*}{N_h}\left(4 - \frac{S_h^*}{S_h} - \frac{I_v^* A_h}{I_v A_h^*} - \frac{A_h^* I_h}{A_h I_h^*} - \frac{I_h^* S_h I_v}{I_h S_h^* I_v^*}\right).\end{aligned}$$

The arithmetic mean is greater than the geometric mean, i.e., the terms $\left(2 - \frac{S_h^*}{S_h} - \frac{S_h}{S_h^*}\right)$, $\left(2 - \frac{I_v^*}{I_v} - \frac{I_v}{I_v^*}\right)$, $\left(3 - \frac{S_h^*}{S_h} - \frac{I_v^* I_h}{I_v I_h^*} - \frac{I_h^* S_h I_v}{I_h S_h^* I_v^*}\right)$, $\left(2 - \frac{A_h^* I_h}{A_h I_h^*} - \frac{A_h I_h^*}{A_h^* I_h}\right)$ and $\left(4 - \frac{S_h^*}{S_h} - \frac{I_v^* A_h}{I_v A_h^*} - \frac{A_h^* I_h}{A_h I_h^*} - \frac{I_h^* S_h I_v}{I_h S_h^* I_v^*}\right)$ are negative. Consequently, $dL/dt \leq 0$ for any coordinate values (S_h, I_h, A_h, I_v) and $dL/dt = 0$ if and only if $S_h = S_h^*$, $I_h = I_h^*$, $A_h = A_h^*$ and $I_v = I_v^*$. Therefore, the largest compact invariant set in $\{(S_h, I_h, A_h, I_v) : dL/dt = 0\}$ is the singleton $\{P^*\}$. If $\hat{R}_0 > 1$, by the classical LaSalle invariance principle (Theorem 5.3 of [15]), the endemic equilibrium P^* is globally asymptotically stable in $int(\Delta)$. □

4. Bayesian approach

4.1. Bayesian model

We consider the model

$$y_i = X_{\boldsymbol{\theta}}(t_i) + \varepsilon(t_i), \qquad i = 1, \ldots, n, \tag{4.1}$$

where y_i is the *i-th* observation of the data that represents the number of infected humans, $\boldsymbol{\theta} = (\beta_h, \beta_v, b, \mu_v, \gamma, p, \delta_h, \kappa, N_v)$ is the unknown vector of parameters of the model in (2.2) to estimate, $X_{\boldsymbol{\theta}}$

is the numerical solution of the system (2.2) for the state variable I_h according to the Runge–Kutta fourth-order method and $\varepsilon(t_i)$ is the random error. The Bayesian statistical model is used in situations in which the dynamics of the expected value $E(y_i) = X_{\boldsymbol{\theta}}(t_i)$ are described by the host-vector model and there is an error around it, i.e, $y_i - E(y_i) = \varepsilon(t_i)$. The errors in each measurement are assumed to be independent even if the expected values $E(y_i)$ follow the host-vector model.

We estimate $\boldsymbol{\theta}$ by using Bayesian inference, which allowed us to add previous information from the literature to the data to generate the distribution for each parameter in $\boldsymbol{\theta}$. According to Bayes' theorem,

$$P(\boldsymbol{\theta}|\boldsymbol{y}) \propto P(\boldsymbol{y}|\boldsymbol{\theta})P(\boldsymbol{\theta}),$$

where $P(\boldsymbol{\theta})$ is the prior distribution, $P(\boldsymbol{y}|\boldsymbol{\theta})$ is the likelihood function and $P(\boldsymbol{\theta}|\boldsymbol{y})$ is the posterior distribution. We assume that $\varepsilon(t_i) \sim N(0, \sigma^2)$ and $y_i \sim N(X_\theta(t_i), \sigma^2)$. The likelihood function is given by

$$P(\boldsymbol{y}|\boldsymbol{\theta}) = \prod_{i=1}^{n} \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{1}{2\sigma^2}\left(y_i - X_{\boldsymbol{\theta}}(t_i)\right)^2\right].$$

