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Modeling the importation and local transmission of vector-borne diseases in Florida: The case of Zika outbreak in 2016☆

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ABSTRACT

Chikungunya, dengue, and Zika viruses are all transmitted by *Aedes aegypti* and *Aedes albopictus* mosquito species, had been imported to Florida and caused local outbreaks. We propose a deterministic model to study the importation and local transmission of these mosquito-borne diseases. The purpose is to model and mimic the importation of these viruses to Florida via travelers, local infections in domestic mosquitoes by imported travelers, and finally non-travel related transmissions to local humans by infected local mosquitoes. As a case study, the model will be used to simulate the accumulative Zika cases in Florida. Since the disease system is driven by a continuing input of infections from outside sources, orthodox analytic methods based on the calculation of the basic reproduction number are inadequate to describe and predict their behavior. Via steady-state analysis and sensitivity analysis, effective control and prevention measures for these mosquito-borne diseases are tested.

1. Introduction

In modern times, humans travel more frequently on scales from local to global. More than a million people are reported to travel internationally each day (Garrett, 1996). Such movements can spread disease pathogens and their vectors over long distances and can threaten public health. Throughout recorded history, non-indigenous vectors that arrive, establish, and spread in new areas have fomented epidemics of human diseases (Lounibos, 2002). Human movements contribute to the spread of vector-borne diseases (Reiner et al., 2014; Stoddard et al., 2009; Wesolowski et al., 2015). Over one million people lose their lives due to mosquito-borne diseases every year (Diseases, 2016). Thus, it is essential to consider current and future influences of host movement on the transmission dynamics and spatial spread of vector-borne diseases such as dengue fever, Chikungunya, and Zika virus.

1.1. Chikungunya

Chikungunya (CHIK) is an emerging disease caused by an *alphavirus*, Chikungunya virus (CHIKV), and transmitted predominantly by *A. aegypti* and *A. Albopictus* mosquitoes. CHIKV was first isolated from human serum and mosquitoes in an epidemic in Tanzania in 1952–1953 (Lumsden, 1955). In 2004, an outbreak originating on the coast of Kenya subsequently spread to Comoros, La Réunion, several other Indian Ocean islands, and India in the following two years. Once introduced in India, CHIKV spread to 17 of its 28 states, infecting more than 1.39 million people before the end of 2006. Viremic travelers then spread outbreaks from India to the Andaman and Nicobar Islands, Sri Lanka, the Maldives, Singapore, Malaysia and Indonesia (PAHO/CDC, 2011).

The first evidence of autochthonous Chikungunya transmission in the Americas was recorded in December 2013, subsequently autochthonous transmission were detected in 33 countries and

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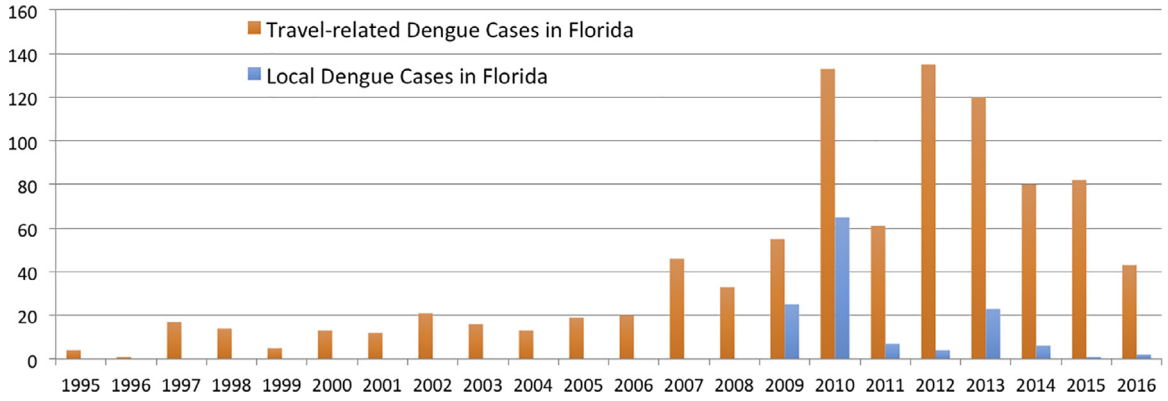

Fig. 1.1. Annual travel-related and local dengue data in the state of Florida from 1995 to 2016 (Florida Department of Health, 2016).

territories of the Americas. The Pan American Health Organization (PAHO) reported a total of 1,071,696 and 635,955 suspected cases (including 169 and 82 deaths) in 2014 and 2015, respectively, in the Americas (PAHO, 2018a).

Prior to 2006, CHIK was rarely identified in the U.S. From 2006 to 2013, studies identified an average of 28 people per year in the U.S. with positive tests for recent CHIKV infection (CDC, 2016b). All were travelers visiting or returning to the U.S. from affected areas in Asia, Africa, or the Indian Ocean (Morens and Fauci, 2014). Beginning in 2014, CHIK cases were reported among U.S. travelers returning from affected areas in the Americas and local transmission was identified in Florida, Puerto Rico, and the U.S. Virgin Islands. In 2014, a total of 2811 CHIK cases were reported to ArboNET from 47 states in the U.S. (452 in Florida). Twelve locally-transmitted cases were also reported from Florida. In 2015, a total of 896 CHIK cases were reported from 44 U.S. states (73 in FL) and the disease became a nationally notifiable condition. In 2016, a total of 175 CHIKV disease cases were reported from 37 U.S. states (6 in FL). All reported cases occurred in travelers returning from affected areas (CDC, 2016b; Florida Department of Health, 2017).

1.2. Dengue

Dengue fever (DF) is caused by any of the four closely related viruses or serotypes (DENV 1, DENV 2, DENV 3, DENV 4) and is transmitted between people by the mosquitoes *Aedes aegypti* and *Aedes albopictus*, which are found throughout the world. Dengue is a viral disease of great global public health concern that causes more illness and death than any other arbovirus and is endemic in more than 100 countries. Today about 2.5 billion people live in areas where there is a risk of dengue transmission with 50 to 100 million infections occur yearly, including 500,000 DHF cases and 22,000 deaths (WHO, 2015).

In the US, nearly all dengue cases reported in the 48 continental states were acquired elsewhere by travelers or immigrants (CDC, 2016c). In Florida, the numbers of cases in the state as a whole have been increased steadily in the last 20 years (see Fig. 1.1; Florida Department of Health, 2016). In 2009 and 2010, an outbreak of dengue was identified in Key West with a total of 88 cases. Small numbers of local cases were reported in Martin County (22 cases) in 2013, Miami-Dade County (6 cases) in 2014, Broward County (1 cases) in 2015, Monroe County (1 case) and Miami-Dade County (1 case) in 2016 (Florida Department of Health, 2016; Linares et al., 2007; Rey, 2014).

1.3. Zika

Zika virus (ZIKV), a *Flavivirus* transmitted mainly by *Aedes* mosquitos, was first isolated from a rhesus monkey in the Zika forest of Uganda in 1947 (Dick et al., 1952). In 1953, three human ZIKV infection cases were first confirmed in Nigeria (Macnamara, 1954). Only a dozen cases were reported in the next 54 years in Africa and Southeast Asia (Petersen et al., 2016). In 2007, the first severe ZIKV outbreak occurred on Yap Island, Federated States of Micronesia, in the North Pacific with an estimated 5000 infections among a population of 6700 (Duffy, 2009). In 2013 and 2014, another large-scale ZIKV outbreak was reported in French Polynesia, South Pacific, with an estimated 28,000 cases (Musso et al., 2014). Subsequent outbreaks occurred on other Pacific islands, including New Caledonia, Easter Island, and Cook Island in 2014 (Musso et al., 2014; Petersen et al., 2016).

It is believed (Musso, 2015; Zanluca et al., 2015) that at the Va'a World Sprint Championship canoe race, held in Rio de Janeiro, Brazil in August 2014, participants from French Polynesia, New Caledonia, Easter Island, and Cook Island brought ZIKV to Brazil. The first ZIKV outbreak in Brazil was reported in Bahia (Campos et al., 2015; Zanluca et al., 2015). From Brazil, ZIKV was subsequently spread to other countries and territories in the Americas (MMWR, 2016). By August 2017, 47 countries and territories in the Americas have confirmed vector-borne transmission of ZIKV disease since 2015 with more than one million suspected cases (PAHO, 2018b).

In January 2016, CDC reported that there were three travel-associated cases of Zika virus in Florida – two were Miami-Dade County residents who traveled to Colombia in December; the third case was a Hillsborough County resident who traveled to Venezuela in December. Starting from February, more and more travel-related Zika cases were reported. On July 7th, the Florida Department of Health began its investigation into possible local transmissions of Zika, and on July 29, the department confirmed Florida's first local transmissions of the Zika virus in four individuals in Miami-Dade and Broward Counties. Consequently, two Zika zones in Wynwood and Miami Beach were identified. On September 1, three mosquito samples in Miami Beach tested positive for the Zika virus in the Miami area, further confirming reports of local Florida transmission of the Zika virus. By the end of 2016, Florida had reported a total of 1016 travel-related Zika cases (320 in Miami-Dade County) and 256 local-acquired cases (241 in Miami-Dade; Florida Department of Health, 2018a; see Fig. 1.2). There were 5102 Zika cases in total in the U.S., among them 4830 were travel related (CDC, 2018). In 2017, there were 452 ZIKV disease cases reported in the U.S. (262 in Florida), among them 437 cases were travel-related, 7 cases were locally transmitted in Florida and Texas, and 8 cases were acquired through sexual transmission (CDC, 2018).

1.4. Epidemiology of these vector-borne diseases

Aedes aegypti and *Aedes albopictus* are two main vectors of these viruses and are widely distributed throughout the tropics with *A.*

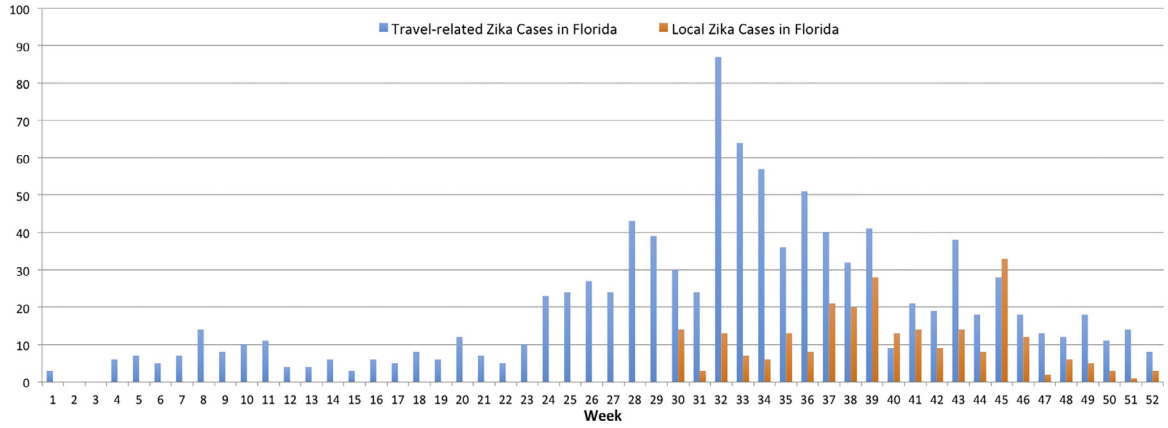

Fig. 1.2. Weekly travel-related Zika human cases reported in Miami-Dade County and the State of Florida in 2016 (Florida Department of Health, 2018).

albopictus at more temperate latitudes, including Florida. Vector-borne diseases transmitted by *Aedes* mosquitoes are generally considered diseases of urban areas and their epidemiology is highly related to the biology of the mosquito vector and human behavior, as well as the environment (Gubler, 1998). Humans serve as the primary reservoir of these viruses during epidemics. Mosquitoes acquire the virus from a viremic host. Following an average extrinsic incubation of 10 days, the mosquito is then able to transmit the virus to a naïve human host. In humans bitten by an infected mosquito, disease symptoms typically occur after an average intrinsic incubation period of 3–7 days (range: 1–12 days). All individuals not previously infected with these viruses are at risk of acquiring infection and developing disease. Pregnant women who become infected with Zika can transmit the disease to their unborn babies, with potentially serious consequences. Zika can be passed through sex from a person with Zika to his or her partners (CDC, 2018; Foy et al., 2011; Gao et al., 2016).

