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สำนักหอสมุด

รายงานวิจัยฉบับสมบูรณ์

แบบจำลองทางคณิตศาสตร์ของการระบาดของโรคไวรัสซิก้าระหว่างยุงกับคน และการศึกษาการควบคุมโดยการเว้นระยะห่างทางสังคม

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กองทุนวิจัยมหาวิทยาลัยนเรศวร

บทคัดย่อ

งานวิจัยนี้ได้ศึกษาเกี่ยวกับการระบาดของโรคอหิวาและการควบคุมโดยการพิจารณาแยกอายุกลุ่มคน ซึ่งแบบจำลองทางคณิตศาสตร์ที่ได้เป็นระบบสมการเชิงอนุพันธ์ย่อยสี่สมการในการอธิบายการระบาดของโรค โดยที่หนึ่งสมการเพิ่มเติมเป็นสมการเชิงอนุพันธ์สำหรับการเติบโตของแบคทีเรีย ความสมดุลของจุดวิกฤติได้รับการตรวจพิสูจน์และผลเฉลยเชิงตัวเลขถูกใช้เป็นเครื่องมือในการยืนยันผล โดยงานวิจัยนี้ได้ศึกษาต่อยอดโดยใช้ทฤษฎีควบคุมอย่างงเหมาะสม (optimal control theory) ในการหาแนวทางเพื่อป้องกัน ควบคุม และรักษาการติดเชื้อของโรคอหิวา ซึ่งงานวิจัยนี้มีประโยชน์สำหรับประเทศยากจนที่ไม่มีงบประมาณเพียงพอในการฉีดวัคซีนกับประชาชนในประเทศทั้งหมด นั่นคือองค์กรที่เกี่ยวข้องต้องมีการวางแผนควบคุมการระบาดโดยใช้แนวทางต่างๆควบคู่กันไปเชิงนโยบาย อย่างเช่น การบำบัดน้ำเสีย การรณรงค์ไม่ให้คนทิ้งเศษขยะลงแม่น้ำลำคลอง หรือการป้องกันการติดเชื้อโดยการรักษาสุขอนามัยให้อยู่ในเกณฑ์ที่ดี

คำสำคัญ : โรคอหิวา การรักษาด้วยการฉีดวัคซีน การหาค่าเหมาะสม การควบคุมโรค การแบ่งกลุ่มคน

Abstract

Zika virus infection is caused by the Zika Virus belonging to the *Flaviviridae* family. The virus is transmitted to people through the bite of an infected *Aedes* mosquito. However, although rare, sexual and mother-to-child are also other modes of transmission. The incubation time in infected humans is a few days to a week. The spread of the disease still presents in some developing countries and remote areas that cannot afford basic public health intervention and vaccine, hence, investigating other options are necessary. In this study, we formulate a diffusion mathematical model of the Zika virus with controls (personal protection, medical treatment, and insecticide). In this model, we will be able to observe the spatial movement of individuals and investigate if the disease can be controlled by performing social distancing combined with other control strategies. Further, we investigate the essential dynamics of the model through equilibrium analyses. The basic reproduction number with the spatial movement of the model is derived. Meanwhile, a time-dependent optimal control study is applied to the model to seek a cost-effective strategy to eradicate Zika virus outbreaks. Numerical results show that strategically deployed personal protection, treatment, and insecticide can significantly reduce the number of infectious individuals and mosquitoes. Also, applying a social connection program can additionally reduce the spread from one place to another, and thus the number of infections in total is reduced.

Keyword: Zika virus model, Disease control, Stability, Optimal control

Executive Summary

1. ความสำคัญและที่มาของปัญหาที่ทำการวิจัย

โรคไวรัสซิก้าเป็นโรคที่สามารถติดต่อกันโดย ผ่านยุงกัด จากแม่สู่ทารก ผ่านการมีเพศสัมพันธ์ และผ่านการให้เลือด ซึ่งตัวไวรัสที่กำลังระบาดอยู่เป็นสายพันธ์พันธ์ที่แพร่ผ่านยุงตระกูล Aedes หรือตระกูลเดียวกับยุงลายที่แพร่ไข้เลือดออกนั่นเอง หลังจากได้รับเชื้อ บางคนจะไม่แสดงอาการหรือมีอาการเพียงเล็กน้อย จึงทำให้ไม่ทราบว่าได้รับเชื้อ ส่วนบางคนที่มีอาการ ก็จะรู้สึก เป็นไข้ มีผื่นขึ้น ปวดหัว ปวดตามกล้ามเนื้อ ตาแดง และปวดตามข้อ ซึ่งอาการที่เป็นอาจมีระยะเป็นอาทิตย์ โดยส่วนใหญ่แล้วผู้ที่ได้รับเชื้อจะไม่แสดงอาการถึงขั้นโคม่าจนต้องนำตัวส่งโรงพยาบาล และคนที่ได้รับเชื้อและหายแล้ว ส่วนใหญ่จะมีภูมิคุ้มกันทำให้ไม่สามารถติดเชื้อรอบสองได้ กลุ่มที่ได้รับผลกระทบมากจะเป็นกลุ่มคนตั้งครรภ์ เนื่องจากว่าเชื้อไวรัสจะกระทบต่อพัฒนาการของทารกและอาจทำให้เกิดการแท้งได้ หรือเกิดมามีความพิการทางด้านร่างกายและสมอง

การป้องการการติดเชื้อจากซิก้านั้นอาจทำได้หลายทาง เช่น การป้องกันยุงกัด โดยการสวมเสื้อผ้าที่มิดชิดเวลาเดินทางไปบริเวณเสี่ยง การครีมหรือสารป้องกันยุง ใช้ถุงยางอนามัยระหว่างการมีเพศสัมพันธ์ กำจัดแหล่งเพาะพันธ์ของยุงพาหะ เป็นต้น

การศึกษาพฤติกรรมของไวรัสซิก้า มีการศึกษาโดยใช้แบบจำลองคณิตศาสตร์มากมาย เพื่อทำความเข้าใจเกี่ยวกับโรค พฤติกรรมของการแพร่ระบาดของโรค รวมทั้งการควบคุมการแพร่ระบาด ในปี 2009 Mukandavire เสนอแบบจำลองทางคณิตศาสตร์ที่ไม่ซับซ้อนมากนัก ง่ายต่อการเข้าใจ และมีความซับซ้อนในการหาผลเฉลยทางตัวเลขน้อย ซึ่งเป็นแบบจำลองที่ผู้วิจัยมากมายนำไปต่อยอด โดยที่โมเดลคือ

$$\frac{dS}{dt} = \mu N - \beta_e S\frac{B}{k+B} - \beta_h SI - \mu S$$
$$\frac{dI}{dt} = \beta_e S\frac{B}{k+B} + \beta_h SI - (\gamma + \mu)I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$
$$\frac{dB}{dt} = \varepsilon I - \delta B$$

โดยที่ S คือ กลุ่มสุ่มเสี่ยงของผู้ติดเชื่อ I คือ กลุ่มผู้ติดเชื้อ R คือ กลุ่มผู้ที่ได้รับการรักษาหายแล้ว และ B คือ กลุ่มประชากรของแบคทีเรีย โดยที่พารามิเตอร์อื่น ๆ คือค่าคงตัวต่าง ๆ

2. วัตถุประสงค์

2.1 เพื่อศึกษาปัจจัยที่ทำให้จำนวนผู้ติดเชื้อซิก้ารายใหม่อยู่ในระดับคงที่และมีแนวโน้มเพิ่มขึ้นทุกปี

2.2 เพื่อศึกษาหาแนวทางในการป้องกันการเพิ่มจำนวนของผู้ติดเชื้อซิก้ารายใหม่ โดยการคำนึงถึงงบประมาณการดำเนินการเป็นเป้าหมายหลัก

2.3 เพื่อใช้กระบวนการทางสถิติ คณิตศาสตร์ และคอมพิวเตอร์ ในการสร้างแบบจำลองทางคณิตศาสตร์

2.4 เพื่อนำองค์ความรู้ที่ได้จากการศึกษานำไปพัฒนาต่อยอดในการวางแผนเชิงนโยบายทางสาธารณสุขเพื่อการป้องกันและควบคุมการระบาดของโรค

3. ระเบียบวิธีวิจัย

3.1 ศึกษาแบบจำลองทางคณิตศาสตร์ต้นแบบที่นำเสนอโดย Mukandavire

3.2 ศึกษาแบบจำลองทางคณิตศาสตร์อื่น ๆ ที่เกี่ยวข้องเพื่อเป็นประโยชน์ต่อการขยายโมเดล

3.3 สร้างแบบจำลองทางคณิตศาสตร์ขั้นสูง

3.4 ตรวจสอบความถูกต้องของโมเดล

3.5 ศึกษาความเป็นไปได้ในการขยายแบบจำลองทางคณิตศาสตร์เพื่องานวิจัยในอนาคตและการประยุกต์ใช้

3.6 สรุปและเขียนงานวิจัย เพื่อตีพิมพ์ในวารสารและรายงานไปยังเจ้าของทุนวิจัย

4. แผนการดำเนินงานวิจัย

กิจกรรม	เดือนที่											
	1	2	3	4	5	6	7	8	9	10	11	12
1. ศึกษาแบบจำลองทางคณิตศาสตร์ต้นแบบที่นำเสนอโดย Mukandavire												
2. ศึกษาแบบจำลองทางคณิตศาสตร์อื่น ๆ ที่เกี่ยวข้องเพื่อเป็นประโยชน์ต่อการขยายโมเดล												
3. สร้างแบบจำลองทางคณิตศาสตร์ขั้นสูง												
4. ศึกษาความเป็นไปได้ในการขยายแบบจำลองทางคณิตศาสตร์เพื่องานวิจัยในอนาคตและการประยุกต์ใช้												
5. สรุปและเขียนงานวิจัย เพื่อตีพิมพ์ในวารสารและรายงานไปยังเจ้าของทุนวิจัย												

5. ตัวชี้วัดเพื่อการเมินผลสำเร็จของโครงการ

5.1 ตีพิมพ์ในวารสารระดับนานาชาติที่มีค่า Impact Factor **จำนวน 1 เรื่อง**

5.2 เจ้าของโครงการเป็น Corresponding Author

เนื้อหางานวิจัย

(ดูรายระเอียดทั้งหมดดังเอกสารแนบหน้าถัดไป)

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ผู้วิจัยขอขอบคุณกองทุนวิจัยมหาวิทยาลัยนเรศวร ที่ได้มอบทุนวิจัยเพื่อให้โอกาสสำหรับผู้วิจัยในการพัฒนาต่อยอดความรู้ทางด้านวิชาการด้วยดีเสมอมา ด้วยทุนที่ได้รับ ทำให้ผู้วิจัยสามารถขอความร่วมมือจากนิสิตในหลายระดับในการช่วยเหลืองานวิจัย และสามารถทำให้นิสิตได้เรียนรู้กระบวนการทำงานวิจัยมากขึ้น

ผู้ช่วยศาสตราจารย์ ดร.ชัยรัตน์ มดนาค

Abstract

Zika virus infection is caused by the Zika Virus belonging to the *Flaviviridae* family. The virus is transmitted to people through the bite of an infected *Aedes* mosquito. However, although rare, sexual and mother-to-child are also other modes of transmission. The incubation time in infected humans is a few days to a week. The spread of the disease still presents in some developing countries and remote areas that cannot afford basic public health intervention and vaccine, hence, investigating other options are necessary. In this study, we formulate a diffusion mathematical model of the Zika virus with controls (personal protection, medical treatment, and insecticide). In this model, we will be able to observe the spatial movement of individuals and investigate if the disease can be controlled by performing social distancing combined with other control strategies. Further, we investigate the essential dynamics of the model through equilibrium analyses. The basic reproduction number with the spatial movement of the model is derived. Meanwhile, a time-dependent optimal control study is applied to the model to seek a cost-effective strategy to eradicate Zika virus outbreaks. Numerical results show that strategically deployed personal protection, treatment, and insecticide can significantly reduce the number of infectious individuals and mosquitoes. Also, applying a social connection program can additionally reduce the spread from one place to another, and thus the number of infections in total is reduced.