To choose the prior distributions, we conducted a literature review of the parameters β_h, β_v, b, μ_v and γ reported in host-vector models for Chikungunya [3–7], the relapse period $1/\delta_h$ from the epidemiological literature [8, 12] and the parameters of the town (Acapulco, Mexico) where the epidemic outbreak occurred (μ_h, N_h and N_v) [12,21]. The parameter values are given in the third column of Table 1. We used uniform densities for most of the parameters, whose support includes the values collected from the literature. We only use beta informative prior distributions for the transmission probability parameters. The prior distributions are given in the fourth column of Table 1. Cole [22] showed that the lack of identifiability results in a strong dependence on the prior information, and that, if you use informative prior information, the estimates will be close to the true parameter values.

To sample from the posterior distributions of nine parameters, we use the No-U-Turn-Sampler algorithm, which is a Hamiltonian Monte Carlo method. The reader is referred to [23] for a description of the method. Three independent Hamiltonian Monte Carlo chains were initialized with a random initial value and run with 20,000 iterations. For each parameter, we calculated the potential scale reduction factor, commonly known as Rhat [24]. Rhat values less than or equal to 1.2 indicate convergence to a stationary distribution. Furthermore, we verified that the trace plots showed good mixing. The libraries *DifferentialEquations* [25] and *turing* [26] of the Julia software [27] were used.

The Bayesian point estimators were the means of the posterior distributions corresponding to a minimization of the expected squared error loss function. The 95% credible interval (CrI) was calculated by using the 2.5th and 97.5th percentiles.

4.2. Bayesian estimation

In Table 2, we report the point and interval estimations of parameters and the basic reproductive number. We will discuss the convergence criteria of the Markov chain Monte Carlo method in the Appendix. The estimated fraction of infected individuals who become asymptomatic, p, was approximately 0.6536, and with a probability of 0.95, this value is between 0.3916 and 0.8324. The estimated fraction of transmission from asymptomatic humans to vectors was approximately 0.2558, and with a probability of 0.95, this value is between 0.0385 and 0.6030. The estimated relapse rate δ_h was 0.7506 (95% CrI: 0.2914–0.9906). The estimated basic reproductive number R_0 was 2.80 (95% CrI:

2.65–4.50). In Figure 2, we show the fit of the model to the number of humans infected with Chikungunya and numerical simulations of the susceptible human, infected human, asymptomatic human and infected vector compartments as performed by using the Bayesian mean estimation of the parameters.

Table 1. A review of the values of the model parameters and the selected prior distributions. For the beta distributions $Beta(\alpha,\beta)$, α and β are the shape parameters. For the uniform distributions $U(a,b)$, a and b are the minimum and maximum values.

Parameter	Description	Reference	Mean value or range of values	Prior distribution
β_h	Transmission probability: from vector to human	[7]	0.9999 [0.6,1]	$Beta(5,2)$
		[4]	0.375	
		[3]	[0.5, 0.8]	
		[5]	0.67 [0.26, 1]	
β_v	Transmission probability: from human to vector	[7]	0.6 [0.6,1]	$Beta(5,2)$
		[4]	0.375	
		[3]	0.37	
b	Number of bites	[7]	2.4676 [1,3]	$U(0,4)$
		[4]	1	
		[3]	0.5 or 1	
μ_v	Birth and death rates of mosquitoes $[month^{-1}]$	[4]	2.72	$U(2,4.5)$
		[3]	4.28	
		[6]	2.143	
γ	Recovery rate $[month^{-1}]$	[7]	[3.7,4.5]	$U(2.5,7.5)$
		[6]	[2,6]	
p	Fraction of infected becoming asymptomatic	Supposed		$U(0,1)$
δ_h	Relapse rate $[month^{-1}]$	[8]	0.5	$U(0,1)$
		[12]	0.66	
κ	Transmission fraction: from asymptomatic humans to vectors	Supposed		$Beta(2,5)$
N_v	Total number of vectors	Supposed	2 to 4.5 times more than the number of humans	$U(11740,26415)$
μ_h	Birth and death rates of humans $[month^{-1}]$	[21]	$\frac{1}{75\times12} \approx 0.0011$	Fixed value
N_h	Total number of humans	[12]	5870	Fixed value

Table 2. Results from the Bayesian estimation of the model parameters and basic reproductive number, including their Rhat values.