1.5. Mathematical modeling of these vector-borne diseases

Various mathematical models have been proposed to describe the transmission dynamics of Chikungunya (Dumont and Chiroleu, 2010; Manore et al., 2014; Moulay et al. 2011; Robinson et al., 2014; Ruiz-Moreno et al., 2012; Yakob and Clements 2013), dengue (Chowell et al., 2013; Esteva and Vargas 1998; Manore et al., 2014; Pinho et al., 2010; Stoddard et al., 2009), and Zika (Funk et al., 2016; Gao et al., 2016; Kucharski et al., 2016; Manore et al., 2017; Towers et al., 2016; Zhang et al., 2017). In particular, mathematical models have been proposed to study the dynamic introduction of Chikungunya virus (Manore et al., 2017; Ruiz-Moreno et al., 2012), dengue virus (Robert et al., 2016) and Zika virus (Manore et al., 2017; Zhang et al., 2017) into the U.S.

1.6. Our goals

So far most of these VBD cases in Florida are related to international travel and Florida is vulnerable to transmission of these viruses in urban and rural areas where *A. aegypti* and A. albopictus are present. The study of Grubaugh et al. (2017) showed that at least 4 introductions but potentially as many as 40 contributed to the Zika outbreaks in Florida and that local transmission is likely to have started in the spring. The standard vector-borne disease models certainly cannot be used to study the transmission processes on how these viruses were introduced, established and caused local outbreaks since the importation of exposed and infectious individuals are not modeled explicitly. The purpose of this paper is to propose a deterministic vector-borne disease model focusing on the importation, establishment and local spread of the viruses, in which importation of exposed and infectious individuals is included. The model can mimic the importation of these viruses into Florida via international travelers, the local infections of domestic mosquitoes by biting the imported infectious humans, and the local transmission of these viruses to local residents. Our model is different from previous models as we use explicit terms to describe the importation of the exposed and infectious human cases. Since the disease system is driven by a continuing input of infections from outside sources, orthodox analytic methods based on the calculation of the basic reproduction number are inadequate to describe and predict their behavior. Thus, the mathematical analysis of our model is also different from that of the standard models. As a case study, the model will be used to simulate the accumulative Zika cases for the outbreak in Florida in 2016. Via steady-state analysis and sensitivity analysis, effective control and prevention measures for these mosquito-borne diseases are tested.

2. Model formulation

We consider a deterministic model with importation to describe the transmission of mosquito-borne diseases. The mosquito population is separated into susceptible, exposed and infectious classes and the number of each subpopulation at time t is denoted as $S_M(t)$, $E_M(t)$ and $I_M(t)$, respectively. Meanwhile, human population is divided into susceptible, exposed, infectious and recovered subclasses and the number of each subpopulation at time t is denoted as $S_H(t)$, $E_H(t)$, $I_H(t)$ and $R_H(t)$, respectively. Let λ_M and λ_{SH} denote the recruitment rates of susceptible mosquitoes and susceptible humans, and λ_{EH} and λ_{IH} be the rates of importing exposed and infectious human populations. Our assumptions are given in the flowchart (Fig. 2.1).

Based on the frequency-dependent biting assumption of mosquitoes, we model the cross-infection between humans and mosquitoes by $a_H\beta_{HM}\frac{S_M I_H}{N_H}$ and $a_H\beta_{MH}\frac{S_H I_M}{N_H}$. Here β_{HM} and β_{MH} denote the probabilities of transmission from humans to mosquitoes and from mosquitoes to humans, respectively, while a_H is per capital biting rate of mosquitoes on humans. We focus on studying how imported human cases transmit the virus to local mosquitoes and induce outbreaks and ignore the human-to-human transmission of the virus, which can be studied similarly as in Gao et al. (2016).

Studies on the immunity of these vector-borne diseases are still on-going (Rivino and Lim, 2017; Rothman, 2011; Verma et al., 2018). For dengue and Chikungunya, when an individual is exposed to one strain, he/she will get a life-long immunity for that particular strain (Rothman, 2011; Verma et al., 2018). Dudley (2016) have shown the existence of protective immunity against homologous

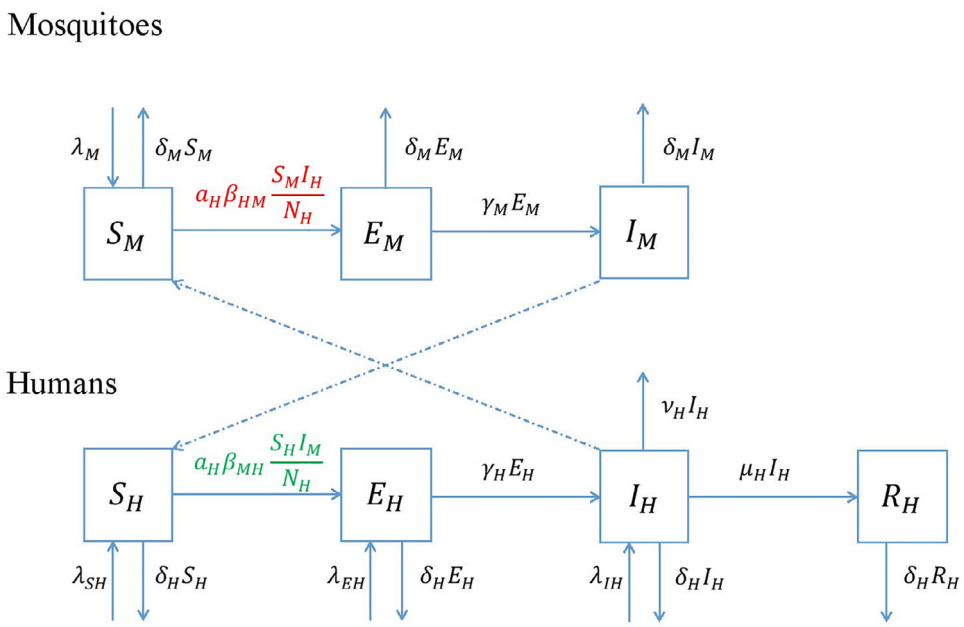

Fig. 2.1. Flowchart of the model.

strains of ZIKA in rhesus macaques monkeys and Osuna (2016) also suggest that primary Zika virus infection elicits protective immunity. So for the sake of simplicity in modeling, we assume that individuals recovered from these vector-borne diseases confer permanent immunity.

Following these assumptions and the flowchart, the model is given as:

$$
\begin{cases}
\text{For mosquitoes}: \\
\begin{cases}
\underbrace{\frac{dS_M}{dt}}_{\text{change rate}} = \underbrace{\lambda_M}_{\text{recruitment}} - \underbrace{a_H\beta_{HM}\frac{S_M I_H}{N_H}}_{\text{infection}} - \underbrace{\delta_M S_M}_{\text{death}} \\
\underbrace{\frac{dE_M}{dt}}_{\text{change rate}} = \underbrace{a_H\beta_{HM}\frac{S_M I_H}{N_H}}_{\text{exposure}} - \underbrace{\delta_M E_M}_{\text{death}} - \underbrace{\gamma_M E_M}_{\text{progression}} \\
\underbrace{\frac{dI_M}{dt}}_{\text{change rate}} = \underbrace{\gamma_M E_M}_{\text{progression}} - \underbrace{\delta_M I_M}_{\text{death}}
\end{cases} \\
\text{For humans}: \\
\begin{cases}
\underbrace{\frac{dS_H}{dt}}_{\text{change rate}} = \underbrace{\lambda_{SH}}_{\text{recruitment}} - \underbrace{a_H\beta_{MH}\frac{S_H I_M}{N_H}}_{\text{infection}} - \underbrace{\delta_H S_H}_{\text{death}} \\
\underbrace{\frac{dE_H}{dt}}_{\text{change rate}} = \underbrace{\lambda_{EH}}_{\text{importation}} + \underbrace{a_H\beta_{MH}\frac{S_H I_M}{N_H}}_{\text{exposure}} - \underbrace{\delta_H E_H}_{\text{death}} - \underbrace{\gamma_H E_H}_{\text{progression}} \\
\underbrace{\frac{dI_H}{dt}}_{\text{change rate}} = \underbrace{\lambda_{IH}}_{\text{importation}} + \underbrace{\gamma_H E_H}_{\text{progression}} - \underbrace{\delta_H I_H}_{\text{death}} - \underbrace{\mu_H I_H}_{\text{disease death}} - \underbrace{\nu_H I_H}_{\text{recovery}} \\
\underbrace{\frac{dR_H}{dt}}_{\text{change rate}} = \underbrace{\nu_H I_H}_{\text{recovery}} - \underbrace{\delta_H R_H}_{\text{death}}.
\end{cases}
\end{cases}
\tag{2.1}
$$

All parameters are nonnegative constants which are listed and interpreted in Table 1.

3. From importation to local transmission

Recall that the traditional approach to calculate the basic reproduction number for an epidemic model (Diekmann et al., 1990, 2009; van den Driessche and Watmough, 2002) starts from considering a disease-free equilibrium. Notice that there are imported exposed and infectious terms in the importation model (2.1) (i.e., $\lambda_{EH} > 0,\ \lambda_{IH} > 0$) which does not have any disease-free equilibrium. Thus the traditional approach of calculating the basic reproduction number does not work for the importation model (2.1). However, endemic equilibrium points always exist. In this section, we will discuss the endemic equilibria which can be classified in three types at three different stages: (i) at the early stage when there were only imported human cases ($\beta_{HM} = \beta_{MH} = 0$); (ii) at the intermediate stage when there were infected local mosquitoes ($\beta_{HM} > 0, \beta_{MH} = 0$); and (iii) at the last stage when there were infected local mosquitoes as well infected local humans ($\beta_{HM} > 0$, $\beta_{MH} > 0$).

3.1. Early stage - with only imported human cases ($\beta_{HM} = \beta_{MH} = 0$)

In the early stage, the mosquito-borne pathogens enter a territory through both of the exposed and infectious travelers. However, local mosquitoes (and thus local humans) are not infected yet by the virus. Mathematically, we assume that $\beta_{HM} = \beta_{MH} = 0$, which implies that the imported humans have not spread the virus to local mosquitoes yet (thus, no transmission from local mosquitoes to local humans).