บทคัดย่อ

การติดเชื้อไวรัสซิก้านั้น ส่วนใหญ่มาจากเชื้อไวรัสตระกูล Flaviviridae ซึ่งผ่านจากยุงสู่คน อย่างไรก็ตาม การติดเชื้อผ่านการมีเพศสัมพันธ์และจากแม่สู่ลูกก็สามารถเกิดขึ้นได้เช่นเดียวกัน แม้ว่าจะพบเห็นไม่บ่อยครั้งนัก ระยะฟักตัวของเชื้อไวรัสซิก้าจะอยู่ระหว่าง 2 วันหรือเป็นอาทิตย์ ในปัจจุบันยังมีการระบาดของโรคไวรัสซิก้าอยู่ในประเทศกำลังพัฒนา หรือพื้นที่ห่างไกล ที่ระบบสาธารณสุขของประเทศนั้น ๆ ยังเข้าไม่ถึง ซึ่งการศึกษาวิธีการควบคุมการระบาดในรูปแบบอื่น ๆ จึงมีความจำเป็น ในงานวิจัยนี้ ผู้วิจัยได้สร้างแบบจำลองทางคณิตศาสตร์ เพื่อศึกษาการระบาดของโรคซิก้าที่การระบาดเป็นกลุ่ม ๆ และศึกษาการควบคุมโดยใช้การเว้นระยะห่างระหว่างกลุ่ม จากผลการศึกษาพบกว่า กลุ่มติดเชื้อลดลงและการใช้การควบคุมแบบเว้นระยะห่าง เห็นว่า โรคไม่สามารถแพร่จากสถานที่หนึ่งไปยังอีกที่หนึ่งอย่างชัดเจน ทำให้โรคแพร่ได้ช้าลงและจำนวนผู้ติดเชื้อโดยรวมลดลงอย่างรวดเร็ว

Chapter 1
Introduction

Zika virus disease is a mosquito-borne which was first identified in Uganda in 1947 among Rhesus monkeys. The Zika virus is transmitted by the *Aedes* mosquitoes which these mosquitoes also transmit dengue, chikungunya, yellow fever and Japanese encephalitis viruses [1]. At least one in five infected people usually develops symptoms such as mild fever, rash, conjunctivitis (red eyes), muscle, and joint pain [1]. These symptoms can last for a few days to a week [2].

Also, an infected person can transmit the virus to his or her partner(s) through vaginal sex, anal sex, and likely oral sex. The sharing of sex toys may also put someone at risk. However, there is no evidence that the virus can be transmitted through saliva during deep kissing [3]. The transmission can be transferred even if the infected person has no symptoms. On the other hand, mother-to-child transmission during the pregnancy or around the time of birth has been reported [4]. Besides, fetuses infected with the Zika virus can develop underdeveloped brain resulting microcephaly where a baby has a head size much smaller compared with other babies of the same age and sex. However, there is no report of infants getting the Zika virus through breastfeeding up to date.

There have been several mathematical models and scientific reports [1, 4 – 11] to study the transmission dynamics of Zika virus disease. However, there are only a few studies conducted optimal control theory to gain guidelines for prevention, treatment, and insecticide. In March 2016, Moreno et al. [5] studied the role of short-term dispersal on the dynamics of Zika. The result verified that the density of community matters and the spread of the disease depends on the entries of the mobility of the residents. To eliminate the Zika virus, one would have to stop mobility and that would cause the economy to a halt.

In May 2016, Onuorah et al. [4] extended some published Zika virus models by including the death rate of infected individuals due to the virus. Meanwhile, there are a few other studies that have already included that into their models. [1] studied the impact of mosquito-borne and sexual transmission on the spread of the Zika virus in June 2016. In this study, the prevention and control of the disease have also been investigated. The results showed that prevention and control efforts against the Zika virus should target both the mosquito-borne and sexual transmission routes. In July 2016, Chunxiao et al. [6] introduced an optimal control mathematical model of the Zika virus by including three effective intervention strategies; personal protection, increasing the autoimmunity and using insecticide. However, the stability analyses and numerical

simulations of the model were not provided. In 2018, Naba et al. [7] proposed a mathematical model of the Zika virus with nonlinear incidence. The study observed that an optimal control problem was the key to reduce the number of Zika infectives, however, the study required some conditions for its endemic equilibrium stability.

In the same year, Suparit et al. [8] presented a mathematical model of Zika that focused on a time-dependent biting rate. The study developed a vector-borne compartmental model to analyze the Zika virus outbreak in Bahia. The results suggested that reducing the mosquito biting rates were found to be a more effective control measure than reducing the mosquito population size. The study mainly focused on numerical simulations and discussions. In 2019, Banulelos et al. [12] simulated an outbreak of the vector-borne Zika virus and found that the vector birth control seems to be more effective to control the outbreak. The main contribution of the present work is a modified-modeling framework that incorporates personal protection, medical treatment, and using insecticide as control measures to seek optimal control strategies to eradicate Zika virus outbreaks. We will utilize both analytical and numerical means to gain deeper insight into the disease dynamics. Meanwhile, our analysis and simulation results regarding the control strategies will provide useful information for public health administrations in the prevention of the Zika virus outbreak. The model will also explore in the case of the spatial movement through a diffusion problem to investigate the basic reproduction number, which represents how infectious the disease is.

The organization of this paper is as follows. Details of our Zika virus model is provided in Section 2, followed by a careful analysis of the disease-free equilibria (DFE) in Section 3. The global stability of the DFE for the system is also established. Section 4 is devoted to the analysis of the endemic dynamics. The Zika virus model with spatial movement will be rigorously analyzed in Section 5. An optimal control problem for our Zika virus model will be conducted and analyzed in Section 6. Finally, the conclusion will be drawn in Section 7.

Chapter 2

Mathematical Model

We describe the Zika virus dynamics using a system of five differential equations. The population of mosquitoes is divided into two compartments: S_v and I_v, where S_v represents the susceptible mosquitoes and I_v represents the infected mosquitoes with Zika virus. The population of humans is compartmentalized into three classes: susceptible (S_h), infectious (I_h), and recovered (R). A diagram to illustrate our model is presented in Figure 1.

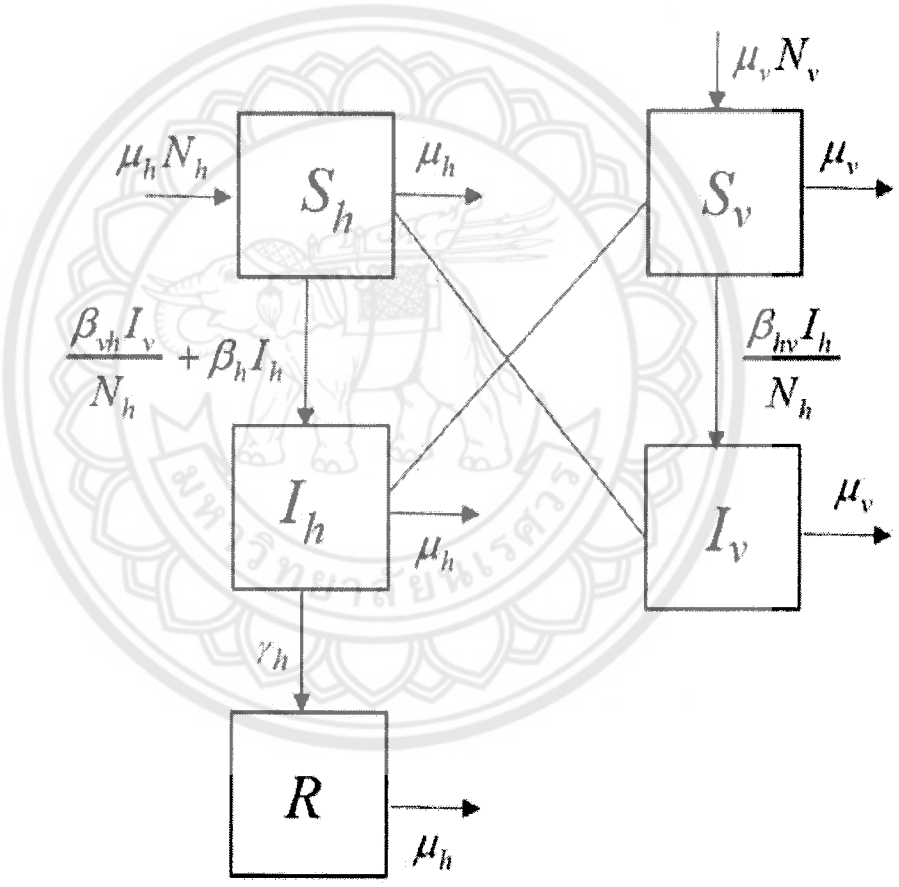

Fig. 1 Diagram of the model

We use an SI model to represent the disease dynamics among mosquitoes. Susceptible mosquitoes are infected through bites (at a rate of β_{hv}) with infectious humans. The infected mosquitoes then transmit the disease to human hosts at a rate of

β_{vh}. Meanwhile, the infection also spreads among the human population through the person-to-person pathway (sex or mother to child) with a transmission rate of β_h. The infectious people may recover from the disease with a rate of γ_h and enter into the recovered class.

We assume the natural birth and death rates are the same and denote that by μ_v and μ_h for mosquitoes and humans, respectively. Finally, we incorporate personal protection, medical treatment, and insecticide through source into the model as disease control measures. Our model thus takes the form below:

$$\begin{aligned}
\frac{dS_v}{dt} &= \mu_v N_v - \left(\mu_v + \frac{\beta_{hv} I_h}{N_h} + \phi_3\right) S_v, \\
\frac{dI_v}{dt} &= \frac{\beta_{hv} I_h}{N_h} S_v - \mu_v I_v, \\
\frac{dS_h}{dt} &= \mu_h N_h - \left(\mu_h + \frac{\beta_{vh} I_v}{N_h} + \beta_h I_h\right) S_h - \phi_1 S_h, \\
\frac{dI_h}{dt} &= \frac{\beta_{vh} I_v}{N_h} S_h + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h, \\
\frac{dR}{dt} &= \gamma_h I_h - \mu_h R + \phi_1 S_h + \phi_2 I_h.
\end{aligned}$$

The definition and numerical values of all the model parameters are provided in Table 1. Written in a vector form, the above equations become

$$\frac{dX}{dt} = F(X) \text{ with } X = (S_v, I_v, S_h, I_h, R)^T.$$

Epidemic analysis

We start our analysis of the model by studying the disease-free equilibrium (DFE) and calculating the basic reproduction numbers. Since our model contains two populations: mosquitoes and humans, it is important that we first investigate the mosquito subsystem, represented by equations (1) and (2), and then proceed to the human subsystem that consists equations (3) - (5). We will follow the same strategy when analyzing the endemic equilibrium as well.