Parameter	Mean	Median	95% Credible interval	Rhat
β_h	0.7379	0.7531	(0.4377, 0.9574)	1.0001
β_v	0.7570	0.7737	(0.4633, 0.9638)	1.0002
b	3.2158	3.2528	(2.2392, 3.9579)	1.0002
μ_v	3.3510	3.3914	(2.0874, 4.4459)	1.0000
γ	4.5821	4.4888	(2.6747, 7.0150)	1.0002
p	0.6536	0.6710	(0.3916, 0.8324)	1.0001
δ_h	0.7506	0.7910	(0.2914, 0.9906)	1.0000
κ	0.2558	0.2321	(0.0385 , 0.6030)	1.0001
N_v	19440.1813	19580.1146	(12254.6677, 26040.5418)	1.0001
R_0	2.8057	1.8199	(2.6528, 4.5063)	*

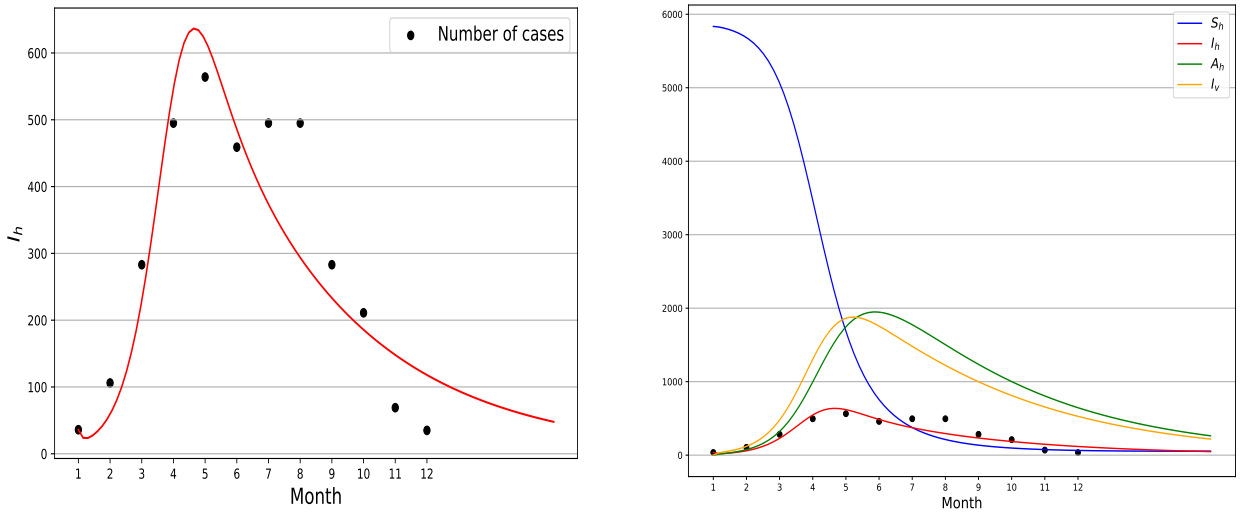

Figure 2. Fitted model: (a) Fit of the model to the number of infected humans with Chikungunya by using means as point estimators; (b) Numerical simulations of the four compartments of humans based on a Bayesian mean estimation of the parameters. The solid dots represent the epidemiological data obtained from [12].

5. Local sensitivity analysis

We performed a sensitivity analysis to measure the dependency of a variable on the parameters and thus identify the parameters that have the highest impact. The sensitivity index approximates the fractional change in a variable X that results from a unit fractional change in a parameter α when the other parameters are kept constant, and it is given by $E_\alpha = \frac{\alpha}{X}\frac{\partial X}{\partial \alpha}$ [28]. If $E_\alpha < 0$, the relationship between the parameter α and X is inversely proportional. Otherwise, if E_α is positive, the relationship is directly proportional.