System (2.1) with $\beta_{HM} = \beta_{MH} = 0$ has one unique equilibrium with imported human cases which is given by

$$
E_0^\lambda = \left(\frac{\lambda_M}{\delta_M}, 0, 0, \frac{\lambda_{SH}}{\delta_H}, \frac{\lambda_{EH}}{\delta_H+\gamma_H}, \frac{(\delta_H+\gamma_H)\lambda_{IH}+\gamma_H\lambda_{EH}}{(\delta_H+\mu_H+\nu_H)(\delta_H+\gamma_H)}, \right.
$$
$$
\left. \frac{\nu_H((\delta_H+\gamma_H)\lambda_{IH}+\gamma_H\lambda_{EH})}{\delta_H(\delta_H+\mu_H+\nu_H)(\delta_H+\gamma_H)}\right). \tag{3.1}
$$

Notice that when $\lambda_{EH} = \lambda_{IH} = 0$ (i.e., there is no importation of exposed and infectious human cases), then E_0^λ becomes E_0, the disease-free equilibrium given in (4.2). One can verify that all eigenvalues of the Jacobian matrix at E_0^λ are negative. Thus, this equilibrium with only imported human cases is asymptotically stable.

This case describes the Zika scenario in Miami-Dade County and the state of Florida from February to sometimes in the spring of 2016, where there were imported Zika virus infected human cases every week, but the virus had not yet been spread to local mosquitoes. In fact, by sequencing ZIKV genomes from patients

Table 1
Parameters used for Zika of model (2.1) and their interpretations.

Parameter	Description	Values
λ_M	Recruitment rate of susceptible mosquitoes	Estimated
λ_{SH}	Recruitment rate of susceptible humans	3.47×10^5 per year (USCB (2013))
λ_{EH}	Number of imported exposed humans population	Estimated
λ_{IH}	Number of imported Zika cases	Assumed
$\frac{1}{\delta_M}$	Average lifespan of mosquitoes	14–21 days (Andraud et al. (2012); Chikaki and Ishikawa (2009))
$\frac{1}{\delta_H}$	Average lifespan of human	1/78years
$\frac{1}{\gamma_M}$	Extrinsic incubation period of Zika	10 (8–12) days (Andraud et al. (2012); Boorman and Porterfield (1956))
$\frac{1}{\gamma_H}$	Intrinsic incubation period of Zika	4.5 (2–7) days (Bearcroft (1956))
$\frac{1}{\mu_H}$	Zika-induced death rate of humans	Almost zero
ν_H	Average recovery time of Zika for humans	6 (3–7)days (Bearcroft (1956))
a_H	Per capita biting rate of mosquitoes on humans	0.03–0.16 per day (Bearcroft (1956))
β_{HM}	Probability of Zika transmission from humans to mosquitoes	0.3–0.75 (Chikaki and Ishikawa (2009))
β_{MH}	Probability of Zika transmission from mosquitoes to humans	0.1–0.75 (Andraud et al. (2012))

and mosquitoes, Grubaugh et al. (2017) showed that there were at least 4 introductions of Zika human cases but potentially as many as 40 introductions in Florida in the spring of 2016.

3.2. Intermediate stage - with infected local mosquitoes ($\beta_{HM}>0$ and $\beta_{MH}=0$)

When the imported cases accumulate to a certain level, in particular when the mosquito season starts in July, these imported human cases can spread the virus to local mosquitoes. At this stage, the transmission only occurs from humans to mosquitoes. Thus we assume $\beta_{HM}>0$ and $\beta_{MH}=0$.

System (2.1) with $\beta_{HM}>0$ and $\beta_{MH}=0$ also has a unique equilibrium and we denote it as

$$\bar{E}^\lambda=(\bar{S}_M^\lambda,\bar{E}_M^\lambda,\bar{I}_M^\lambda,\bar{S}_H^\lambda,\bar{E}_H^\lambda,\bar{I}_H^\lambda,\bar{R}_H^\lambda).$$

Obviously we have

$$\bar{S}_H^\lambda=\frac{\lambda_{SH}}{\delta_H},\ \bar{E}_H^\lambda=\frac{\lambda_{EH}}{\delta_H+\gamma_H},\ \bar{I}_H^\lambda=\frac{(\delta_H+\gamma_H)\lambda_{IH}+\gamma_H\lambda_{EH}}{(\delta_H+\mu_H+\nu_H)(\delta_H+\gamma_H)},$$
$$\bar{R}_H^\lambda=\frac{\nu_H\bar{I}_H^\lambda}{\delta_H},$$

and

$$\frac{\bar{I}_H^\lambda}{\bar{N}_H^\lambda}=\frac{\lambda_{SH}+\lambda_{EH}+\lambda_{IH}-\mu_H\bar{I}_H^\lambda}{\delta_H}$$

provided that

$$\lambda_{SH}+\lambda_{EH}+\lambda_{IH}>\frac{\mu_H[(\delta_H+\gamma_H)\lambda_{IH}+\gamma_H\lambda_{EH}]}{(\delta_H+\mu_H+\nu_H)(\delta_H+\gamma_H)}. \tag{3.2}$$

Thus, we obtain that

$$\bar{S}_M^\lambda=\frac{\lambda_M\delta_H}{a_H\beta_{HM}(\lambda_{SH}+\lambda_{EH}+\lambda_{IH}-\mu_H\bar{I}_H^\lambda)+\delta_M\delta_H},\ \bar{E}_M^\lambda=\frac{\lambda_M-\delta_M\bar{S}_M^\lambda}{\delta_M+\gamma_M},$$
$$\bar{I}_M^\lambda=\frac{\gamma_M(\lambda_M-\delta_M\bar{S}_M^\lambda)}{\delta_M(\delta_M+\gamma_M)}.$$

Note that once condition (3.2) is satisfied, then $\bar{S}_M^\lambda>0$ and $\lambda_M-\delta_M\bar{S}_M^\lambda>0$, so that $\bar{E}_M^\lambda>0$ and $\bar{I}_M^\lambda>0$. The Jacobian matrix evaluated at $\bar{E}^\lambda$ is

$$J(\bar{E}^\lambda)=\begin{pmatrix}A_{11}&A_{12}\\0&A_{22}\end{pmatrix},$$

where

$$A_{11}=\begin{pmatrix}-\delta_M-a_H\beta_{HM}\frac{\bar{I}_H^\lambda}{\bar{N}_H^\lambda}&0&0\\a_H\beta_{HM}\frac{\bar{I}_H^\lambda}{\bar{N}_H^\lambda}&-(\delta_M+\gamma_M)&0\\0&\gamma_M&-\delta_M\end{pmatrix}.$$

$$A_{22}=\begin{pmatrix}-\delta_H&0&0&0\\0&-(\gamma_H+\delta_H)&0&0\\0&\gamma_H&-(\delta_H+\mu_H+\nu_H)&0\\0&0&\nu_H&-\delta_H\end{pmatrix}.$$

$$A_{12}=\begin{pmatrix}a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}&a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}&-a_H\beta_{HM}\frac{\bar{S}_M^\lambda(\bar{N}_H^\lambda-\bar{I}_H^\lambda)}{(\bar{N}_H^\lambda)^2}&a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}\\-a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}&-a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}&a_H\beta_{HM}\frac{\bar{S}_M^\lambda(\bar{N}_H^\lambda-\bar{I}_H^\lambda)}{(\bar{N}_H^\lambda)^2}&-a_H\beta_{HM}\frac{\bar{S}_M^\lambda\bar{I}_H^\lambda}{(\bar{N}_H^\lambda)^2}\\0&0&0&0\end{pmatrix}.$$

Also, we have

$$\begin{aligned}&\mathrm{Det}(J(\bar{E}^\lambda))\\&=(\lambda+\delta_H)^2(\lambda+\gamma_H+\delta_H)(\lambda+\delta_M)(\lambda+\gamma_M+\delta_M)\\&\times(\lambda+\delta_M+a_H\beta_{HM}\frac{\bar{I}_H^\lambda}{\bar{N}_H^\lambda})(\lambda+\delta_H+\mu_H+\nu_H).\end{aligned}$$

All eigenvalues are negative and the equilibrium $\bar{E}^\lambda$ is locally asymptotically stable under the condition (3.2), which indicates that if there are enough introductions of exposed and infectious human cases (i.e., either λ_{EH} or λ_{IH} or both are large enough), soon or later local mosquitoes will be infected by biting these imported human cases.

This case mimics the Zika situation in Miami-Dade County before July 20, 2016: the number of imported Zika virus infected human cases kept increasing, local mosquitoes were believed to be infected with Zika virus (Grubaugh et al., 2017) though it was only confirmed in mosquito samples on September 1, 2016 in Miami Beach by the Florida Department of Agriculture (Mack, 2016), but the virus had not been spread to local humans yet.

3.3. Late stage - with infected local mosquitoes and humans ($\beta_{HM}>0$ and $\beta_{MH}>0$)

The unique stable equilibrium of system (2.1) with ($\beta_{HM}>0$ and $\beta_{MH}=0$) indicates local epidemic of the disease among mosquitoes. At a late stage, local residents can acquire mosquito-borne pathogens through being bitten by local infectious mosquitoes and non-travel-related human cases will be reported as the result of the amplification of the transmission circle. The fact that both of the local mosquitoes and humans are infected indicates the local establishment of this disease in the region. At this stage, we study model (2.1) with the following assumption: $\beta_{HM}>0$ and $\beta_{MH}>0$. Thus we study the transmission dynamics between humans and mosquitoes with the consideration of imported humans.

The existence of endemic equilibria is decided by the existence of roots of the third-order polynomial equation

$$b_0 + b_1 I_H + b_2 I_H^2 + b_3 I_H^3 = 0$$

in the interval $(\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H}, \frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)})$, where

$$\begin{aligned}
b_0 &= -\delta_M^2(\gamma_M+\delta_M)(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})^2(\delta_H\lambda_{IH}+\gamma_H(\lambda_{EH}+\lambda_{IH}));\\
b_1 &= (\gamma_H+\delta_H)\delta_H^2(\gamma_M+\delta_M)(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})^2(\delta_H+\mu_H+\nu_H)\\
&\quad + \delta_M(\gamma_M+\delta_M)(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})(\delta_H\lambda_{IH}+\gamma_H(\lambda_{EH}+\lambda_{IH}))\\
&\quad \times(-a_H\beta_{HM}\delta_H+2\delta_M\mu_H) - a_H^2\beta_{HM}\beta_{MH}\gamma_M\delta_H^2\lambda_{IH}\lambda_M\\
&\quad - a_H^2\beta_{HM}\beta_{MH}\gamma_H\gamma_M\delta_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})\lambda_M;\\
b_2 &= \delta_M(\gamma_M+\delta_M)(\delta_H\lambda_{IH}+\gamma_H(\lambda_{EH}+\lambda_{IH}))\mu_H(a_H\beta_{HM}\delta_H-\delta_M\mu_H)\\
&\quad + a_H^2\beta_{HM}\beta_{MH}\gamma_M\delta_H(\gamma_H+\delta_H)\lambda_M(\delta_H+\mu_H+\nu_H) + (\gamma_H+\delta_H)\\
&\quad \times\delta_M(\gamma_M+\delta_M)(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})(a_H\beta_{HM}\delta_H-2\delta_M\mu_H)\\
&\quad \times(\delta_H+\mu_H+\nu_H));\\
b_3 &= -(\gamma_H+\delta_H)\delta_M(\gamma_M+\delta_M)\mu_H(a_H\beta_{HM}\delta_H-\delta_M\mu_H)\\
&\quad \times(\delta_H+\mu_H+\nu_H).
\end{aligned}$$