It is straightforward to obtain the DFE for the mosquito subsystem:

$$\epsilon_v = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, 0\right)$$

Since infected mosquitoes will not spread the disease to other susceptible mosquitoes, thus we will not calculate the reproduction number for mosquitoes here. Also, we assume that the biting rate is constant and thus the reproduction number mainly depends on factors on the human's side. However, if the population size of the mosquito gets large, the infection rate of humans should be proportional. To calculate the reproduction number by using the coupled system is our future interest but we will not show it here for this study. The DFE for the human subsystem is given by

$$\epsilon_h = \left(\frac{\mu_h N_h}{\mu_h + \phi_1}, 0, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right).$$

To compute the basic reproduction number for humans, we use the well-known method of van den Driessche and Watmough, [13], with the associated next-generation matrices

$$F = \left[\beta_h \frac{\mu_h N_h}{\mu_h + \phi_1}\right] \quad \text{and} \quad V = \left[\mu_h + \gamma_h + \phi_2\right].$$

The basic reproduction number is then determined as the spectral radius of FV^{-1}; thus we obtain

$$R_0 = \frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)(\mu_h + \gamma_h + \phi_2)}.$$

Consequently, based on work in \cite{van}, we immediately obtain the result below:

Theorem 1

The disease-free equilibrium of the model (1) - (5) is locally asymptotically stable if $R_0 < 1$, and unstable if $R_0 > 1$.

Next, we examine the global asymptotic stability of the DFE. To that end, we state the following result introduced by Castillo-Chavez et al., [14].

Lemma 1

Consider a model system written in the form

$$\frac{dX_1}{dt} = F(X_1, X_2),$$
$$\frac{dX_2}{dt} = G(X_1, X_2), G(X_1, 0) = 0$$

where $X_1 \in \mathbf{R}^m$ denotes (its components) the number of uninfected individuals and $X_2 \in \mathbf{R}^m$ denotes (its components) the number of infected individuals including latent, infectious, etc; $X_0 = (X_1^*, 0)$ denotes the disease-free equilibrium of the system. Also, assume the two conditions (H1) and (H2) below:

(H1) For $\frac{dX_1}{dt} = F(X_1, 0), X_1^*$ is globally asymptotically stable;

(H2) $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2), \hat{G}(X_1, X_2) \geq 0$ for $(X_1, X_2) \in \Omega$,

where the off-diagonal elements of the Jacobian matrix $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$ are non-negative, and Ω is the region where the model makes biological sense.

Then the DFE $X_0 = (X_1^*, 0)$ is globally asymptotically stable provided that $R_0 < 1$

.

We now apply this lemma to our model.

Theorem 2

When $R_0 < 1$, the disease-free equilibrium of the model (6) is globally asymptotic stable.

Proof We show that the conditions (H1) and (H2) hold when $R_0 < 1$. In our ODE system (1) - (5), $X_1 = (S_v, S_h, R), X_2 = (I_v, I_h)$, and $X_1^* = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, \frac{\mu_h N_h}{\mu_h + \phi_1}, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right)$. We note that

$$\frac{dX_1}{dt} = F(X_1, 0) = \begin{bmatrix} \mu_v N_v - (\mu_v + \phi_3) S_v \\ \mu_h N_h - (\mu_h + \phi_1) S_h \\ \phi_1 S_h - \mu_h R \end{bmatrix}$$

is linear and its solution can be easily found as

$$S_v(t) = \frac{\mu_v N_v}{\mu_v + \phi_3} + \left(S_v(0) - \frac{\mu_v N_v}{\mu_v + \phi_3}\right) e^{-(\mu_v + \phi_3)t},$$

$$S_h(t) = \frac{\mu_h N_h}{\mu_h + \phi_1} + \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1}\right) e^{-(\mu_h + \phi_1)t},$$

$$R(t) = \frac{\phi_1 N_h}{\mu_h + \phi_1} - \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1}\right) e^{-(\mu_h + \phi_1)t} + \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1} + R(0) - \frac{\phi_1 N_h}{\mu_h + \phi_1}\right) e^{-\mu_h t}.$$

As $t \to \infty$, we have $S_v(t) \to \frac{\mu_v N_v}{\mu_v + \phi_3}, S_h(t) \to \frac{\mu_h N_h}{\mu_h + \phi_1}$ and $R(t) \to \frac{\phi_1 N_h}{\mu_h + \phi_1}$. Thus, $X_1^* = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, \frac{\mu_h N_h}{\mu_h + \phi_1}, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right)$ is globally asymptotically stable for the system $dX_1 / dt = F(X_1, 0)$.

Next, we have

$$G(X_1, X_2) = \begin{bmatrix} \frac{\beta_{hv} I_h S_v}{N_h} - \mu_v I_v \\ \frac{\beta_{vh} I_v S_h}{N_h} + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h. \end{bmatrix}.$$

We can then obtain

$$A = \begin{bmatrix} -\mu_v & \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \\ \frac{\beta_{vh} \mu_h N_h}{(\mu_h + \phi_1) N_h} & \frac{\beta_h M_h N_h}{\mu_h + \phi_1} - (\mu_h + \gamma_h + \phi_2) \end{bmatrix}$$

with all non-negative off-diagonal elements. Meanwhile, we find

$$\hat{G}(X_1, X_2) = \begin{bmatrix} \frac{\beta_{hv} I_h}{N_h} \left(\frac{\mu_v N_v}{\mu_v + \phi_3} - S_v \right) \\ a_{11} \end{bmatrix}.$$

where $a_{11} = \frac{\beta_{vh} I_v}{N_h} \left(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h \right) + \beta_h I_h \left(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h \right)$.

From equation (3), we observe that

$$\frac{dS_h}{dt} \le \mu_h N_h - (\mu_h + \phi_1) S_h$$

which yields

$$S_h \le \frac{\mu_h N_h}{\mu_h + \phi_1}$$

and similarly, from equation (1) we have

$$S_v \le \frac{\mu_v N_v}{\mu_v + \phi_3}.$$

Hence, $\hat{G}(X_1, X_2) \ge 0$.

Chapter 3

Endemic Analysis

The stability at the DFE determines the short-term epidemics of the disease, whereas its dynamics over a length of time is characterized by the stability at the endemic equilibrium. In this section, we will analyze the endemic properties of our Zika virus model.

Endemic equilibrium

We first examine the existence of the positive endemic equilibrium. Denote the endemic equilibrium of the model by

$$\epsilon^* = (S_v^*, I_v^*, S_h^*, I_h^*, R^*)$$

Setting equations (1) and (2) are equal to zero, we obtain

$$\frac{\beta_{hv} I_h^*}{N_h} S_v^* - \mu_v I_v^* = 0$$

$$\frac{\beta_{hv} I_h^*}{N_h} S_v^* = \mu_v I_v^*$$

and

$$\mu_v N_v - \left(\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3\right) S_v^* = 0$$

$$\mu_v N_v = \left(\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3\right) S_v^*.$$

Thus

$$I_v^* = \frac{\beta_{hv} I_h^*}{\mu_v N_h} S_v^* \quad \text{and} \quad S_v^* = \frac{\mu_v N_v}{\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3}.$$

Hence, with some algebraic manipulations, we have

$$I_v^* = \frac{\beta_{hv} I_h^*}{\mu_v N_h} \left(\frac{\mu_v N_v}{\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3} \right) = \frac{\beta_{hv} I_h^* N_v}{N_h \mu_v + \beta_{hv} I_h^* + \phi_3 N_h}.$$

Now set equation (4) is equal to zero, we obtain

$$\frac{\beta_{vh}I_v^*}{N_h}S_h^* + \beta_h I_h^* S_h^* - (\mu_h + \gamma_h + \phi_2)I_h^* = 0$$

$$\frac{\beta_{vh}I_v^*}{N_h}S_h^* + \beta_h I_h^* S_h^* = (\mu_h + \gamma_h + \phi_2)I_h^*$$

$$S_h^* = \frac{(\mu_h + \gamma_h + \phi_2)I_h^*}{\left(\frac{\beta_{vh}I_v^*}{N_h}S_h^* + \beta_h I_h^*\right)}$$

When we substitute I_v^* into it then we find

$$S_h^* = \frac{(\mu_h + \gamma_h + \phi_2)I_h^*}{\frac{\beta_{hv}\beta_{vh}N_v I_h^*}{N_h(N_h\mu_v + \beta_{hv}I_h^* + \phi_3 N_h)} + \beta_h I_h^*}.$$

Next, we substitute I_v^* and S_h^* into (3) to obtain

$$\mu_h N_h - \left(\mu_h + \frac{\beta_{vh}\beta_{hv}I_h^* N_v}{N_h(\mu_v N_h + \beta_{hv}I_h^* + \phi_3 N_h)} + \beta_h I_h^* + \phi_1\right) \times \left(\frac{(\mu_h + \gamma_h + \phi_2)I_h^*}{\frac{\beta_{hv}\beta_{vh}N_v I_h^*}{N_h(N_h\mu_v + \beta_{hv}I_h^* + \phi_3 N_h)} + \beta_h I_h^*}\right) = 0.$$

This equation, after some algebra, yields a quadratic equation

$$A_1 I_h^{*2} + B_1 I_h^* + C_1 = 0,$$

where

$$A_1 = -\beta_h\beta_{hv}aN_h,$$

$$B_1 = \beta_h\mu_h\beta_{hv}N_h^2 - \mu_h aN_h\beta_{hv} - \beta_{vh}\beta_{hv}N_v a - \beta_h aN_h^2\mu_v - \beta_h a\phi_3 N_h^2 - \phi_1 aN_h\beta_{hv},$$

$$C_1 = \mu_h N_h\beta_{vh}\beta_{hv}N_v + \beta_h\mu_h\mu_v N_h^3 + \beta_h\mu_h N_h^3\phi_3 - \mu_h\mu_v aN_h^2 - \mu_h a\phi_3 N_h^2 - \phi_1 aN_h^2\mu_v - a\phi_1\phi_3 N_h^2,$$

and where $a = \mu_h + \gamma_h + \phi_2$.

The roots of equation (12) have to satisfy

$$I_{h1}^* I_{h2}^* = \frac{C_1}{A_1} \text{ and } I_{h1}^* + I_{h2}^* = -\frac{B_1}{A_1}.$$

It is obvious that $A_1 < 0$. Meanwhile we have

$$C_1 = \mu_h N_h\beta_{vh}\beta_{hv}N_v + \beta_h\mu_h\mu_v N_h^3 + \beta_h\mu_h N_h^3\phi_3 - \mu_h\mu_v aN_h^2 - \mu_h a\phi_3 N_h^2 - \phi_1 aN_h^2\mu_v - a\phi_1\phi_3 N_h^2$$

$$= \mu_h N_h\beta_{vh}\beta_{hv}N_v + \left(\beta_h\mu_h\mu_v N_h^3 - (\mu_h + \phi_1)aN_h^2\mu_v\right)$$

$$
\begin{aligned}
&+\left(\beta_h\mu_h N_h^3\phi_3-(\mu_h+\phi_1)a\phi_3N_h^2\right)\\
&=\mu_hN_h\beta_{vh}\beta_{hv}N_v+(\mu_h+\phi_1)aN_h^2\mu_v\left(\frac{\beta_h\mu_hN_h}{(\mu_h+\phi_1)a}-1\right)\\
&+(\mu_h+\phi_1)a\phi_3N_h^2\left(\frac{\beta_h\mu_hN_h}{(\mu_h+\phi_1)a}-1\right)\\
&=\mu_hN_h\beta_{vh}\beta_{hv}N_v+(\mu_h+\phi_1)aN_h^2\mu_v(R_0-1)\\
&+(\mu_h+\phi_1)a\phi_3N_h^2(R_0-1).
\end{aligned}
$$

It can be clearly seen that $C_1>0$ when $R_0>1$. Thus $I_{h1}^*I_{h2}^*<0$ in this case; that are the two roots of equation (12) are both real: one must be positive and the other must be negative. Consequently, we have the result below:

Theorem 3

The positive endemic equilibrium ϵ^* of the system (1)-(5) exists and is unique when $R_0>1$.