Using the basic reproductive number R_0, as determined by using (3.3), we calculated the sensitivity index for each parameter:

$$E_{\mu_h} = -\frac{1}{2}\frac{\mu_h[(\mu_h+\delta_h)^2 + \kappa p\gamma(2\mu_h+\delta_h+\gamma) + \delta_h p\gamma]}{(\kappa p\gamma+\mu_h+\delta_h)[(\mu_h+\gamma)(\mu_h+\delta_h) - \delta_h p\gamma]},$$

$$E_p = \frac{1}{2}\frac{p\gamma(\mu_h+\delta_h)[(\mu_h+\gamma)\kappa + \delta_h]}{(\kappa p\gamma+\mu_h+\delta_h)[(\mu_h+\gamma)(\mu_h+\delta_h) - \delta_h p\gamma]},$$

$$E_\gamma = \frac{1}{2}\frac{\gamma(\mu_h+\delta_h)[\mu_h(p\kappa-1) + \delta_h(p-1)]}{(\kappa p\gamma+\mu_h+\delta_h)[(\mu_h+\gamma)(\mu_h+\delta_h) - \delta_h p\gamma]},$$

$$E_{\delta_h} = \frac{1}{2}\frac{\delta_h p\gamma[-\kappa(\mu_h+\gamma(1-p)) + \mu_h]}{(\kappa p\gamma+\mu_h+\delta_h)[(\mu_h+\gamma)(\mu_h+\delta_h) - \delta_h p\gamma]},$$

$$E_\kappa = \frac{1}{2}\frac{\kappa p\gamma}{\kappa p\gamma+\mu_h+\delta_h},$$

$$E_b = 1,$$

$$E_{N_v} = E_{\beta_h} = E_{\beta_v} = \frac{1}{2},$$

$$E_{N_h} = E_{\mu_v} = -\frac{1}{2}.$$

We have used the fixed values of μ_h and N_h from Table 1 and the Bayesian mean estimation of the model parameters from Table 2 to create Figure 3. The sensitivity indices shown in this figure indicate that the parameters β_h, β_v, b, p, κ and N_h have direct relationships with R_0. This implies that decreasing the values of these parameters will reduce R_0. On the contrary, the parameters μ_v, γ, δ_h, μ_v and N_h have inverse relationships with R_0. This implies that increasing the values of these parameters will decrease R_0. From Figure 3, we observe that the fraction of infected individuals who become asymptomatic, p, has the greatest (direct or inverse) impact on R_0, followed by the number of bites b, the transmission probability (β_h and β_v), the total number of vectors N_v and the death rate of mosquitoes μ_v.

Among the new parameters incorporated into the Chikungunya model, we note that the relapse rate δ_h and the fraction of transmission from asymptomatic humans to vectors κ have a weak impact on R_0. We interpret the negative relationship between δ_h and R_0 as increasing the relapse rate, which decreases R_0, that is to say, by decreasing the relapse period ($1/\delta_h$), R_0 is reduced. On the other hand, the fraction of infected individuals who become asymptomatic, p, has a strong impact on R_0.