Let $H(x) = b_3x^3 + b_2^2 + b_1x + b_0$, we have

$$H\left(\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H}\right) = p_0 + p_1\lambda_{IH} + p_2\lambda_{IH}^2$$

with

$$\begin{aligned}
p_0 &= -\gamma_H\delta_M^2(\gamma_M+\delta_M)\lambda_{EH}(\lambda_{SH}+\lambda_{EH})^2 < 0,\\
p_1 &= \frac{-\gamma_H(\lambda_{SH}+\lambda_{EH})(\delta_H+\mu_H+\nu_H)(a_H\beta_{HM}\delta_H(\delta_M^2\lambda_{EH}+\gamma_M(\delta_M\lambda_{EH}+a_H\beta_{MH}\lambda_M))+2\delta_M^2(\gamma_M+\delta_M)\lambda_{EH}(\delta_H+\mu_H))}{(\delta_H+\mu_H+\nu_H)^2} < 0,\\
p_2 &= \frac{-\gamma_H\delta_M(\gamma_M+\delta_M)\lambda_{EH}(\delta_H+\nu_H)(a_H\beta_{HM}\delta_H+\delta_M(\delta_H+\mu_H))}{(\delta_H+\mu_H+\nu_H)^2} < 0
\end{aligned}$$

and

$$H\left(\frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)}\right) = q_0 + q_1\lambda_{IH} + q_2\lambda_{IH}^2$$

with

$$\begin{aligned}
q_0 &= \frac{\gamma_H\delta_M(\gamma_M+\delta_M)\lambda_{SH}}{(\gamma_H+\delta_H)^2(\delta_H+\mu_H+\nu_H)^2}(\lambda_{SH}+\lambda_{EH})^2(\gamma_H(\delta_H+\nu_H)+\delta_H(\delta_H+\mu_H+\nu_H))(a_H\beta_{HM}\gamma_H\delta_H\\
&\quad +\delta_M(\gamma_H(\delta_H+\nu_H)+\delta_H(\delta_H+\mu_H+\nu_H))) > 0,\\
q_1 &= \frac{\gamma_H\delta_M(\gamma_M+\delta_M)\lambda_{SH}}{(\gamma_H+\delta_H)^2(\delta_H+\mu_H+\nu_H)^2}(\gamma_H+\delta_H)(\lambda_{SH}+\lambda_{EH})(2\delta_M(\delta_H+\nu_H)(\gamma_H(\delta_H+\nu_H\\
&\quad +\delta_H(\delta_H+\mu_H+\nu_H)) + a_H\beta_{HM}\delta_H(2\gamma_H(\delta_H+\nu_H)+\delta_H(\delta_H+\mu_H+\nu_H)))) > 0,\\
q_2 &= \frac{\gamma_H\delta_M(\gamma_M+\delta_M)\lambda_{SH}}{(\gamma_H+\delta_H)^2(\delta_H+\mu_H+\nu_H)^2}(\gamma_H+\delta_H)^2(\delta_H+\nu_H)(a_H\beta_{HM}\delta_H+\delta_M(\delta_H+\nu_H)) > 0.
\end{aligned}$$

Thus, we have $H(\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H}) < 0$ and $H(\frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)}) > 0$. These imply that there exists at least one positive equilibrium in system (2.1).

To explore other endemic equilibria, we denote

$$H'(x) = 3b_3x^2 + 2b_2x + b_1,\ \Delta_1 = b_2^2 - 3b_3b_1.$$

Notice that $\Delta_1 = d_2\lambda_M^2 + d_1\lambda_M + d_0$ is a quadratic polynomial of λ_M, where we can easily verify that $d_1^2 - 4d_0d_2 > 0$ when $\delta_M > \frac{a_H\beta_{HM}\delta_H}{\mu_H}$. We can see that if $\delta_M \le \frac{a_H\beta_{HM}\delta_H}{\mu_H}$, system (2.1) has only one endemic equilibrium since $b_3 \le 0$.

Now we only discuss the case $b_3 > 0$. Denote $\lambda_1 = \frac{-d_1-\sqrt{d_1^2-4d_0d_2}}{2d_2}$ and $\lambda_2 = \frac{-d_1+\sqrt{d_1^2-4d_0d_2}}{2d_2}$. Then $\Delta_1 > 0$ if one of the following holds: $\lambda_M < \lambda_1$ or $\lambda_M > \lambda_2$. Denote the possible reflection points by

$$R_1 = \frac{b_2-\sqrt{\Delta_1}}{3b_3},\quad R_2 = \frac{b_2+\sqrt{\Delta_1}}{3b_3}.$$

To have multiple equilibria, the two reflection points must locate in the above interval; that is,

$$\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H} < R_1 < R_2 < \frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)}$$

and both of the following conditions hold: $H(R_1) > 0$ and $H(R_2) < 0$.

In summary, system (2.1) always has at least one endemic equilibrium and can have up to three endemic equilibrium.

(i) If $\delta_M \le \frac{a_H\beta_{HM}\delta_H}{\mu_H}$, then there exists only one endemic equilibrium;

(ii) If $\delta_M > \frac{a_H\beta_{HM}\delta_H}{\mu_H}$ and $b_2^2 - 3b_1b_3 \le 0$, then there exists only one endemic equilibrium;

(iii) If $\delta_M > \frac{a_H\beta_{HM}\delta_H}{\mu_H}$ and $b_2^2 - 3b_1b_3 > 0$, then

(a) system (2.1) has three endemic equilibria if $H(R_1) > 0$, $H(R_2) < 0$, and

$$\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H} < R_1 < R_2 < \frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)};$$

the three endemic equilibria collapse to two if $H(R_1) = 0$ or $H(R_2) = 0$;

(b) Otherwise, the system still has only one endemic equilibrium.

We will show all possibilities of equilibria numerically in the Appendix.

This case explains the Zika situation in Miami-Dade County and in the State of Florida after July 20, 2016: locally acquired human cases were confirmed and the Zika virus had successfully been imported to Florida.

4. Transmission dynamics after introduction

In this section we first consider the case when the viruses have been introduced to a náive population, so the importation of exposed and infectious human cases is ignored by assuming that $\lambda_{EH} = \lambda_{IH} = 0$ in model (2.1); that is, we consider the following standard vector-borne disease model:

$$\begin{aligned}
\frac{dS_M}{dt} &= \lambda_M - a_H\beta_{HM}\frac{S_MI_H}{N_H} - \delta_MS_M,\\
\frac{dE_M}{dt} &= a_H\beta_{HM}\frac{S_MI_H}{N_H} - \delta_ME_M - \gamma_ME_M,\\
\frac{dI_M}{dt} &= \gamma_ME_M - \delta_MI_M,\\
\frac{dS_H}{dt} &= \lambda_{SH} - a_H\beta_{MH}\frac{S_HI_M}{N_H} - \delta_HS_H,\\
\frac{dE_H}{dt} &= a_H\beta_{MH}\frac{S_HI_M}{N_H} - \delta_HE_H - \gamma_HE_H,\\
\frac{dI_H}{dt} &= \gamma_HE_H - \delta_HI_H - \mu_HI_H - \nu_HI_H,\\
\frac{dR_H}{dt} &= \nu_HI_H - \delta_HR_H.
\end{aligned} \tag{4.1}$$

4.1. Disease-free equilibrium and basic reproduction number

Model (4.1) has a disease-free equilibrium (DFE) given by

$$E_0 = \left(\frac{\lambda_M}{\delta_M}, 0, 0, \frac{\lambda_{SH}}{\delta_H}, 0, 0, 0\right). \tag{4.2}$$

Following Diekmann et al. (1990, 2009) and van den Driessche and Watmough (2002), we obtain the basic reproduction number as follows:

$$\mathcal{R}_0 = \sqrt{\frac{a_H^2\gamma_H\gamma_M\beta_{HM}\beta_{MH}\lambda_M\delta_H}{\delta_M^2\lambda_{SH}(\delta_M+\gamma_M)(\delta_H+\gamma_H)(\delta_H+\mu_H+\nu_H)}}. \tag{4.3}$$

By Theorem 2 of van den Driessche and Watmough (2002), we know that the disease-free equilibrium E_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

4.2. Endemic equilibra

To discuss the existence of positive equilibria of model (4.1), following Chen et al. (2016) we have the quadratic equation

$$a_2 I_H^2 + a_1 I_H + a_0 = 0, \tag{4.4}$$

where

$$\begin{aligned}
a_2 &= (\gamma_H+\delta_H)(\delta_H+\mu_H+\nu_H)(\gamma_M+\delta_M)\delta_M\mu_B(\delta_M\mu_H - a_H\beta_{HM}\delta_H),\\
a_1 &= (\gamma_H+\delta_H)(\delta_H+\mu_H+\nu_H)[\lambda_{SH}\delta_M(\gamma_M+\delta_M)\\
&\quad\times(a_H\beta_{HM}\delta_H - 2\delta_M\mu_H) + a_H^2\beta_{HM}\beta_{MH}\gamma_M\lambda_M\delta_H],\\
a_0 &= \lambda_{SH}^2\delta_M^2(\gamma_H+\delta_H)(\gamma_M+\delta_M)(1-\mathcal{R}_0^2).
\end{aligned} \tag{4.5}$$

Denote

$$\Delta = a_1^2 - 4a_2a_0, \quad I_H^{**} = \frac{\gamma_H\lambda_{SM}}{(\gamma_H+\delta_H)(\delta_H+\mu_H+\nu_H)}.$$

Thus, system (4.1) can have up to two endemic equilibria which are classified as follows:

(i) If $\mathcal{R}_0 < 1$ and
  (a) $a_2 \le 0$, then there is no positive equilibrium;
  (b) $a_2 > 0$, then system (4.1) has two positive equilibria $E^1(S_M^1, E_M^1, I_M^1, S_H^1, E_H^1, I_H^1, R_H^1)$ and $E^2(S_M^2, E_M^2, I_M^2, S_H^2, E_H^2, I_H^2, R_H^2)$ if and only if

$$\Delta > 0 \quad \text{and} \quad 0 < \frac{-a_1}{2a_2} < I_H^{**}, \tag{4.6}$$

where $I_H^1 = \frac{-a_1-\sqrt{\Delta}}{2a_2}$, $I_H^2 = \frac{-a_1+\sqrt{\Delta}}{2a_2}$, and for $i = 1, 2$

$$\begin{aligned}
S_M^i &= \frac{\lambda_M}{\delta_M} + \frac{a_H\beta_{HM}\delta_H\lambda_M I_H^i}{\delta_M(I_H^*(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
E_M^i &= -\frac{a_H\beta_{HM}\delta_H\lambda_M I_H^i}{(\gamma_M+\delta_M)(I_H^i(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
I_M^i &= -\frac{a_H\beta_{HM}\gamma_M\delta_H\lambda_M I_H^i}{\delta_M(\gamma_M+\delta_M)(I_H^i(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
S_H^i &= \frac{\gamma_H\lambda_{SH} - (\gamma_H+\delta_H)(\delta_H+\mu_H+\nu_H)I_H^i}{\gamma_H\delta_H},\\
E_H^i &= \frac{(\delta_H+\mu_H+\nu_H)I_H^i}{\gamma_H},\\
R_H^i &= \frac{\nu_H I_H^i}{\delta_H}.
\end{aligned}$$

  (c) Moreover, these two positive equilibria coalesce when $\Delta = 0$.