Also, we note that if $I_v^*=0$ (i.e., no infection persistent in mosquitoes, and thus no disease contributed to the humans from infectious mosquitoes and vice versa), then $\beta_{vh}=\beta_{hv}=0$, and thus

$$C_1=(\mu_h+\phi_1)aN_h^2\mu_v(R_0-1)+(\mu_h+\phi_1)a\phi_3N_h^2(R_0-1).$$

It is obvious that $C_1<0$ when $R_0<1$ and $C_1>0$ when $R_0>1$. Since A_1 is always negative, thus $I_{h1}^*I_{h2}^*>0$ when $R_0<1$; that is, the two roots of equation (12) can be either both negative or both positive real numbers. Meanwhile we have

$$B_1=-\beta_haN_h^2\mu_v-\beta_ha\phi_3N_h^2\le 0.$$

Consequently, equation (12) has only one biologically meaningful root $I_{h1}^*=I_{h2}^*=0$ since $I_{h1}^*+I_{h2}^*\le 0$. These analytical findings show that in the absence of mosquitoes, the human subsystem (3) - (5) is reduced to a normal SIR model. We observe that the infected mosquitoes directly contribute to the positive growth of infectious humans in our model. Hence, using personal protection and insecticide through source would be important control measures to protect humans against the infection and to contain the disease outbreak.

Local stability

We proceed to analyze the stability properties of the endemic equilibrium. First, we establish the following result regarding local stability.

Theorem 4

When $R_0 > 1$ and $I_v^* > 0$, the endemic equilibrium ϵ^* is locally asymptotically stable.

Proof

The Jacobian of the system (3)- (4) at ϵ^* is given by

$$J(\epsilon^*) = \begin{bmatrix} J_{11} & -\beta_h S_h \\ \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* & \beta_h S_h - (\mu_h + \gamma_h + \phi_2) \end{bmatrix}$$

where $J_{11} = -\mu_h - \frac{\beta_{vh}}{N_h} I_v^* - \beta_h I_h^* - \phi_1$.

The characteristic equation of the matrix $J(\epsilon^*)$ is

$$\begin{aligned} 0 &= det[\lambda I - J(\epsilon^*)] \\ &= \left(\lambda + \left(\mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1\right)\right) \\ &\times \left(\lambda - \left(\beta_h S_h^* - (\mu_h + \gamma_h + \phi_2)\right)\right) \\ &+ \beta_h S_h^* \left(\frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^*\right) \end{aligned}$$

The above equation can be put into a quadratic equation of the form

$$a_2 \lambda^2 + a_1 \lambda + a_0 = 0,$$

where

$$\begin{aligned} a_2 &= 1, \\ a_1 &= \mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1 + a - \beta_h S_h^*, \\ a_0 &= -(\mu_h + \phi_1)\beta_h S_h^* + (\mu_h + \phi_1)a \\ &+ \left(\frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^*\right)a. \end{aligned}$$

The Routh-Hurwitz criterion requires

$$a_1 > 0, a_2 > 0 \text{ and } a_3 > 0$$

as the necessary and sufficient conditions for the locally asymptotical stability; i.e., all roots of the polynomial (13) have negative real parts. Meanwhile, we have

$$a_1 = \mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1 + a - \beta_h S_h^*,$$

$$= \mu_h . + \frac{\beta_{vh}\beta_{hv} I_h^* N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h I_h^* + \phi_1$$

$$+ a\left(1 - \frac{\beta_h}{\frac{\beta_{vh}\beta_{hv} N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h}\right)$$

From equation (3) we observe that

$$\frac{dS_h^*}{dt} \le \mu_h N_h - (\mu_h + \phi_1) S_h^*,$$

which yields $S_h^* \le \frac{\mu_h N_h}{\mu_h + \phi_1}$. Next, we proceed to show that $a_0 > 0$. We can write a_0 as

$$a_0 = \mu_h N_h \left(\frac{\beta_{vh}\beta_{hv} N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h\right) - (\mu_h + \phi_1)\beta_h S_h^*$$

$$= \frac{\mu_h \beta_{vh}\beta_{hv} N_v}{N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h} + \beta_h(\mu_h + \phi_1)\left(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h^*\right).$$

It can be clearly seen that $a_0 > 0$. This completes the proof.

Chapter 4

Zika Virus Model with Spatial Movement and Optimal Control

Model Framework

As mentioned before, vectors and humans can be a key factor in the spread of the Zika virus. Thus, in this section, we will extend our model to a PDE system to investigate the spatial dynamics of Zika virus. We consider a one-dimensional spatial domain, $x \in [0,1]$ and we assume that both the human population and the virus undergo a diffusion process. Let $D_i > 0 \ \ (0 \le i \le 5)$ is the diffusion coefficient of $S_v(x,t)$, $I_v(x,t)$, $S_h(x,t)$, $I_h(x,t)$, and $R(x,t)$, respectively. Then the Zika model (1)-(5) with the inclusion of diffusion takes the form:

$$
\begin{aligned}
\frac{\partial S_v}{\partial t} &= \mu_v N_v - (\mu_v + \frac{\beta_{hv} I_h}{N_h} + \phi_3) S_v + D_1 \frac{\partial^2 S_v}{\partial x^2}, \\
\frac{\partial I_v}{\partial t} &= \frac{\beta_{hv} I_h}{N_h} S_v - \mu_v I_v + D_2 \frac{\partial^2 I_v}{\partial x^2}, \\
\frac{\partial S_h}{\partial t} &= \mu_h N_h - (\mu_h + \frac{\beta_{vh} I_v}{N_h} + \beta_h I_h) S_h - \phi_1 S_h + D_3 \frac{\partial^2 S_h}{\partial x^2}, \\
\frac{\partial I_h}{\partial t} &= \frac{\beta_{vh} I_v}{N_h} S_h + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h + D_4 \frac{\partial^2 I_h}{\partial x^2}, \\
\frac{\partial R}{\partial t} &= \gamma_h I_h - \mu_h R + \phi_1 S_h + \phi_2 I_h + D_5 \frac{\partial^2 R}{\partial x^2}.
\end{aligned}
$$

Meanwhile, we assume the entire domain represents a closed community of our interest with an assumption; that is, no individual would cross the boundary. Hence, we impose the Neumann (no-flux) boundary conditions for $x \in [0,1], t > 0$:

$$
\frac{\partial S_i}{\partial x} = \frac{\partial I_i}{\partial x} = \frac{\partial R}{\partial x} = 0, \qquad i = v, h.
$$

Turing Instability

It is known that in many reaction-diffusion systems with multiple components is the occurrence of Turing instability [15]; that is, loss of stability due to inclusion of diffusion (i.e. there exist conditions under which the spatial uniform steady state in the absence of diffusion and can become unstable because of diffusion). We linearize system

(12)-(16) at the DFE; $\epsilon^0 = (S_v^0, I_v^0, S_h^0, I_h^0, R^0)^T = (\frac{\mu_v N_v}{\mu_v + \phi_3}, 0, \frac{\mu_h N_h}{\mu_h + \phi_1}, 0, \frac{\phi_1 N_h}{\mu_h + \phi_1})^T$ of the system (1)-(5) in the absence of diffusion. Introducing the new coordinates $Y = (Y_1, Y_2, Y_3, Y_4, Y_5)^T = (S_v - S_v^0, I_v - I_v^0, S_h - S_h^0, I_h - I_h^0, R - R^0)^T$, we obtain the linear system as follows:

$$\frac{\partial Y}{\partial t} = D\frac{\partial^2 Y}{\partial x^2} + JY,$$

where J is the Jacobian matrix of the associated ODE system evaluated at the DFE:

$$J(\epsilon^0) = \begin{bmatrix} -(\mu_v + \phi_3) & 0 & 0 & -\frac{\beta_{hv} S_v^0}{N_h} & 0 \\ 0 & -\mu_v & 0 & \frac{\beta_{hv} S_v^0}{N_h} & 0 \\ 0 & -\frac{\beta_{vh} S_h^0}{N_h} & -(\mu_h + \phi_1) & -\beta_h S_h^0 & 0 \\ 0 & \frac{\beta_{vh} S_h^0}{N_h} & 0 & a_{22} & 0 \\ 0 & 0 & \phi_1 & \gamma_h + \phi_2 & -\mu_h \end{bmatrix},$$

where $a_{22} = \beta_h S_h^0 - (\mu_h + \gamma_h + \phi_2)$ and $D =$ diag $[D_1, D_2, D_3, D_4, D_5]$. Consider the eigenvalue problem

$$\frac{\partial^2 \psi(x)}{\partial x^2} = -\rho\psi(x), \qquad x \in (0,1),$$
$$\frac{\partial \psi(x)}{\partial x} = 0, \qquad x = 0, 1.$$

One can easily verify that the eigenvalues of the boundary value problem (21) are $\rho_k = (k\pi)^2 \geq 0$ and the corresponding eigenfunctions are $\psi_k(x) = cos(k\pi x)$. Now let us return to our system (20). Since the system is linear, the solution $Y(x,t)$ can be written as the sum of eigenfunctions

$$Y(x,t) = \sum_j a_j e^{\lambda t} \psi_j(x) \qquad (1 \leq j \leq 5)$$

where $\psi_j(x)$ is the solution of the eigenvalue problem (21), λ and a_j are constants. Substituting (22) into (20) yields

$$|J-\rho D-\lambda I_5|=0,$$

where I_5 is a 5×5 identity matrix. We are interested in whether there exists λ such that $Re(\lambda)>0$ at the DFE. Solving (23), we find that the associated eigenvalues are given by

$$|J-\rho D-\lambda I_5|=[-a_1-\rho D_1-\lambda][-\mu_h-\rho D_5-\lambda]$$
$$\times\begin{vmatrix} -\mu_v-\rho D_2-\lambda & 0 & \frac{\beta_{hv}S_v^0}{N_h} \\ -\frac{\beta_{vh}S_h^0}{N_h} & -a_3-\rho D_3-\lambda & -\beta_h S_h^0 \\ \frac{\beta_{vh}S_h^0}{N_h} & 0 & \beta_h S_h^0-a_4-\rho D_4-\lambda \end{vmatrix}=0$$

where $a_1=\mu_v+\phi_3, a_3=\mu_h+\phi_1$, and $a_4=\mu_h+\gamma_h+\phi_2$.

This implies that

$$\lambda_1=-\frac{k_1+k_4}{2}+\frac{\sqrt{(k_1-k_4)^2+4k_2k_3}}{2},$$
$$\lambda_2=-\frac{k_1+k_4}{2}-\frac{\sqrt{(k_1-k_4)^2+4k_2k_3}}{2},$$
$$\lambda_3=-(a_1+\rho D_1),$$
$$\lambda_4=-(a_3+\rho D_3),$$
$$\lambda_5=-(\mu_h+\rho D_5),$$

where

$$k_1=\mu_v+\rho D_2,$$
$$k_2=\frac{\beta_{vh}\mu_h}{(\mu_h+\phi_1)},$$
$$k_3=\frac{\beta_{hv}\mu_v N_v}{(\mu_v+\phi_3)N_h},$$
$$k_4=-\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)}+(\mu_h+\gamma_h+\phi_2)+\rho D_4.$$

Proposition 1

If $R_0^{ODE}<1$, inclusion of diffusion spatial spread into model (1)-(5) will not produce a Turing instability.