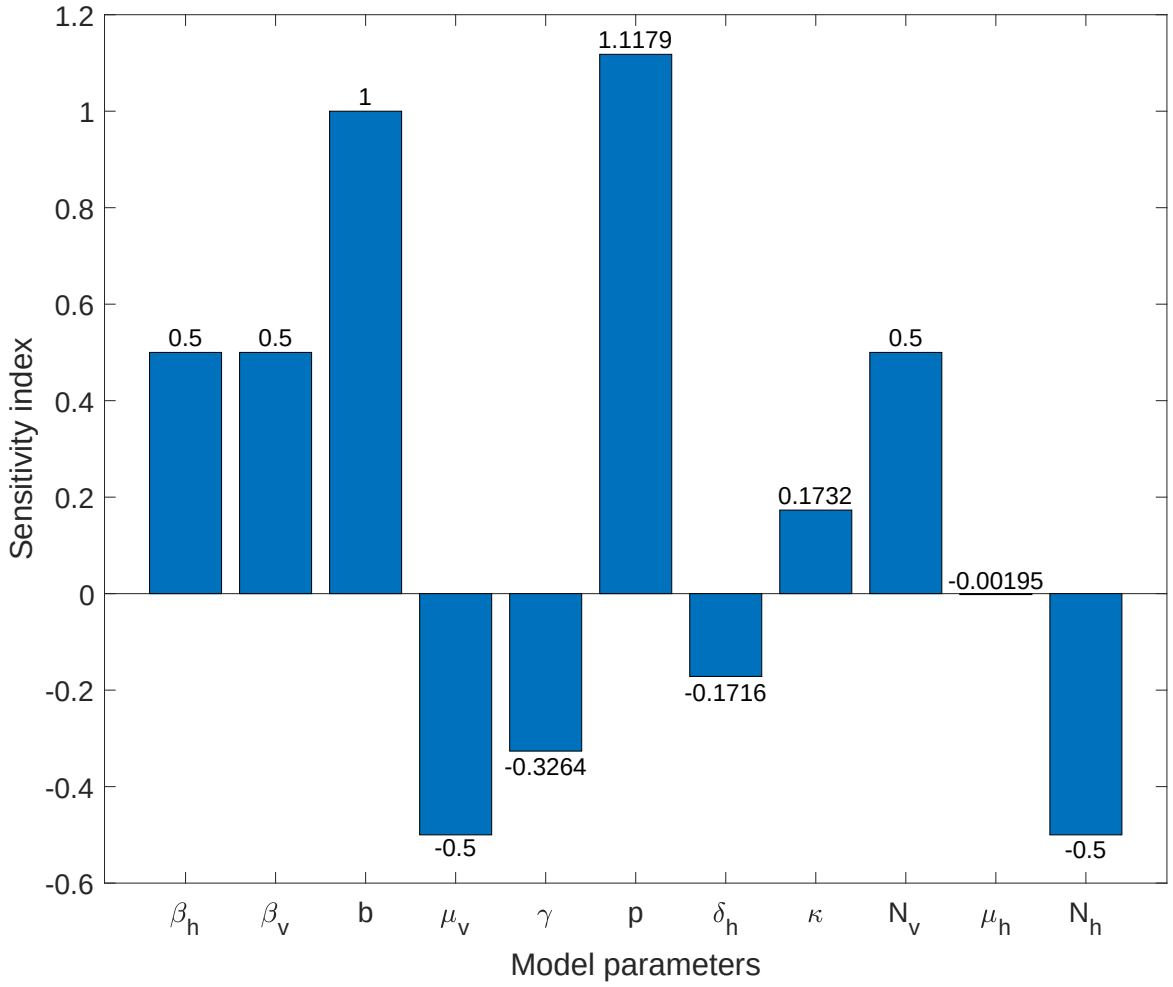

Figure 3. Local sensitivity analysis of the basic reproductive number R_0 using the Bayesian mean estimation of the parameters.

6. Concluding remarks

Mathematical models for Chikungunya have incorporated the aquatic phase of the mosquito [3,29], control mechanics [4,7] and the incorporation of intrinsic and extrinsic incubation periods [6,29]. The phenomenon of relapses in Chikungunya virus infections has been reported in many studies [8–12], but it has not been considered in mathematical models. In this paper, we proposed the first model that incorporates the recurrence of symptoms into the dynamics of Chikungunya.

First, we carried out a qualitative analysis of the Chikungunya model with relapses. The system has the classic equilibrium points, namely, disease-free and endemic equilibrium points. We calculated the basic reproductive number ($R_0 = \sqrt{\hat{R}_0}$) for the disease by using the next-generation operator method. We proved that the disease-free equilibrium point P_0, when $\hat{R}_0 = 1$, presents a forward bifurcation. We analyzed the global stability of the equilibrium points by using the Lyapunov function method. We proved that the disease-free equilibrium is globally asymptotically stable when $\hat{R}_0 \leq 1$, and that the endemic equilibrium is globally asymptotically stable when $\hat{R}_0 > 1$ in the interior of the feasible region.