(ii) If $\mathcal{R}_0 > 1$, then system (4.1) has one positive equilibrium $E^*(S_M^*, E_M^*, I_M^*, S_H^*, E_H^*, I_H^*, R_H^*)$, where

$$\begin{aligned}
S_M^* &= \frac{\lambda_M}{\delta_M} + \frac{a_H\beta_{HM}\delta_H\lambda_M I_H^*}{\delta_M(I_H^*(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
E_M^* &= -\frac{a_H\beta_{HM}\delta_H\lambda_M I_B^*}{(\gamma_M+\delta_M)(I_H^*(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
I_M^* &= -\frac{a_H\beta_{HM}\gamma_M\delta_H\lambda_M I_H^*}{\delta_M(\gamma_M+\delta_M)(I_H^*(\delta_M\mu_H - a_H\beta_{HM}\delta_H) - \delta_M\lambda_{SH})},\\
S_H^* &= \frac{\gamma_H\lambda_{SH} - (\gamma_H+\delta_H)(\delta_H+\mu_H+\nu_H)I_H^*}{\gamma_H\delta_H},\\
E_H^* &= \frac{(\delta_H+\mu_H+\nu_H)I_H^*}{\gamma_H},\\
I_H^* &= \begin{cases} \frac{-a_0+\sqrt{\Delta}}{2a_2} & \text{if } a_2 > 0;\\ \frac{-a_0}{a_1} & \text{if } a_2 = 0;\\ \frac{-a_0+\sqrt{\Delta}}{2a_2} & \text{if } a_2 > 0, \end{cases}\\
R_H^* &= \frac{\nu_H I_H^*}{\delta_H}.
\end{aligned}$$

4.3. Backward bifurcation

From the results in Section 4.2 we know that when $\mathcal{R}_0 < 1$ and

$$a_2 > 0, \ \Delta > 0 \text{ and } 0 < \frac{-a_1}{2a_2} < I_H^{**},$$

system (4.1) has two positive equilibria

$$E^1(S_M^1, E_M^1, I_M^1, S_H^1, E_H^1, I_H^1, R_H^1) \text{ and } E^2(S_M^2, E_M^2, I_M^2, S_H^2, E_H^2, I_H^2, R_H^2).$$

In fact, following Theorem 3.3 in Chen et al. (2016), we have that if $\mathcal{R}_0 < 1$ and

$$\delta_M < \frac{a_H\beta_{HM}\gamma_H\delta_H}{(\delta_H+\gamma_H)(\delta_H+\mu_H+\nu_H)}, \tag{4.7}$$

then system (4.1) exhibits a backward bifurcation. Thus, in such a case $\mathcal{R}_0 < 1$ cannot guarantee the stability of the disease-free equilibrium E_0 due to the existence of the positive equilibria.

The existence of backward bifurcation indicates that the vector-borne disease cannot be eradicated by simply reducing the basic reproduction number $\mathcal{R}_0$ to be less than unity. Instead, it is important to discuss the backward bifurcation condition (4.7) since it may provide some qualitative implications to control the disease.

5. Numerical simulations

In this section we use model (2.1) to simulate the different stages of introduction of Zika to Florida and to fit the accumulative local Zika infected cases in Florida in 2016. To carry out some numerical simulations of model (2.1), some parameters are adapted from the literature about Zika outbreaks, some parameter values about Florida are taken from Chen et al. (2016), and some other values are estimated, which are listed in Table 1. We then use our model (2.1) to fit the accumulative weekly data of local Zika infected cases in Florida from July 29, which is given in Fig. 5.3.

5.1. Local mosquitoes were infected

With parameter values given in Table 1, some others given in Chen et al. (2016) and $\beta_{HM} > 0$, $\beta_{MH} = 0$, numerical simulations show that some local mosquitoes are infected from biting the imported infectious humans (Fig. 5.1).

The existence of this equilibrium represents the situation in Miami-Dade as well as in the State of Florida before July 20, 2016: there were imported Zika virus infected human cases who had

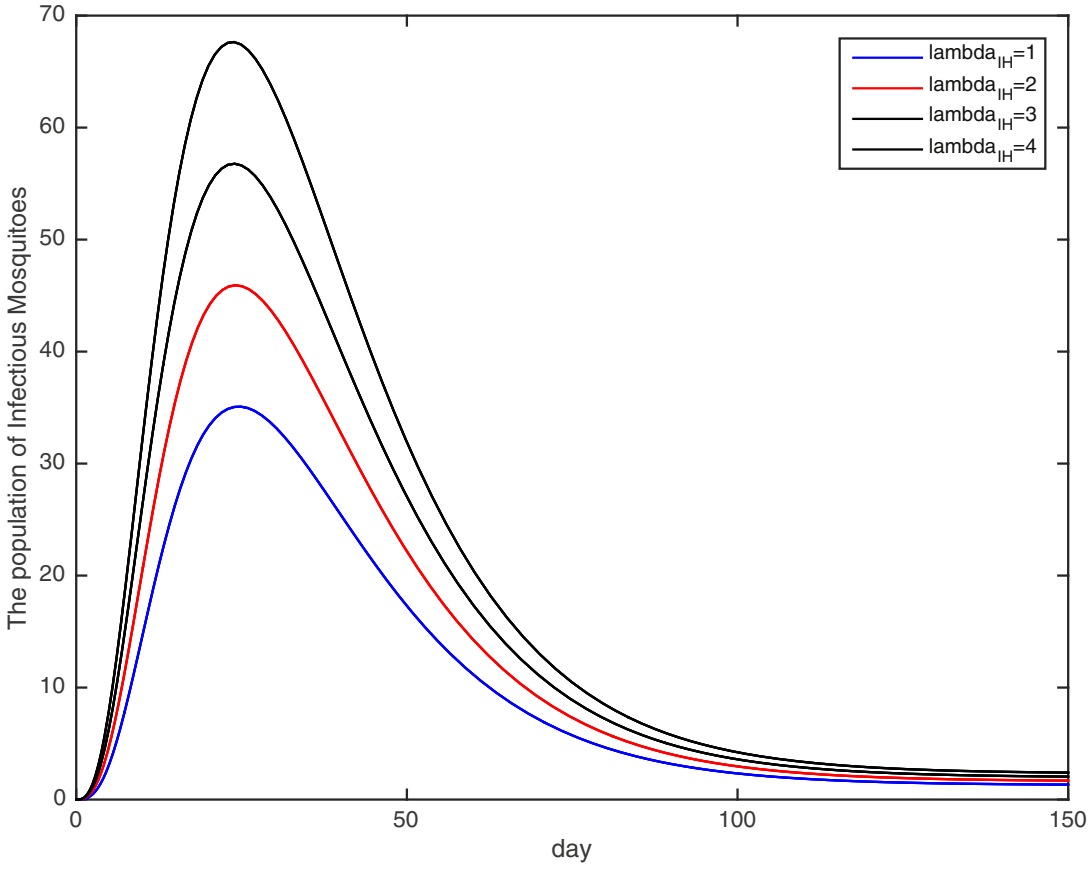

Fig. 5.1. Number of local mosquitoes infected by biting imported infectious humans with $\beta_{HM} > 0$ and $\beta_{MH} = 0$.

spread the virus to some local mosquitoes, but the virus had not been spread to local humans yet. On September 1, 2016, the Florida Department of Agriculture confirmed that three Zika-positive mosquito samples were found in Miami Beach (Mack, 2016), but local mosquitoes were believed to be infected with Zika virus earlier (Grubaugh et al., 2017).

5.2. Both local mosquitoes and humans were infected

With parameter values given in Table 1, some others given in Chen et al. (2016) and $\beta_{HM} > 0$, $\beta_{MH} > 0$, numerical simulations show that local mosquitoes spread the virus to local humans (Fig. 5.2). This explains the situation in Miami-Dade and in the State of Florida after July 20, 2016: there were still imported Zika virus infected human cases reported, locally acquired human cases were reported continuously in the following months (Florida Department of Health, 2018a).

5.3. Fit the accumulative local zika data in florida

Now we use model (2.1) to fit the accumulative local Zika infected cases in Florida (Fig. 5.3). The first local Zika infected cases were identified in Miami-Dade and Broward Counties on July 29. By September 30, there were 124 local on-travel related infections in Florida (Florida Department of Health, 2018b).

5.4. Effects of initial population sizes

Now we examine the influence of initial numbers of susceptible mosquitoes, exposed humans, and infectious humans on the number of infections mosquito population. From Fig. 5.4, we can see that the initial population sizes of susceptible mosquitoes, exposed humans, and infectious humans affect $I_M(t)$, the number of infectious mosquitoes. Since the virus is transmitted directly from infectious humans to susceptible mosquitoes, the number of infectious mosquitoes reaches peak faster with increasing number of infectious humans.

Note that Fig. 5.2 (a) and Fig. 5.4 (c) provide a comparison on the numbers of infected mosquitoes from the imported model (Fig. 5.2 (a)) and the standard model (Fig. 5.4 (c)). Once the virus is introduced into the region via imported hosts, it is the interaction between local mosquitoes and local hosts that determines the transmission dynamics. So the difference between the two cases is not significant.

5.5. Sensitivity analysis

One potential control strategy is to quarantine or isolate the imported infectious individuals when there is no effective treatment or vaccine for the specific disease. To examine such a measure, we assume that $\lambda_{IH} = 0$. Then the number of equilibria of this system depends on the number of roots of the third-order polynomial equation $H(x) = 0$ in the interval $(0, \frac{\gamma_H(\lambda_{SH}+\lambda_{EH})}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)})$. Here $H(0) = p_0 < 0$ and $H(\frac{\gamma_H(\lambda_{SH}+\lambda_{EH})}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)}) = q_0 > 0$ if $\lambda_{EH} > 0$. These imply that the existence of imported exposed individuals guarantees the existence of at least one endemic equilibrium even if no infectious individuals are allowed to enter or all imported infectious individuals are quarantined or isolated. Therefore, the virus will be eventually transmitted to both local humans and mosquitoes.