Proof

Suppose that $R_0^{ODE}<1$. We obtain that

$$0 < (\mu_h + \gamma_h + \phi_2) - \frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)}.$$

Thus $k_4 = -\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) + \rho D_4 > 0$. This implies that $k_i > 0$ for all $i = 1,2,3,4$. It follows that $\lambda_i < 0, (i = 2,3,4)$ and the only eigenvalue that could have a sign change is λ_1. We now demonstrate that $\lambda_1 < 0$. Notice that

$$\begin{aligned}
\lambda_1 \lambda_2 &= \left(-\frac{k_1 + k_4}{2} \right)^2 - \left(\frac{\sqrt{(k_1 - k_4)^2 + 4k_2 k_3}}{2} \right)^2 \\
&= \frac{k_1^2 + 2k_1 k_4 + k_4^2 - k_1^2 + 2k_1 k_4 - k_4^2 - 4k_2 k_3}{4} \\
&= k_1 k_4 - k_2 k_3
\end{aligned}$$

where

$$\begin{aligned}
k_1 k_4 - k_2 k_3 &= -\mu_v \frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + \mu_v (\mu_h + \gamma_h + \phi_2) + \mu_v \rho D_4 \\
&\quad - \frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} \rho D_2 + (\mu_h + \gamma_h + \phi_2) \rho D_2 \\
&\quad + \rho^2 D_2 D_4 - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \\
&= \mu_v \rho D_4 + \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) + \rho D_4 \right) \rho D_2 \\
&\quad + \left[\mu_v \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) \right) - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \right]. \\
&= \mu_v \rho D_4 + k_4 \rho D_2 + \left[\mu_v \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) \right) \right. \\
&\quad \left. - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \right].
\end{aligned}$$

It is clear that the first two terms of equation (30) are the sum of two positive terms ($k_4 > 0$). Thus by Theorem 3, $\mu_v \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) \right) + (\mu_h + \gamma_h + \phi_2) - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h}$ is a product of two eigenvalues of $J(\epsilon^0)$ at the DFE, hence it is positive since the system (1)-(5) is stable at the DFE. This yield $\lambda_1 \lambda_2 > 0$, and it implies that $\lambda_1 < 0$ (since $\lambda_2 < 0$). Therefore, we obtain that all eigenvalues of the system (12)-(16) are negative real numbers and hence Turing instability will not occur.

PDE Model Threshold Dynamics

We now study the spatial threshold dynamics of the Zika virus by analyzing the basic reproduction number derived from the PDE model (12)-(16). We will use the ideas presented in [16-18], in which the concept of the basic reproduction number is extended to the reaction-diffusion epidemic system with Neumann (no-flux) boundary conditions. Based on these studies, the basic reproduction number R_0 for a PDE epidemic system is defined as the spectral radius of the operator

$$L[\phi(x)] = \int_0^\infty F(x)T(t)\phi dt = F(x)\int_0^\infty T(t)\phi dt$$

and in [18] they showed that

$$\int_0^\infty T(t)\phi dt = -B^{-1}\phi,$$

where

$$L = -FB^{-1},$$

for $B := \nabla\cdot(d_I\nabla) - \nabla - V$. Here F and V are analogues to the next-generation matrices associated with the corresponding ODE system (i.e. without diffusion terms); $T(t)$ denotes the solution semigroup for the linearized reaction-diffusion system for disease compartments; ϕ describes the distribution of the initial infection; and d_I is the diffusion coefficient vector. For our Zika virus model (12)-(16), we have

$$d_I = diag[D_2, D_4],$$

$$F = \begin{bmatrix} \frac{\beta_h \mu_h N_h}{\mu_h + \phi_1} \end{bmatrix}, \qquad V = \begin{bmatrix} \mu_h + \gamma_h + \phi_2 \end{bmatrix},$$

and

$$B = \begin{bmatrix} D_4 \frac{\partial^2}{\partial x^2} - (\mu_h + \gamma_h + \phi_2) \end{bmatrix}.$$

To analyze the basic reproduction number of the PDE system (12)-(16) which is

$$R_0^{PDE} = \rho(L),$$

we proceed to calculate B^{-1} by solving $B(\phi_1) = y_1$ subject to homogeneous Neumann boundary conditions. First, let us consider the boundary value problem

$$B_1[\phi_1] := D_4 \frac{\partial^2 \phi_1}{\partial x^2} - (\mu_h + \gamma_h + \phi_2)\phi_1 = y_1,$$

$$\phi_1'(0) = 0, \quad \phi_1'(1) = 0, 0 \le x \le 1$$

This problem can be easily solved by using the Laplace transform. Describe the Laplace transforms of $\phi_1(x)$ and $y_1(x)$ by $\psi_1(s)$ and $Y_1(s)$, respectively. Consider

$$L[D_4\phi_1'' - (\mu_h + \gamma_h + \phi_2)\phi_1] = L[y_1],$$
$$(D_4 s^2 - (\mu_h + \gamma_h + \phi_2))\psi_1(s) - D_4 s\psi_1(0) = Y_1(s).$$

It yields

$$\psi_1(s) = \frac{Y_1(s)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)} + \frac{sD_4\psi_1(0)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)}$$

where we have applied the first boundary condition of ψ_1. The inverse Laplace transform and the convolution integral then give

$$\psi_1(x) = \frac{1}{\sqrt{D_4(\mu_h + \gamma_h + \phi_2)}} \times \int_0^x \sinh\left[\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau$$
$$\frac{\cosh\left(\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}}\right)}{\sqrt{D_4(\mu_h + \gamma_h + \phi_2)}\sinh\left(\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}}\right)} \times \int_0^1 \cosh\left[\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}}(1-\tau)\right] y_1(\tau)d\tau.$$

Indeed,

$$\psi_1(x) = L^{-1}[\psi_1(s)] = L^{-1}\left[\frac{Y_1(s)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)}\right] + L^{-1}\left[\frac{sD_4\psi_1(0)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)}\right].$$

Consider,

$$L^{-1}\left[\frac{Y_1(s)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)}\right] = L^{-1}\left[\frac{Y_1(s)\sqrt{D_4(\mu_h + \gamma_h + \phi_2)}}{\sqrt{D_4(\mu_h + \gamma_h + \phi_2)}(\sqrt{D_4})^2 s^2 - (\mu_h + \gamma_h + \phi_2)}\right]$$

Setting

$$f(s)=\frac{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}{(\sqrt{D_4}s)^2-(\sqrt{\mu_h+\gamma_h+\phi_2})^2}$$

and

$$g(s)=\frac{Y_1(s)}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}.$$

We obtain

$$L^{-1}[f*g]=\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}\times\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right]y_1(\tau)d\tau.$$

Next, we consider

$$L^{-1}\left[\frac{sD_4\psi_1(0)}{D_4s^2-(\mu_h+\gamma_h+\phi_2)}\right]=\psi_1(0)L^{-1}\left[\frac{sD_4}{(\sqrt{D_4})^2s^2-(\sqrt{\mu_h+\gamma_h+\phi_2})^2}\right]$$
$$=\psi_1(0)\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right).$$

Consequently, we have

$$\psi_1(x)=\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}\times\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right]y_1(\tau)d\tau$$
$$+\psi_1(0)\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right).$$

We differentiate ψ_1 and applying the boundary condition $\psi_1'(1)=0$, we obtain that

$$\psi_1'(x)=\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}\times\frac{d}{dx}\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right]y_1(\tau)d\tau$$
$$+\psi_1(0)\frac{d}{dx}\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)$$
$$=\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}}\times\int_0^x \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right]y_1(\tau)d\tau$$
$$+\frac{\psi_1(0)}{\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right).$$

Hence

$$\psi_1(0) = -\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)}$$
$$\times\int_0^1 \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(1-\tau)\right] y_1(\tau)d\tau.$$

Now let us focus on the eigenvalue problem $L[\phi]=\lambda\phi$; that is,

$$-FB^{-1}\phi = \lambda\phi = L[\phi] = R_0.$$

With some algebraic manipulation, the eigenvalue problem can be put into the form

$$k_{i1}\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau + k_{i2}\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)$$
$$\times\int_0^1 \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(1-\tau)\right] y_1(\tau)d\tau \quad (i=1)$$

where

$$k_{11} = \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}},$$
$$k_{12} = \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)}.$$

Optimal control

Now we turn to the more general model (1) - (5) with time-dependent control profiles $\phi_1(t),\phi_2(t)$ and $\phi_3(t)$, and conduct an optimal control study [19]. We consider the system on a time interval [0,T]. The functions $\phi_1(t),\phi_2(t)$ and $\phi_3(t)$ are assumed to be at least Lebesgue measurable on [0,T]. The control set is defined as

$$\Gamma = \{(\phi_1(t),\phi_2(t),\phi_3(t) \mid 0\le\phi_1(t)\le\phi_{1max},\ 0\le\phi_2(t)\le\phi_{2max},\ 0\le\phi_3(t)\le\phi_{3max}\}$$

where ϕ_{1max},ϕ_{2max} and ϕ_{3max} are the upper bounds for the control rates. The bound reflects a practical limitation on the maximum rate of controls in a given time.

Our optimal control study aims to minimize the total numbers of infectious people and the cost of controls over the time interval [0,T]; i.e.,

$$\min_{\phi_1,\phi_2,\phi_3\in\Omega} \int_0^T [I_h(t)+I_v(t)+c_1\phi_1(t)S_h(t)+c_2\phi_2(t)I_h(t)+c_3(t)\phi_3(t)S_v(t)$$
$$c_4\phi_1^2(t)+c_5\phi_2^2(t)+c_6\phi_3^2(t)]dt$$

where c_1, c_2, c_3, c_4, c_5 and c_6 are appropriate units defined the appropriate costs associated with the controls.

Let us first define the adjoint functions $\lambda_{S_v}, \lambda_{S_h}, \lambda_{I_h}$ and λ_{I_v} associated with the state equations for S_v, S_h, I_h and I_v, respectively. We then form Hamiltonian, H, by multiplying each adjoint function with the right-hand side of its corresponding state equation and adding each of these products to the integrand of the objective functional.