Second, a Chikungunya outbreak occurred in Acapulco, Mexico, and we used the epidemiological data of self-reported cases from this outbreak obtained in [12] to fit the state variable I_h of the model. We used the Bayesian approach to estimate nine model parameters and two fixed parameter values. For this outbreak, we estimated that the fraction of infected individuals who become asymptomatic, p, is between 0.3916 and 0.8324. These estimates of the infected people who experience relapses with rheumatoid symptoms are consistent with those reported in the literature which ranges from approximately 30% [12] to 72% [8]. The relapse period ($1/\delta_h$) is estimated to be between 1.00 and 3.43. Infected asymptomatic humans play a relatively small role in the transmission of the infection; the fraction of transmission from asymptomatic humans to vectors ranged from 0.0385 to 0.6030. We estimated that the basic reproductive number was equal to 2.80 (95% CrI: 2.65–4.50); this value plays an important role as a bifurcation value and in epidemiological interpretation. Recently, Haider et al. [30] estimated, using a frequentist meta-analysis, the basic reproductive number for Chikungunya based on various studies that have estimated this value; they obtained a value of 3.4 (95% confidence interval: 2.4–4.2). Our Bayesian estimate of R_0 is very similar to that reported in [30].

Third, we performed a local sensitivity analysis of the basic reproductive number by using the Bayesian mean estimation of the model parameters. Among the new parameters incorporated into the Chikungunya model, we found that the fraction of infected individuals who become asymptomatic, p, has a strong impact on R_0. The fraction p and the relapse period $1/\delta_h$ could be reduced with antiviral therapies, and, consequently, R_0 could be decreased. Conversely, the relapse rate δ_h has a weak impact on R_0, but it is not insignificant.

Fourth, to assess the efficiency of insecticide control in the presence and absence of relapses, we varied the mosquito death rate and examined its impact on R_0. The results for these two scenarios are shown in Figure 4. For the case in which the fraction p is considered, we note that we need a higher mortality rate to ensure that the disease is controlled, with an R_0 value below unity. When relapses are not considered in the modeling, it intuitively follows that less control is needed over the mosquito population. This demonstrates the importance of incorporating relapse into Chikungunya models for the estimation of the dynamics of the disease and the study of control measures and protocols.

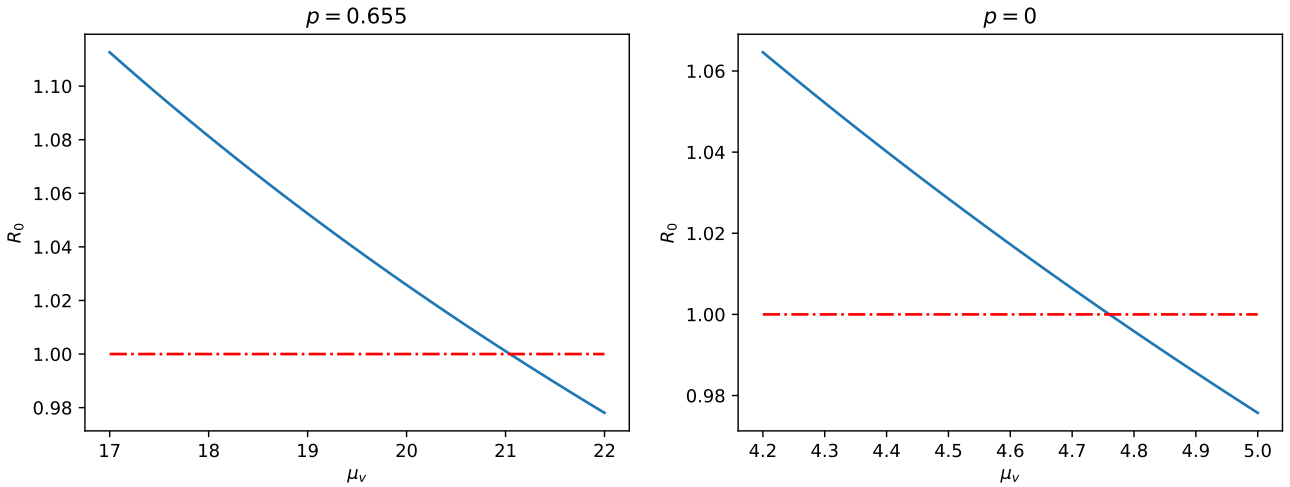

Figure 4. Values of the basic reproductive number obtained by varying the death rate of mosquitoes μ_v. On the left side, the fraction of infected individuals who become asymptomatic (p) is considered, and, on the right side, the fraction p is not considered.