Thus we examine the sensitivity of steady states of both infectious mosquitoes and infectious humans to parameter variations in Fig. 5.5. A larger PRCC in absolute values indicates the importance

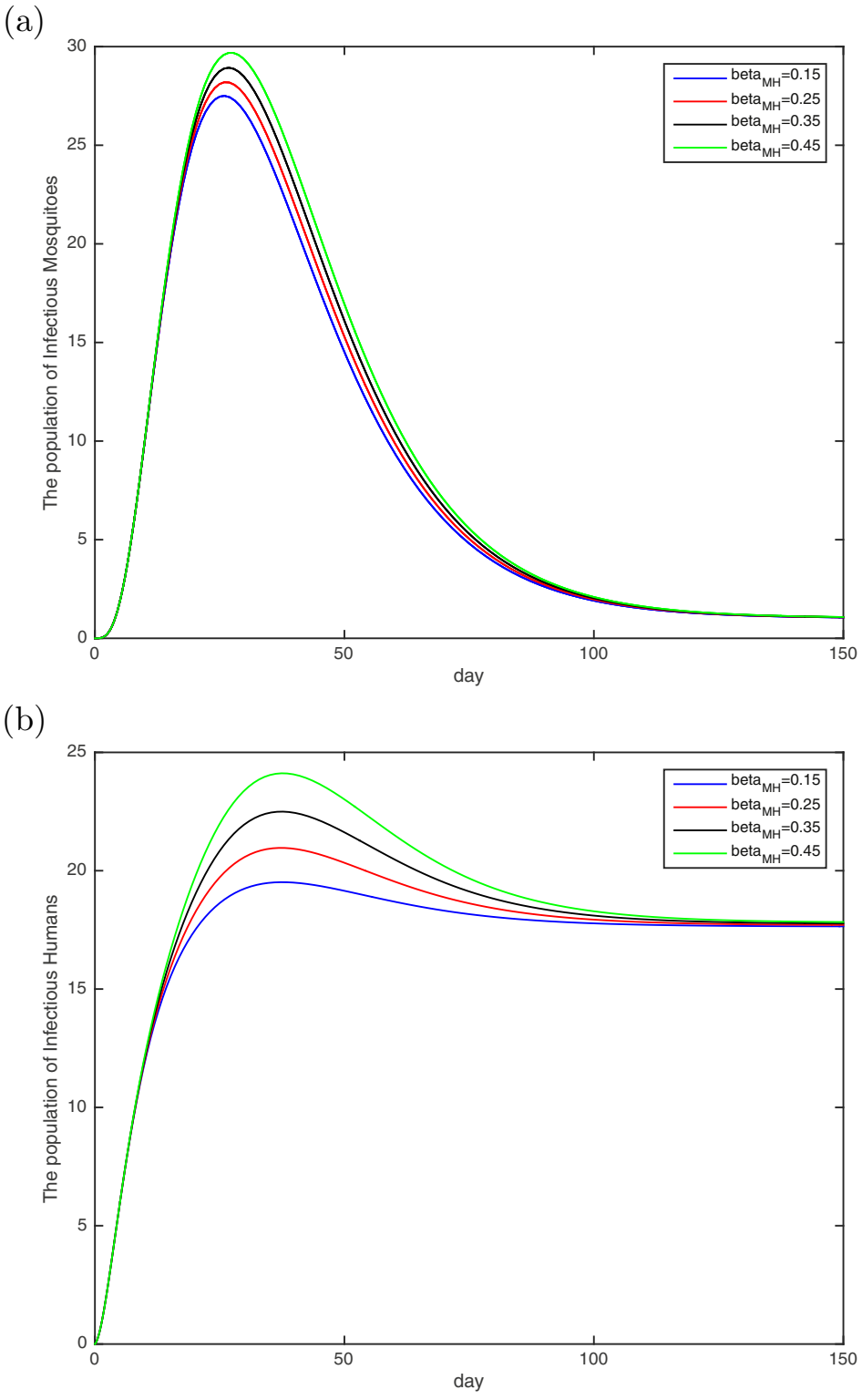

Fig. 5.2. When $\beta_{HM} > 0$ and $\beta_{MH} > 0$, both (a) local mosquitoes and (b) local humans are infected by the virus.

of this parameter to the change in the steady states of infectious populations I_M^* and I_H^*. The values of parameters used to simulate are listed in Table 1. We can see that the death rate of mosquitoes δ_M and the biting rate a_H contribute most to the number of infectious mosquitoes.

5.6. Control strategies after introduction

After the introduction of the virus to a new location, the model without importation (4.1) has a basic reproduction number $\mathcal{R}_0$ given by (4.3), from which various control measures can be tested by carrying out sensitive analysis of $\mathcal{R}_0$ in terms of parameters. Fig. 5.6 presents three important factors to control the disease: the

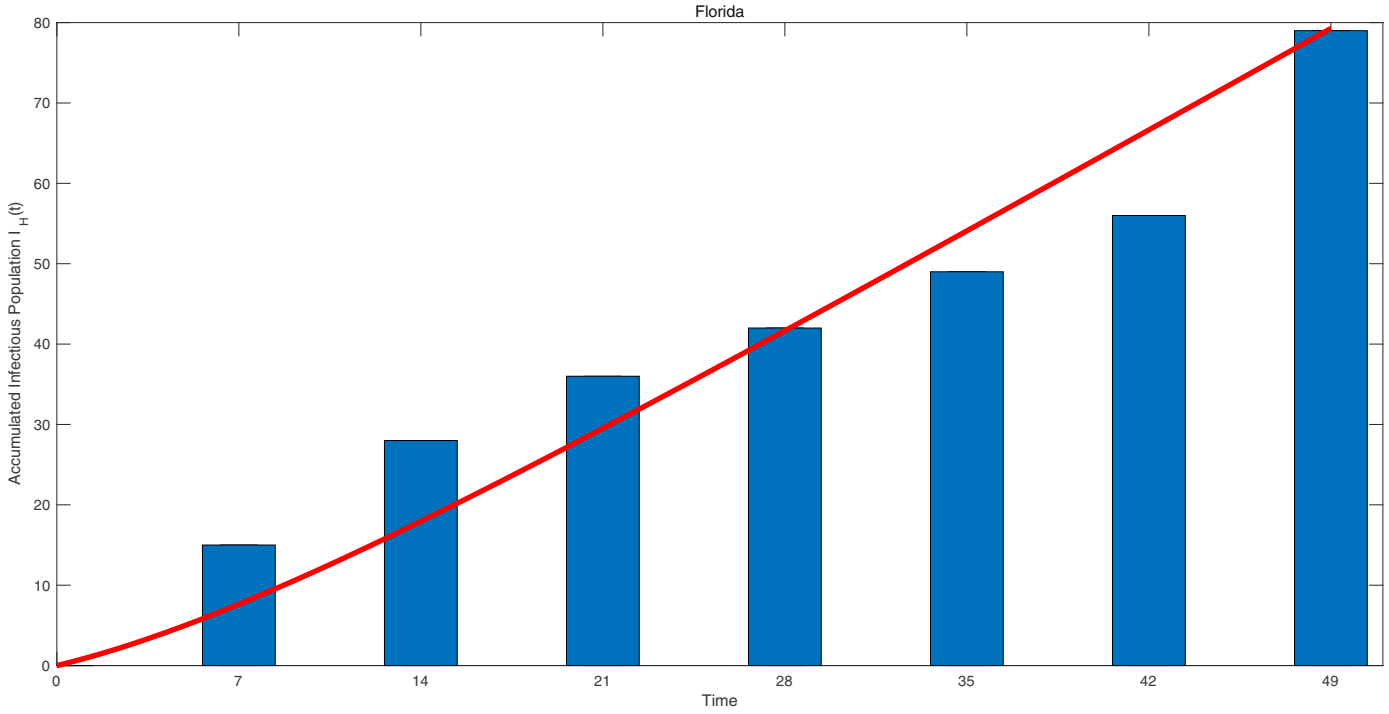

Fig. 5.3. Simulation of the accumulative weekly data of local Zika infected cases in Florida from July 29.

Table 2
Parameters used for Chikungunya of model (2.1) and their interpretations.

Parameter	Description	Values
λ_M	Recruitment rate of susceptible mosquitoes	Estimated
λ_{SH}	Recruitment rate of susceptible humans	3.47×10^5 per year (USCB, 2013)
λ_{EH}	Number of imported exposed humans population	Estimated
λ_{IH}	Number of imported Chikungunya cases	475 per year (CDC, 2016a)
$\frac{1}{\delta_M}$	Average lifespan of mosquitoes	14–21 days (Andraud et al., 2012; Chikaki and Ishikawa, 2009)
$\frac{1}{\delta_H}$	Average lifespan of human	78 years
$\frac{1}{\gamma_M}$	Extrinsic incubation period of Chikungunya	3.5 days (CDC and Prevention, 2016d; Pialoux et al., 2007C)
$\frac{1}{\gamma_H}$	Intrinsic incubation period of Chikungunya	3 (2–4) days (CDC and Prevention, 2016d; Pialoux et al., 2007)
$\frac{1}{\mu_H}$	Chikungunya-induced death rate of humans	0.001 (Gilotra and Shah, 1967)
ν_H	Average recovery time of Chikungunya for humans	6 (3–7) days
a_H	Per capita biting rate of mosquitoes on humans	0.03-0.16 per day
β_{HM}	Probability of Chikungunya transmission from humans to mosquitoes	0.24 (0.001–0.35)
β_{MH}	Probability of Chikungunya transmission from mosquitoes to humans	0.24 (0.005–0.35)

death rate of mosquitoes δ_M, the recruitment rate of mosquitoes λ_M, and the biting rate of mosquitoes a_M. Obviously the biting rate of mosquitoes can be reduced if the population size of mosquitoes decreases significantly. Fig. 5.6 (d) provides the evidence that neither of these two factors by itself plays a dominant role in controlling the disease. So in order to achieve a sufficiently small basic reproduction number a combined strategy (increasing the mosquito death rate, decreasing the mosquito recruitment rate, and reducing the biting rate) is suggested.

5.7. Other vector-borne diseases

Since dengue virus and Chikungunya virus are also transmitted by the same *aedes* mosquito species and have been imported to Florida and caused local outbreaks, we believe model (2.1) can be used to study their introduction and local outbreaks in Florida as well. For example, using parameter values from the literature (see Table 2), we can perform similar PRCC sensitivity analysis of steady states of both infectious mosquitoes I_M^* and infectious humans I_H^* to parameter variations, see Fig. 5.7.

6. Discussion

Though most of the reported cases of dengue, Chikungunya and Zika infections in Florida were returning travelers, local non-travel related infections of all three diseases have also been reported in Florida. Taking into account the fact that dengue virus, Chikungunya virus, and Zika virus are all transmitted by *Aedes aegypti* and *Aedes albopictus* mosquito species, we proposed a deterministic model to study their transmission dynamics as mosquito-borne diseases. Various mathematical models have been proposed to describe the transmission dynamics of Chikungunya (Dumont and Chiroleu, 2010; Manore et al., 2014; Moulay et al., 2011; Robinson et al., 2014; Ruiz-Moreno et al., 2012; Yakob and Clements, 2013), dengue (Chowell et al., 2013; Esteva and Vargas, 1998; Manore et al., 2014; Pinho et al., 2010; Stoddard et al., 2009), and Zika (Funk et al., 2016; Gao et al., 2016; Kucharski et al., 2016; Manore et al., 2017; Towers et al., 2016; Zhang et al., 2017). Our model is different from these models as we used explicit terms to describe the importation of the exposed and infectious human cases. Note that the imported model (2.1) does not have any disease-