As a result, we obtain

$$\begin{aligned}
H &= I_h(t)+I_v(t)+c_1\phi_1(t)S_h(t)+c_2\phi_2(t)I_h(t)\\
&+c_3\phi_3(t)S_v(t)+c_4\phi_1^2(t)+c_5\phi_2^2(t)+c_6\phi_3^2(t)\\
&+\lambda_{S_h}\left(\mu_h N_h-\left(\mu_h+\frac{\beta_{vh}I_v}{N_h}+\beta_h I_h\right)S_h-\phi_1(t)S_h\right)\\
&+\lambda_{I_h}\left(\frac{\beta_{vh}I_v}{N_h}S_h+\beta_h I_h S_h-(\mu_h+\gamma_h+\phi_2(t))I_h\right)\\
&+\lambda_{S_v}\left(\mu_v N_v-(\mu_v+\frac{\beta_{hv}I_h}{N_h})S_v-\phi_3(t)S_v\right)\\
&+\lambda_{I_v}\left(\frac{\beta_{hv}I_h S_v}{N_h}-\mu_v I_v\right)
\end{aligned}$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_{S_h}}{dt}=-\frac{\partial H}{\partial S_h}, \frac{d\lambda_{S_v}}{dt}=-\frac{\partial H}{\partial S_v}, \frac{d\lambda_{I_h}}{dt}=-\frac{\partial H}{\partial I_h}$, and $\frac{d\lambda_{I_v}}{dt}=-\frac{\partial H}{\partial I_v}$. Thus, we have

$$\begin{aligned}
\frac{d\lambda_{S_h}}{dt} &= -c_1\phi_1(t)+\lambda_{S_h}\left(\mu_h+\frac{\beta_{vh}I_v}{N_h}+\beta_h I_h+\phi_1\right)-\lambda_{I_h}\left(\frac{\beta_{vh}I_v}{N_h}+\beta_h I_h\right),\\
\frac{\lambda_{I_h}}{dt} &= -1-c_2\phi_2(t)+\lambda_{S_h}\beta_h S_h-\lambda_{I_h}(\beta_h S_h-(\mu_h+\gamma_h+\phi_2(t)))+\lambda_{S_v}\frac{\beta_{hv}S_v}{N_h}-\lambda_{I_v}\frac{\beta_{hv}S_v}{N_h},\\
\frac{d\lambda_{S_v}}{dt} &= -c_3\phi_3(t)+\lambda_{S_v}\left(\mu_v+\frac{\beta_{hv}I_h}{N_h}+\phi_3(t)\right)-\lambda_{I_v}\frac{\beta_{hv}I_h}{N_h},\\
\frac{d\lambda_{I_v}}{dt} &= -1+\lambda_{S_h}\frac{\beta_{vh}S_h}{N_h}-\lambda_{I_h}\frac{\beta_{vh}S_h}{N_h}+\lambda_{I_v}\mu_v
\end{aligned}$$

with the final-time conditions $\lambda_{S_h}(T)=0, \lambda_{S_v}(T)=0, \lambda_{I_h}(T)=0$, and $\lambda_{I_v}(T)=0$. The characterizations of the optimal controls $\phi_1(t), \phi_2(t)$ and $\phi_3(t)$ are then based on the conditions

$\frac{\partial H}{\partial \phi_1}=0$, $\frac{\partial H}{\partial \phi_2}=0$, and $\frac{\partial H}{\partial \phi_3}=0$ respectively, subject to the constraints $0 \le \phi_1(t) \le \phi_{1max}, 0 \le \phi_2(t) \le \phi_{2max}$ and $0 \le \phi_3(t) \le \phi_{3max}$. Thus, we have

$$\begin{aligned} \phi_1^*(t) &= \backslash max[0, min(\phi_1(t), \phi_{1max})], \\ \phi_2^*(t) &= max[0, min(\phi_2(t), \phi_{2max})], \\ \phi_3^*(t) &= max[0, min(\phi_3(t), \phi_{3max})], \end{aligned}$$

where

$$\phi_1(t) = \frac{(\lambda_{S_h} - c_1)S_h}{2c_4},$$

$$\phi_2(t) = \frac{(\lambda_{I_h} - c_2)I_h}{2c_5},$$

$$\phi_3(t) = \frac{(\lambda_{S_v} - c_3)S_v}{2c_6}$$

Numerical results

The optimal control system, consisting of the state equations, the adjoint equations, and the optimality conditions, has to be solved numerically. We have conducted numerical simulation using various choices of cost parameters and time intervals, and have observed a unique solution in each case. The numerical results demonstrate that optimal control strategies can significantly bring down the number of infectious individuals and infectious mosquitoes.

In the simulation for our diffusion model, we assume that a Zika virus disease outbreak first appears on day 1 of the first month, then it spreads to the neighboring cities (in diffusion way) and reaches its peak of the outbreak in about two months and a half (average mosquitoes' life-span). Also, for each location (in the spatial domain), we assume that the initial number of infected mosquitoes is the same (from reproduction). We further assume that cities in our simulation are about the same size, therefore, in each spatial location, the initial condition for infected humans is also the same. We also extend our numerical study to investigate the time-dependent biting rate that is based on seasonality by assuming that the biting rate of mosquitoes starts small and increases

over time. It will reach its maximum value of about seventy days and decrease to almost zero at the end of the fourth month.

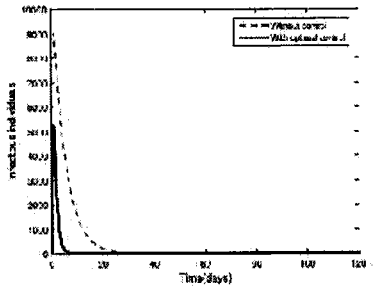

Fig. 2 Infectious humans of the ODE model

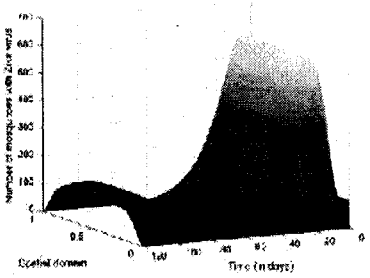

Fig. 4 Mosquitoes with the Zika virus in each spatial location versus time

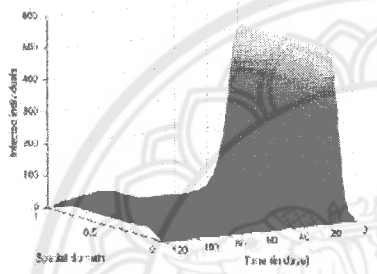

Fig. 3 Infected humans in diffusion model

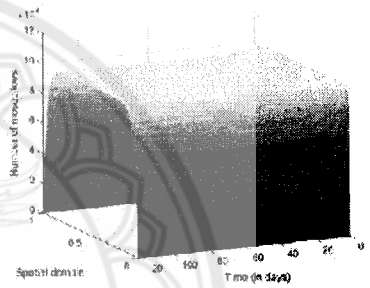

Fig. 5 Susceptible mosquitoes in each spatial location versus time

Fig.2 shows the number of infectious humans, in which without controls is shown in the dashed line and that with optimal controls is shown in the solid line. The controls include personal protection, medical treatment, and insecticide. As the graph presented, the reduction in both the infection level and the outbreak period is significant. To further understand the effects of social connection among humans, we also present the human infectious diffusion curve in Fig.3. As demonstrated, we observe that if an outbreak starts at location $x = 0.5$, it will spread further out to the neighboring cities (the closer to the starting point, the number of infected individuals stays high). From our numerical simulations, the total number of mosquitoes (susceptible and infected as shown in Fig.4 and Fig.5, respectively) near the starting point of the outbreak is high and decreases farther out over time. Thus, the simulations suggest that if we can control the disease to stay close to the starting point, it will not transfer to other neighboring cities and as a result, it reduces the number of infections in humans in total.

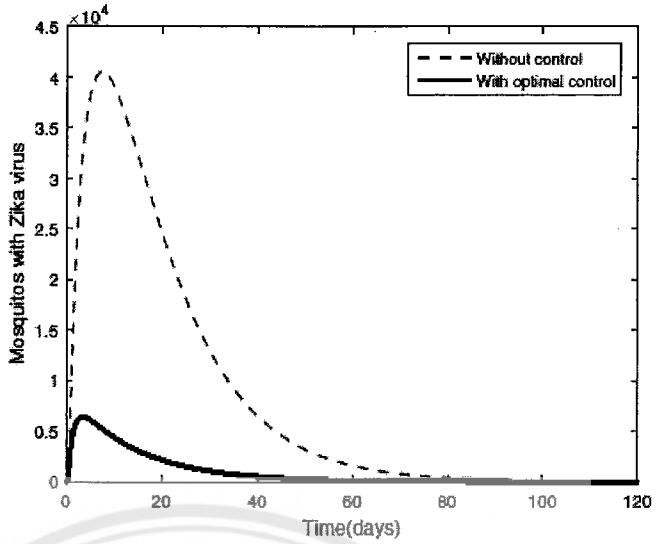

Fig. 6 Infectious mosquitoes

The infection level in humans will not reduce if the population of infected mosquitoes is still high. Fig.6 represents that the infection level of mosquitoes has been significantly reduced due to the incorporation of the three types of controls. Also, the peak of I_v, infectious mosquitoes, without control curve reaches its highest value at $t \approx$ 5 - 8 days, however, the peak of I_v with optimal controls reaches its peak at $t \approx$ 2 days and its value is much lower than that without controls. Fig.7 shows the optimal control profile rates and their zoom-in versions are presented in Fig. 8.

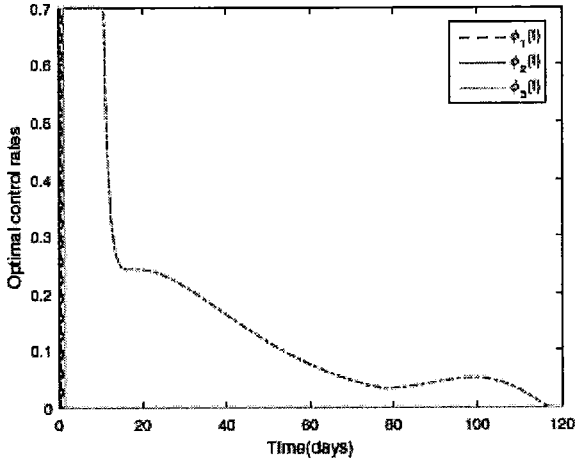

Fig. 7 Rates of controls with $\phi_{1\max} = 0.7$, $\phi_{2\max} = 0.7$ and $\phi_{3\max} = 0.7$. The result shows that medical treatment is needed at its maximum rate for about 7 days to reduce the number of infectious individuals

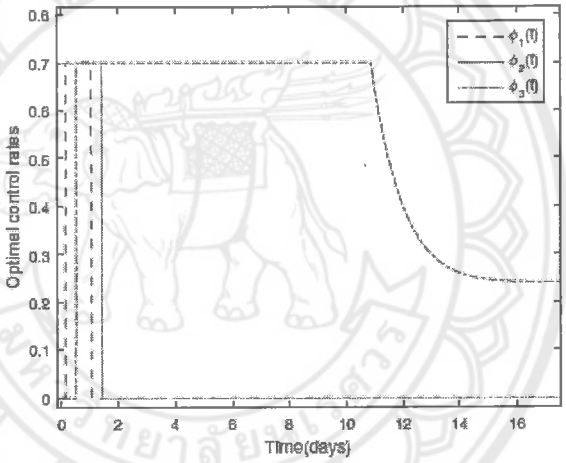

Fig. 8 Zoomed-in rates of controls with $\phi_{1\max} = 0.7$, $\phi_{2\max} = 0.7$ and $\phi_{3\max} = 0.7$. It is seen that the insecticide and personal protection control measures are very important to control Zika virus outbreaks. Also, they should be implemented immediately after the onset of a Zika virus outbreak

Table 1 Parameter values and symbols

Parameter	Symbol	Value
Human birth rate	μ_h	0.0000391/day
Mosquito birth rate	μ_v	0.0714/day
Vector-human contact rate	β_{vh}	0.3/day
Human-vector contact rate	β_{hv}	0.09/day
Human-human contact rate	β_h	0.1/day
The recovery rate	γ_h	0.2
Death rate due to disease	α	0.03

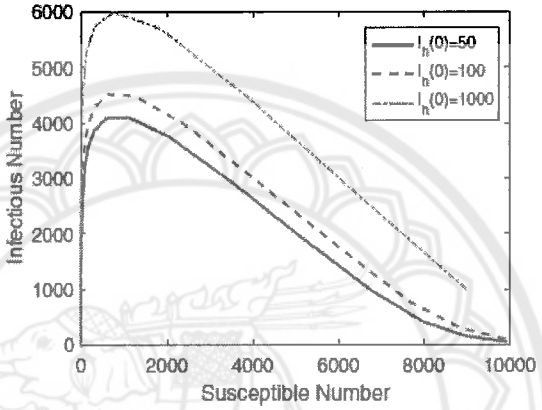

Fig. 9 Phase portraits for the Zika virus model (without controls) with different initial conditions, and $R_0 > 1$. All the curves converge to the endemic equilibrium