Finally, this work has some limitations. The occurrence of Chikungunya cases was self-reported through a designed questionnaire, and the cases were not confirmed by PCR or serological tests. Our model considers that the relapse rate is constant, but the epidemiological literature reports variability in the relapse periods that should be considered in future work.

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 regarding the publication of this manuscript.

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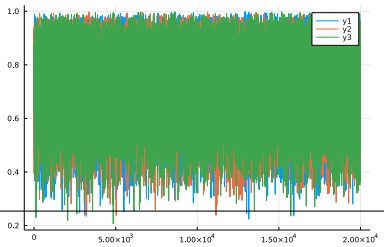
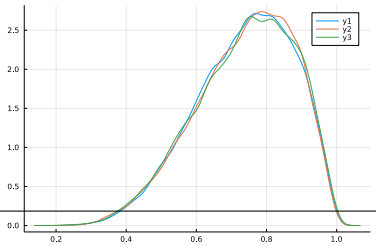
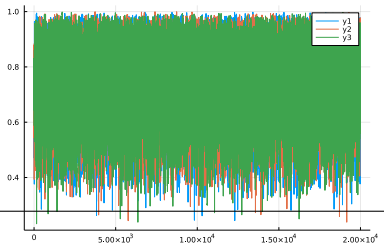
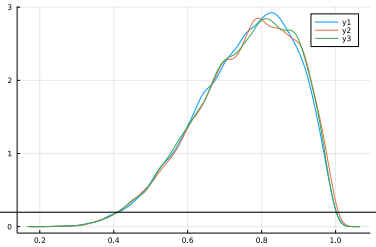
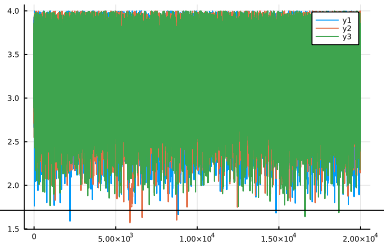
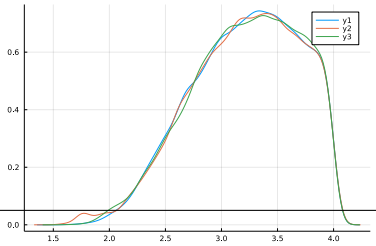
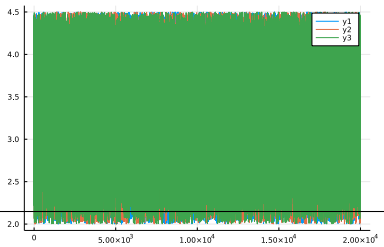
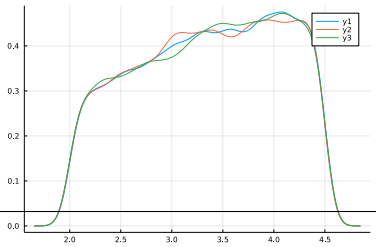
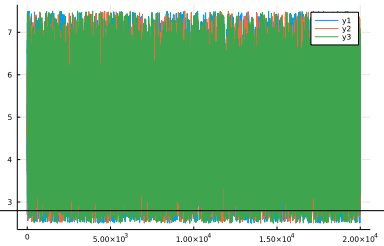
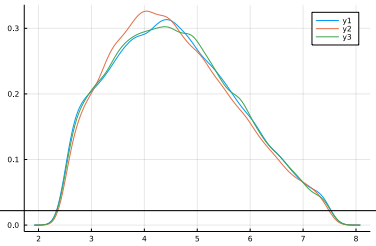
Appendix

In this Appendix, the convergence criteria of the host-vector model for Chikungunya are discussed. The chains of model parameters show good mixing, as shown in Figure 5. Table 2 shows the results of the computation of the Rhat values, thus indicating that both convergence results are consistent.