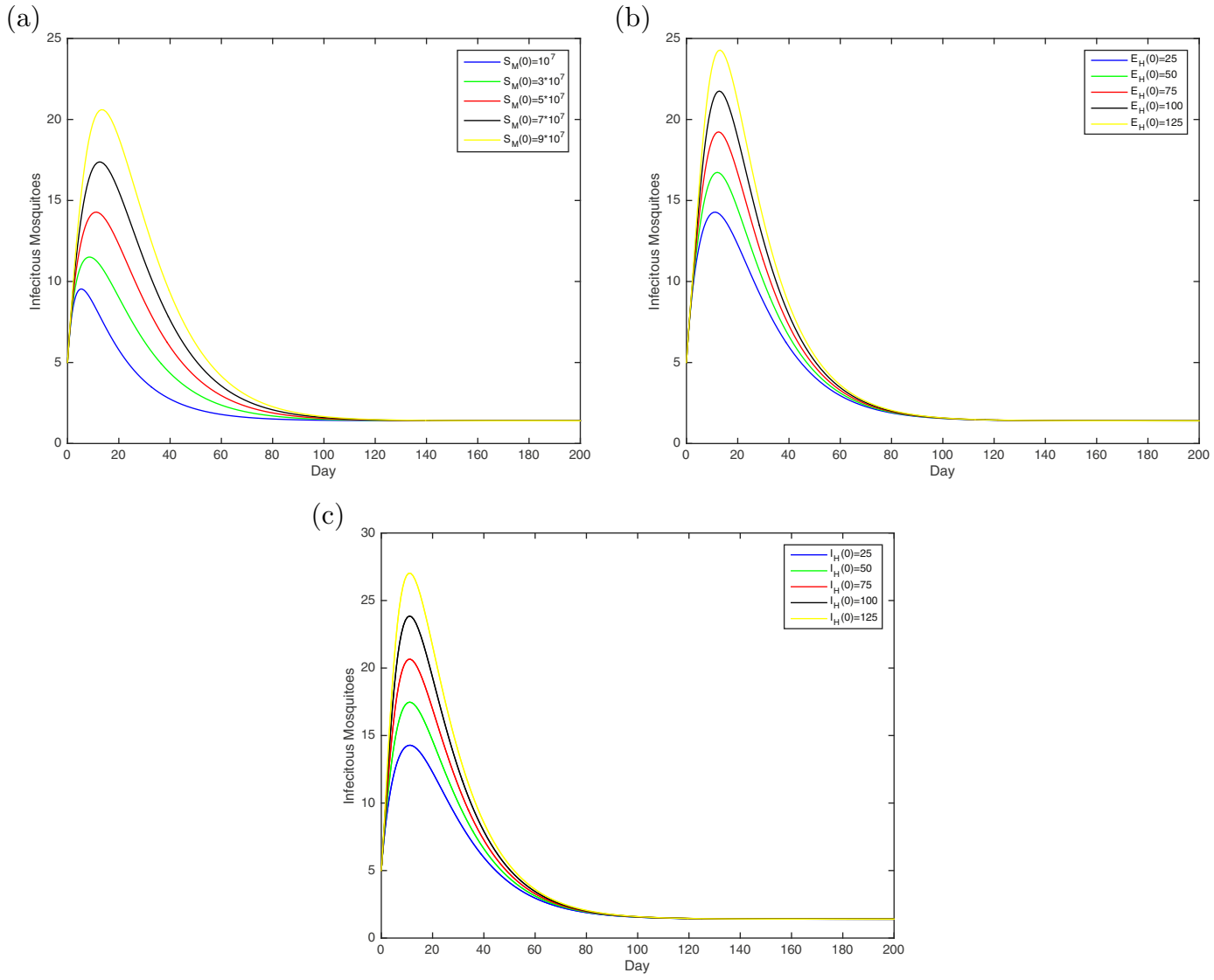

Fig. 5.4. The influence of initial population sizes of (a) susceptible mosquitoes, (b) exposed humans and (c) infectious humans on the number of infectious mosquitoes.

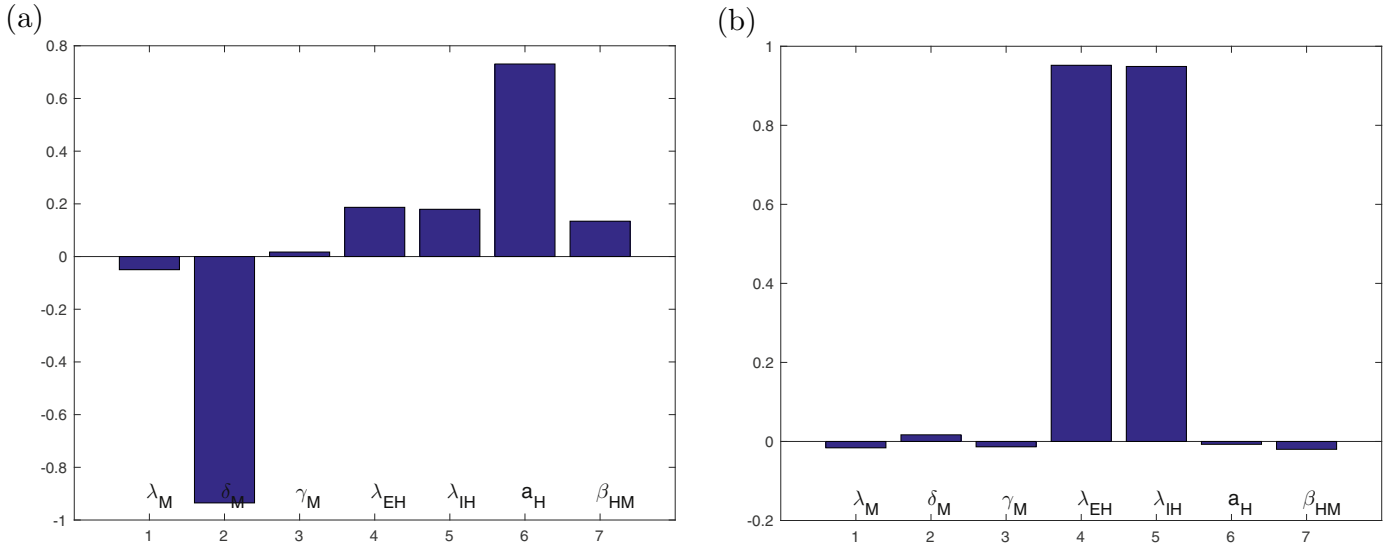

Fig. 5.5. (a) Partial rank correlation coefficients for the steady state of infectious mosquitoes I_M^* and each input parameter variables of Zika virus; (b) Partial rank correlation coefficients for the steady state of infectious humans I_H^* and each input parameter variables of Zika virus.

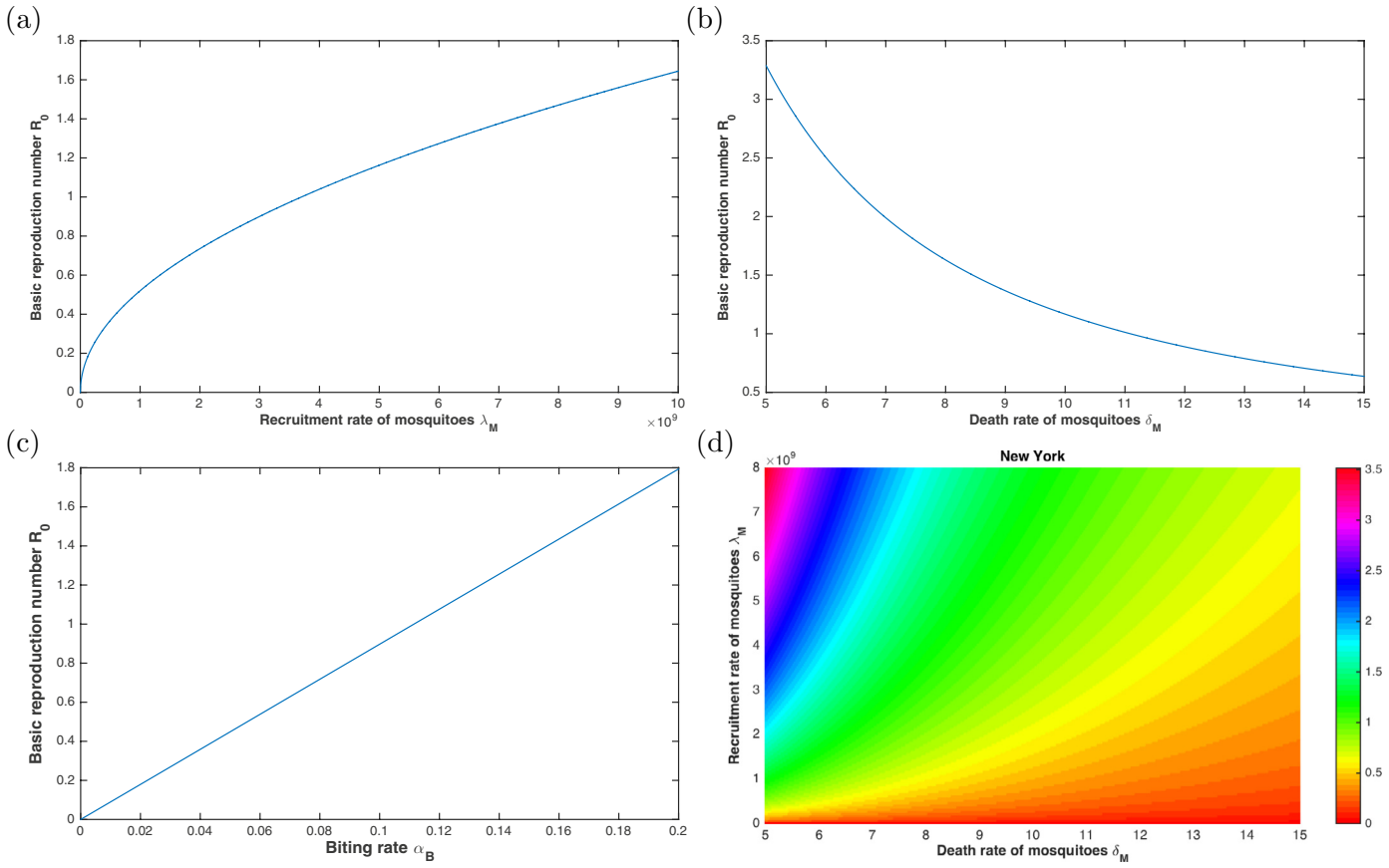

Fig. 5.6. The basic reproduction number $\mathcal{R}_0$ in terms of (a) recruitment rate of mosquitoes λ_M, (b) death rate of mosquitoes δ_M, (c) the biting rate of mosquitoes a_M, and (d) the recruitment rate λ_M and the death rate δ_M of mosquitoes.

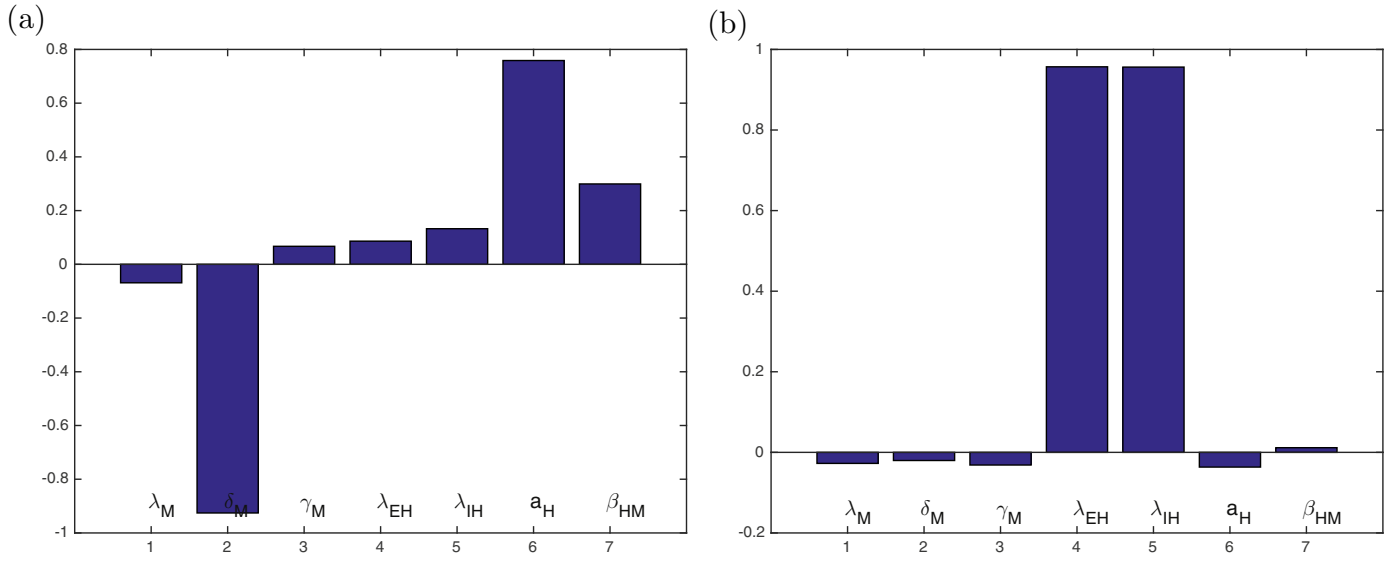

Fig. 5.7. (a) Partial rank correlation coefficients for the steady state of infectious mosquitoes I_M^* and each input parameter variables of Chikungunya; (b) Partial rank correlation coefficients for the steady state of infectious humans I_H^* and each input parameter variables of Chikungunya.

free equilibrium, so the traditional approach of calculating the basic reproduction number R_0 does not work here. Consequently, the mathematical analysis (such as the existence and stability of the positive equilibria) of our model is much harder than that of the standard models and the nonlinear dynamics of our model are much more complicated than that of the standard model. We believe that a threshold value similar to the basic reproduction number exists which can be used to determine the behavior of our model. We think that the imperfect bifurcation theory (Keener and Keller, 1973; Liu et al., 2005) might be used to study the transmission dynamics of our importation model and leave it for future consideration.