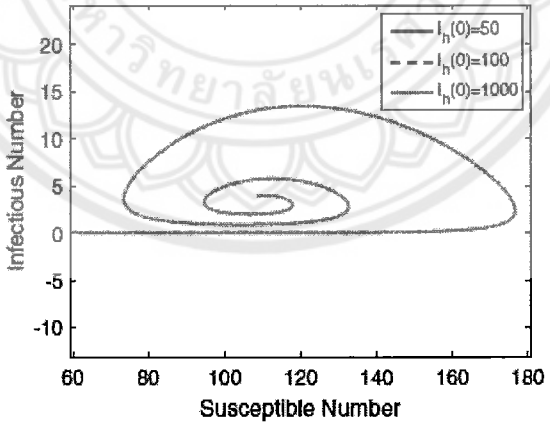

Fig. 10 Phase portraits (zoomed-in) for the Zika virus model (without controls) with different initial conditions, and $R_0 > 1$. All the curves converge to the endemic equilibrium

We have also run the numerical simulation for this model with various parameter values and initial conditions, and the results are consistent with our analytical predictions: when $R_0 < 1$, the disease dies out; when $R_0 > 1$, the disease persists and all solutions converge to the endemic equilibrium. In particular, using the parameter values given in Table 1 (with $R_0 > 1$), we show a set of results in Fig.9, Fig.10 and Fig.11. We observe that all three curves approach the endemic equilibrium over time, indicating the global asymptotic stability of the endemic equilibrium. We also investigate the reproduction number of our optimal control problem as shown in Fig.12 and it shows that the reproduction number decreases in the first few days due to the implementation of controls and starts increasing after day 2 or 3. The result indicates that controls can help to reduce the number of newly infected patients.

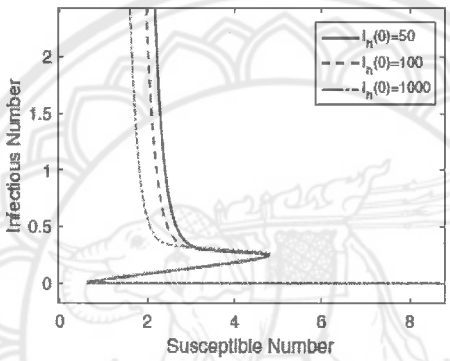

Fig. 11 The zoomed-in phrase plots of infectious individuals with control. All the curves converge to almost zero

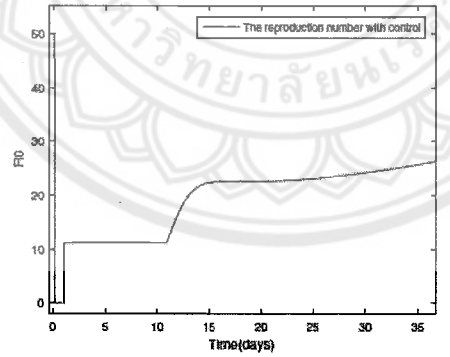

Fig. 12 The reproduction number with control

To investigate our diffusion model, we have used simple finite difference schemes for our PDE systems to facilitate numerical implementation while maintaining good numerical stability. Parameter values used in this numerical simulation are presented in Table 1.

Chapter 5
Conclusion

We have presented a mathematical model for the Zika virus disease that incorporates the control measures; personal protection, medical treatment, and insecticide. The model exhibits two feasible points of equilibrium, namely, the disease-free equilibrium and the endemic equilibrium. The stability of these two feasible points of equilibrium is controlled by the threshold number R_0. If R_0 is less than one, then the disease dies out and the disease-free equilibrium stable. If R_0 is greater than one, then the disease persists and the disease-free equilibrium is unstable. The analytical predictions are verified by our numerical simulation results for our model. We further have extended our work to a diffusion model to study the spatial movement of both mosquitoes and humans via a PDE model to better understand the time-space model for the Zika virus.

We have also performed an optimal control study by investigating three types of controls: personal protection, medical treatment, and insecticide, to seek the optimal control strategy to contain the disease outbreak in humans. Our results show that personal protection and insecticide, when strategically deployed, are very important control measures to reduce the numbers of human and mosquito infectious and to help eradicate the disease outbreak. Also, we have conducted a numerical simulation to investigate the reproduction number under an optimal control problem to gain guidelines for preventing the spread of the Zika virus disease.

The diffusion model also represents that to stop the virus from spreading to other nearby cities or places, we need to additionally implement other control strategies such as social distancing or quarantine. The numerical simulations suggest that if the center of an outbreak is contained, the disease will not spread to other places and it results in stopping the outbreak.

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Output ที่ได้จากโครงการ

1. ได้ผลงานตีพิมพ์ในวารสารวิชาการนานาชาติ

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ภาคผนวก

ประกอบด้วย

1. ผลงานตีพิมพ์ในวารสารวิชาการนานาชาติ เรื่อง

A diffusion model of Zika virus with human-vector transmission dynamics and control strategy including social distancing study

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A diffusion model of Zika virus with human-vector transmission dynamics and control strategy including social distancing study

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Abstract
Zika virus infection is caused by the Zika Virus belonging to the *Flaviviridae* family. The virus is transmitted to people through the bite of an infected *Aedes* mosquito. However, although rare, sexual and mother-to-child are also other modes of transmission. The incubation time in infected humans is a few days to a week. The spread of the disease still presents in some developing countries and remote areas that cannot afford basic public health intervention and vaccine, hence, investigating other options are necessary. In this study, we formulate a diffusion mathematical model of the Zika virus with controls (personal protection, medical treatment, and insecticide). In this model, we will be able to observe the spatial movement of individuals and investigate if the disease can be controlled by performing social distancing combined with other control strategies. Further, we investigate the essential dynamics of the model through equilibrium analyses. The basic reproduction number with the spatial movement of the model is derived. Meanwhile, a time-dependent optimal control study is applied to the model to seek a cost-effective strategy to eradicate Zika virus outbreaks. Numerical results show that strategically deployed personal protection, treatment, and insecticide can significantly reduce the number of infectious individuals and mosquitoes. Also, applying a social connection program can additionally reduce the spread from one place to another, and thus the number of infections in total is reduced.

Keywords Zika virus model · Optimal control theory · Diffusion model · Vector-borne disease · Mathematical biology

1 Introduction

Zika virus disease is a mosquito-borne which was first identified in Uganda in 1947 among Rhesus monkeys. The Zika virus is transmitted by the *Aedes* mosquitoes which these mosquitoes also transmit dengue, chikungunya, yellow fever and Japanese encephalitis viruses [1]. At least one in five infected people usually develops symptoms such as mild fever, rash, conjunctivitis (red eyes), muscle, and joint pain [1]. These symptoms can last for a few days to a week [2].

Also, an infected person can transmit the virus to his or her partner(s) through vaginal sex, anal sex, and likely oral sex. The sharing of sex toys may also put someone at risk. However, there is no evidence that the virus can be transmitted through saliva during deep kissing [3]. The transmission can be transferred even if the infected person has no symptoms. On the other hand, mother-to-child transmission during the pregnancy or around the time of birth has been reported [4]. Besides, fetuses infected with the Zika virus can develop underdeveloped brain resulting microcephaly where a baby has a head size much smaller compared with other babies of the same age and sex. However, there is no report of infants getting the Zika virus through breastfeeding up to date.

There have been several mathematical models and scientific reports [1,4–11] to study the transmission dynamics of Zika virus disease. However, there are only a few studies conducted optimal control theory to gain guidelines for prevention, treatment, and insecticide. In March 2016, Moreno et al. [5] studied the role of short-term dispersal on the dynamics of Zika. The result verified that the density of community matters and the spread of the disease depends on the entries of the mobility of the residents. To eliminate the Zika virus,

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one would have to stop mobility and that would cause the economy to a halt.

In May 2016, Onuorah et al. [4] extended some published Zika virus models by including the death rate of infected individuals due to the virus. Meanwhile, there are a few other studies that have already included that into their models. Daozhou et al. [1] studied the impact of mosquito-borne and sexual transmission on the spread of the Zika virus in June 2016. In this study, the prevention and control of the disease have also been investigated. The results showed that prevention and control efforts against the Zika virus should target both the mosquito-borne and sexual transmission routes. In July 2016, Chunxiao et al. [6] introduced an optimal control mathematical model of the Zika virus by including three effective intervention strategies; personal protection, increasing the autoimmunity and using insecticide. However, the stability analyses and numerical simulations of the model were not provided. In 2018, Naba et al. [7] proposed a mathematical model of the Zika virus with nonlinear incidence. The study observed that an optimal control problem was the key to reduce the number of Zika infectives, however, the study required some conditions for its endemic equilibrium stability.

In the same year, Suparit et al. [8] presented a mathematical model of Zika that focused on a time-dependent biting rate. The study developed a vector-borne compartmental model to analyze the Zika virus outbreak in Bahia. The results suggested that reducing the mosquito biting rates were found to be a more effective control measure than reducing the mosquito population size. The study mainly focused on numerical simulations and discussions. In 2019, Banulelos et al. [12] simulated an outbreak of the vector-borne Zika virus and found that the vector birth control seems to be more effective to control the outbreak. The main contribution of the present work is a modified-modeling framework that incorporates personal protection, medical treatment, and using insecticide as control measures to seek optimal control strategies to eradicate Zika virus outbreaks. We will utilize both analytical and numerical means to gain deeper insight into the disease dynamics. Meanwhile, our analysis and simulation results regarding the control strategies will provide useful information for public health administrations in the prevention of the Zika virus outbreak. The model will also explore in the case of the spatial movement through a diffusion problem to investigate the basic reproduction number, which represents how infectious the disease is.

The organization of this paper is as follows. Details of our Zika virus model is provided in Sect. 2, followed by a careful analysis of the disease-free equilibria (DFE) in Sect. 3. The global stability of the DFE for the system is also established. Section 4 is devoted to the analysis of the endemic dynamics. The Zika virus model with spatial movement will be rigorously analyzed in Sect. 5. An optimal control problem for our Zika virus model will be conducted and analyzed in Sect. 6. Finally, the conclusion will be drawn in Sect. 7.

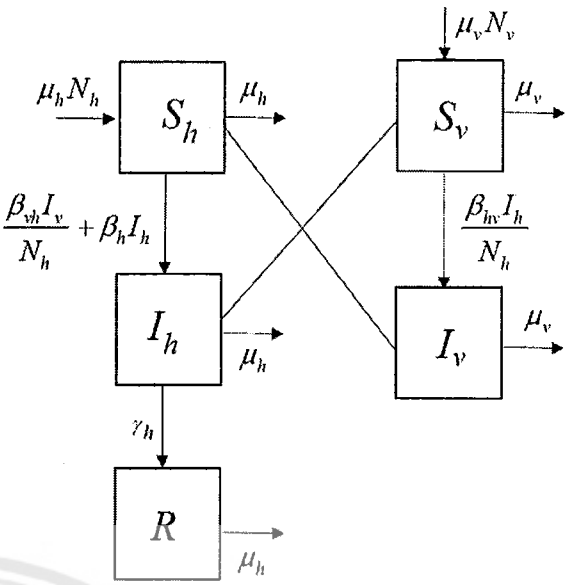

Fig. 1 Diagram of the model

2 Mathematical model

We describe the Zika virus dynamics using a system of five differential equations. The population of mosquitoes is divided into two compartments: S_v and I_v, where S_v represents the susceptible mosquitoes and I_v represents the infected mosquitoes with Zika virus. The population of humans is compartmentalized into three classes: susceptible (S_h), infectious (I_h), and recovered (R). A diagram to illustrate our model is presented in Fig. 1.