Parameter	Trace plot	Posterior distribution
β_h		
β_v		
b		
μ_v		
γ		

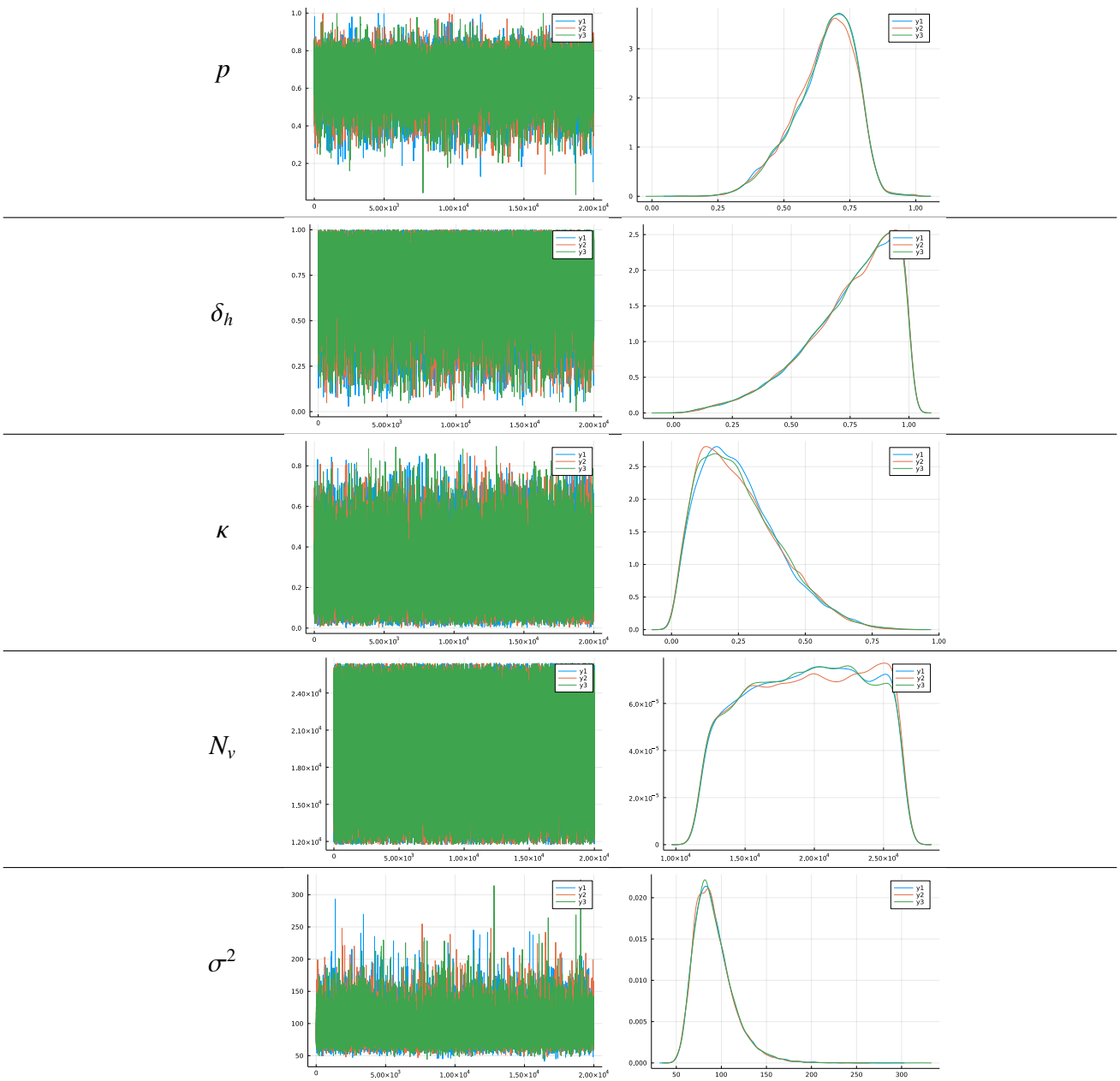


Figure 5. On the left, the convergence chains are shown, and, on the right, the posterior distributions of the parameters of the host-vector model for Chikungunya are shown.