The submodels and their analyses were used to describe the three stages of the introduction of these diseases: the importation

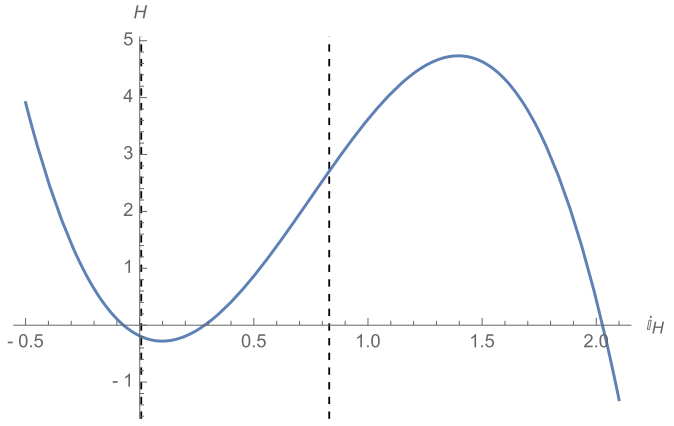

Fig. A.1. If $\delta_M \leq \frac{a_H \beta_{HM} \delta_H}{\mu_H}$, then $b_3 < 0$, there is only one endemic equilibrium.

of these viruses to Florida via travelers, local infections in domestic mosquitoes by imported travelers, and finally non-travel related transmissions to local humans by infected local mosquitoes. As far as we know, there is no model in the literature that can be used to mimic these stages of introduction of vector-borne diseases. The model was also used to simulate the accumulative Zika cases in Florida. By steady-state analysis and sensitivity analysis, we examined control and prevention measures for these mosquito-borne diseases. Our analysis demonstrates that large-scale spraying of insecticides at the infected zones to kill adult mosquitoes, eggs, and larvas are effective in control the outbreaks of these diseases. Personal protections from mosquito bites are also important in preventing the virus infections.

Once the viruses had been introduced to a náive population, the importation of exposed and infectious human cases may be ignored by assuming that $\lambda_{EH} = \lambda_{IH} = 0$ in model (2.1), which yields the standard vector-borne disease model (4.1). We then studied the basic properties of the model in terms of the basic reproduction number, including the existence and stability of the disease-free equilibrium, existence of the endemic equilibria, and existence of backward bifurcation. The existence of backward bifurcation indicates that the vector-borne disease cannot be eradicated by simply reducing the basic reproduction number $\mathcal{R}_0$ to be less than unity. Combined strategies including increasing the mosquito death rate, decreasing the mosquito recruitment rate, and reducing the biting rate, etc. are required to control the vector-borne diseases.

Our modeling scheme was based on the observations that these three mosquito-borne diseases have been imported to Florida and caused outbreaks, and the model was used to simulate the accumulative local Zika infections in Florida. It should be pointed out that the model is in a general setting and can be used to simulate the importation and local transmission of these mosquito-borne diseases in other regions and territories. For example, CHIKV was introduced to Comoros, La Réunion and several other Indian Ocean islands in 2004, our imported model can be used to understand how CHIKV was introduced and caused outbreaks in these regions (Yakob and Clements, 2013). It could be also used to model the introduction of CHIKV into the U.S. (Manore et al., 2017; Ruiz-Moreno et al., 2012). ZIKV was imported into Singapore and caused local transmission (The Singapore Zika Study Group, 2017), our imported model could be applied there too.

Since these mosquito-borne diseases can also be spread geographically by human movement, it will be very important to investigate how human travel affects the spatial transmission of the diseases. Spatial heterogeneities can be modeled by dividing the population into subpopulations and allowing infective individuals in one patch to infect susceptible individuals in another. Such models for various diseases have been studied widely, including in vector-borne disease systems (Cosner et al., 2009; Dye and Hasibeder, 1986; Gao and Ruan, 2012, 2014; Hasibeder and Dye, 1988; Smith et al., 2004). Such modeling scheme will help us better understand how these mosquito-borne diseases were transmitted to Florida from other countries and territories in the Americas and whether if these diseases will be able to spread to other states with competent mosquito species. Using houses or blocks as patches, such multi-patch models can also be used to study how these diseases spread from communities to communities via movements of humans and dispersals of mosquitoes.

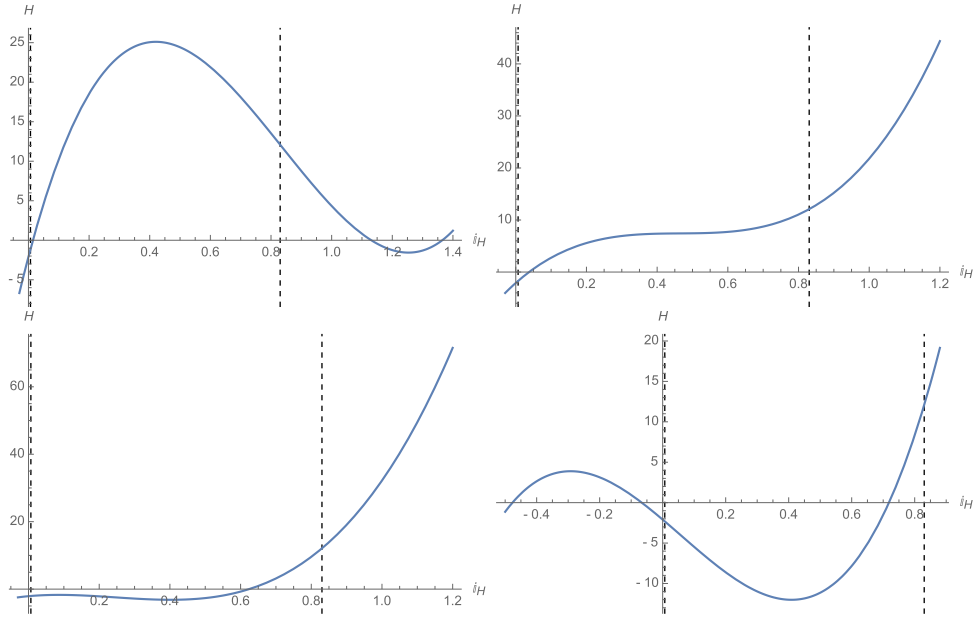

Fig. A.2. Only one root of the equation $H(I_H) = 0$ lies in the interval $(\frac{\lambda_{IH}}{\delta_H+\mu_H+\nu_H}, \frac{\gamma_H(\lambda_{SH}+\lambda_{EH}+\lambda_{IH})+\delta_H\lambda_{IH}}{(\delta_H+\mu_H+\nu_H)(\gamma_H+\delta_H)}) = (0.00666667, 0.830196)$ in the following cases: (a) $\lambda_M < 0.0924647$; (b) $0.0924647 < \lambda_M < 0.680876$; (c) $0.680876 < \lambda_M < 0.897178$; (d) $\lambda_M > 0.897178$.

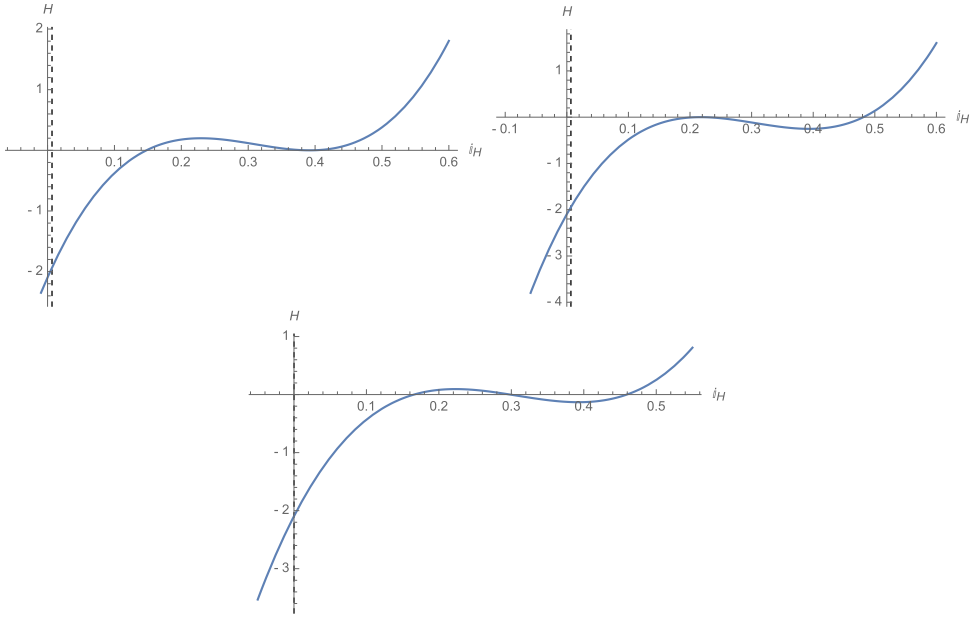

Fig. A.3. There are two roots when (a) $\lambda_M = 0.674874$ and (b) $\lambda_M = 0.680876$. There are three roots when (c) $0.674874 < \lambda_M < 0.680876$.

Appendix

Here we show numerically that all three cases about the roots of the third-order polynomial equation $H(x) == b_3x^3 + b_2^2 + b_1x + b_0 = 0$ can occur. We fix the parameter values as follows: $\gamma_H = 5, \delta_H = 0.1, \mu_H = 0.1, \nu_H = 0.1, a_H = 2, \beta_{HM} = \beta_{MH} = 1, \gamma_M = 0.5, \delta_M = 0.5, \lambda_{SH} = 1, \lambda_{EH} = \lambda_{IH} = 0.008$. If $\delta_M \leq \frac{a_H\beta_{HM}\delta_H}{\mu_H}$ and $b_3 < 0$, there is only one endemic equilibrium (Fig. A.1). If $0.674874 < \lambda_M < 0.680876$, then there exist three endemic equilibria (see Fig. A.3 (c)). The number of endemic equilibria changes from three to two if λ_M is at the two end points of the interval (0.674874,0.680876) (see Fig. A.3(a)(b)). Otherwise, system (2.1) has only one unique endemic equilibrium (see Figs. A.2).

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