We use an SI model to represent the disease dynamics among mosquitoes. Susceptible mosquitoes are infected through bites (at a rate of β_{hv}) with infectious humans. The infected mosquitoes then transmit the disease to human hosts at a rate of β_{vh}. Meanwhile, the infection also spreads among the human population through the person-to-person pathway (sex or mother to child) with a transmission rate of β_h. The infectious people may recover from the disease with a rate of γ_h and enter into the recovered class.

We assume the natural birth and death rates are the same and denote that by μ_v and μ_h for mosquitoes and humans, respectively. Finally, we incorporate personal protection, medical treatment, and insecticide through source into the model as disease control measures. Our model thus takes the form below:

$$\frac{dS_v}{dt} = \mu_v N_v - \left(\mu_v + \frac{\beta_{hv} I_h}{N_h} + \phi_3\right) S_v, \tag{1}$$

$$\frac{dI_v}{dt} = \frac{\beta_{hv} I_h}{N_h} S_v - \mu_v I_v, \tag{2}$$

$$\frac{dS_h}{dt} = \mu_h N_h - \left(\mu_h + \frac{\beta_{vh} I_v}{N_h} + \beta_h I_h\right) S_h - \phi_1 S_h, \tag{3}$$

$$\frac{dI_h}{dt} = \frac{\beta_{vh} I_v}{N_h} S_h + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h, \tag{4}$$

$$\frac{dR}{dt} = \gamma_h I_h - \mu_h R + \phi_1 S_h + \phi_2 I_h. \tag{5}$$

The definition and numerical values of all the model parameters are provided in Table 1. Written in a vector form, the above equations become

$$\frac{dX}{dt} = F(X) \tag{6}$$

with $X = (S_v, I_v, S_h, I_h, R)^T$.

3 Epidemic analysis

We start our analysis of the model by studying the disease-free equilibrium (DFE) and calculating the basic reproduction numbers. Since our model contains two populations: mosquitoes and humans, it is important that we first investigate the mosquito subsystem, represented by Eqs. (1) and (2), and then proceed to the human subsystem that consists equations (3)–(5). We will follow the same strategy when analyzing the endemic equilibrium as well.

It is straightforward to obtain the DFE for the mosquito subsystem:

$$\epsilon_v = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, 0\right). \tag{7}$$

Since infected mosquitoes will not spread the disease to other susceptible mosquitoes, thus we will not calculate the reproduction number for mosquitoes here. Also, we assume that the biting rate is constant and thus the reproduction number mainly depends on factors on the human's side. However, if the population size of the mosquito gets large, the infection rate of humans should be proportional. Calculating the reproduction number using the coupled system is our future work, we will not show it here in this study. The DFE for the human subsystem is given by

$$\epsilon_h = \left(\frac{\mu_h N_h}{\mu_h + \phi_1}, 0, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right). \tag{8}$$

To compute the basic reproduction number for humans, we use the well-known method of van den Driessche and Watmough, [13], with the associated next-generation matrices

$$F = \left[\beta_h \frac{\mu_h N_h}{\mu_h + \phi_1}\right] \tag{9}$$

and

$$V = \left[\mu_h + \gamma_h + \phi_2\right]. \tag{10}$$

The basic reproduction number is then determined as the spectral radius of FV^{-1}; thus we obtain

$$R_0 = \frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)(\mu_h + \gamma_h + \phi_2)}. \tag{11}$$

Consequently, based on work in [13], we immediately obtain the result below:

Theorem 1 *The disease-free equilibrium of the model* (1)–(5) *is locally asymptotically stable if* $R_0 < 1$, *and unstable if* $R_0 > 1$.

Next, we examine the global asymptotic stability of the DFE. To that end, we state the following result introduced by Castillo-Chavez et al., [14].

Lemma 1 *Consider a model system written in the form*

$$\frac{dX_1}{dt} = F(X_1, X_2),$$

$$\frac{dX_2}{dt} = G(X_1, X_2), G(X_1, 0) = 0$$

where $X_1 \in \mathrm{R}^m$ *denotes (its components) the number of uninfected individuals and* $X_2 \in \mathrm{R}^m$ *denotes (its components) the number of infected individuals including latent, infectious, etc;* $X_0 = (X_1^*, 0)$ *denotes the disease-free equilibrium of the system. Also, assume the two conditions (H1) and (H2) below:*

(H1) *For* $\frac{dX_1}{dt} = F(X_1, 0)$, X_1^* *is globally asymptotically stable;*

(H2) $G(X_1, X_2) = AX_2 - \hat{G}(X_1, X_2)$, $\hat{G}(X_1, X_2) \geq 0$ *for* $(X_1, X_2) \in \Omega$, *where the off-diagonal elements of the Jacobian matrix* $A = \frac{\partial G}{\partial X_2}(X_1^*, 0)$ *are non-negative, and* Ω *is the region where the model makes biological sense.*

Then the DFE $X_0 = (X_1^*, 0)$ *is globally asymptotically stable provided that* $R_0 < 1$.

We now apply this lemma to our model.

Theorem 2 *When* $R_0 < 1$, *the disease-free equilibrium of the model* (6) *is globally asymptotic stable.*

Proof We show that the conditions (H1) and (H2) hold when $R_0 < 1$. In our ODE system (1)–(5), $X_1 = (S_v, S_h, R)$, $X_2 = (I_v, I_h)$, and $X_1^* = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, \frac{\mu_h N_h}{\mu_h + \phi_1}, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right)$. We note that

$$\frac{dX_1}{dt} = F(X_1, 0) = \begin{bmatrix} \mu_v N_v - (\mu_v + \phi_3) S_v \\ \mu_h N_h - (\mu_h + \phi_1) S_h \\ \phi_1 S_h - \mu_h R \end{bmatrix}$$

is linear and its solution can be easily found as

$$S_v(t) = \frac{\mu_v N_v}{\mu_v + \phi_3} + \left(S_v(0) - \frac{\mu_v N_v}{\mu_v + \phi_3}\right) e^{-(\mu_v + \phi_3)t},$$
$$S_h(t) = \frac{\mu_h N_h}{\mu_h + \phi_1} + \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1}\right) e^{-(\mu_h + \phi_1)t},$$
$$R(t) = \frac{\phi_1 N_h}{\mu_h + \phi_1} - \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1}\right) e^{-(\mu_h + \phi_1)t} + \left(S_h(0) - \frac{\mu_h N_h}{\mu_h + \phi_1} + R(0) - \frac{\phi_1 N_h}{\mu_h + \phi_1}\right) e^{-\mu_h t}.$$

As $t \to \infty$, we have $S_v(t) \to \frac{\mu_v N_v}{\mu_v + \phi_3}$, $S_h(t) \to \frac{\mu_h N_h}{\mu_h + \phi_1}$ and $R(t) \to \frac{\phi_1 N_h}{\mu_h + \phi_1}$. Thus, $X_1^* = \left(\frac{\mu_v N_v}{\mu_v + \phi_3}, \frac{\mu_h N_h}{\mu_h + \phi_1}, \frac{\phi_1 N_h}{\mu_h + \phi_1}\right)$ is globally asymptotically stable for the system $dX_1/dt = F(X_1, 0)$.

Next, we have

$$G(X_1, X_2) = \begin{bmatrix} \frac{\beta_{hv} I_h S_v}{N_h} - \mu_v I_v \\ \frac{\beta_{vh} I_v S_h}{N_h} + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h \end{bmatrix}.$$

We can then obtain

$$A = \begin{bmatrix} -\mu_v & \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \\ \frac{\beta_{vh} \mu_h N_h}{(\mu_h + \phi_1) N_h} & \frac{\beta_h M_h N_h}{\mu_h + \phi_1} - (\mu_h + \gamma_h + \phi_2) \end{bmatrix}$$

with all non-negative off-diagonal elements. Meanwhile, we find

$$\hat{G}(X_1, X_2) = \begin{bmatrix} \frac{\beta_{hv} I_h}{N_h} \left(\frac{\mu_v N_v}{\mu_v + \phi_3} - S_v\right) \\ a_{11} \end{bmatrix}.$$

where $a_{11} = \frac{\beta_{vh} I_v}{N_h} \left(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h\right) + \beta_h I_h \left(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h\right)$. From Eq. (3), we observe that

$$\frac{dS_h}{dt} \le \mu_h N_h - (\mu_h + \phi_1) S_h$$

which yields

$$S_h \le \frac{\mu_h N_h}{\mu_h + \phi_1}$$

and similarly from Eq. (1) we have

$$S_v \le \frac{\mu_v N_v}{\mu_v + \phi_3}.$$

Hence, $\hat{G}(X_1, X_2) \ge 0$. □

4 Endemic analysis

The stability at the DFE determines the short-term epidemics of the disease, whereas its dynamics over a length of time is characterized by the stability at the endemic equilibrium. In this section, we will analyze the endemic properties of our Zika virus model.

4.1 Endemic equilibrium

We first examine the existence of the positive endemic equilibrium. Denote the endemic equilibrium of the model by

$$\epsilon^* = (S_v^*, I_v^*, S_h^*, I_h^*, R^*)$$

Setting Eqs. (1) and (2) are equal to zero, we obtain

$$\frac{\beta_{hv} I_h^*}{N_h} S_v^* - \mu_v I_v^* = 0$$
$$\frac{\beta_{hv} I_h^*}{N_h} S_v^* = \mu_v I_v^*$$

and

$$\mu_v N_v - \left(\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3\right) S_v^* = 0$$
$$\mu_v N_v = \left(\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3\right) S_v^*.$$

Thus

$$I_v^* = \frac{\beta_{hv} I_h^*}{\mu_v N_h} S_v^* \quad \text{and} \quad S_v^* = \frac{\mu_v N_v}{\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3}.$$

Hence, with some algebraic manipulations, we have

$$I_v^* = \frac{\beta_{hv} I_h^*}{\mu_v N_h} \left(\frac{\mu_v N_v}{\mu_v + \frac{\beta_{hv} I_h^*}{N_h} + \phi_3}\right) = \frac{\beta_{hv} I_h^* N_v}{N_h \mu_v + \beta_{hv} I_h^* + \phi_3 N_h}.$$

Now set Eq. (4) is equal to zero, we obtain

$$\frac{\beta_{vh} I_v^*}{N_h} S_h^* + \beta_h I_h^* S_h^* - (\mu_h + \gamma_h + \phi_2) I_h^* = 0$$
$$\frac{\beta_{vh} I_v^*}{N_h} S_h^* + \beta_h I_h^* S_h^* = (\mu_h + \gamma_h + \phi_2) I_h^*$$
$$S_h^* = \frac{(\mu_h + \gamma_h + \phi_2) I_h^*}{\left(\frac{\beta_{vh} I_v^*}{N_h} S_h^* + \beta_h I_h^*\right)}$$

When we substitute I_v^* into it then we find

$$S_h^* = \frac{(\mu_h + \gamma_h + \phi_2) I_h^*}{\frac{\beta_{hv} \beta_{vh} N_v I_h^*}{N_h (N_h \mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h I_h^*}.$$

Next we substitute I_v^* and S_h^* into (3) to obtain

$$\mu_h N_h - \Big(\mu_h + \frac{\beta_{vh}\beta_{hv} I_h^* N_v}{N_h(\mu_v N_h + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h I_h^* + \phi_1\Big) \times \Big(\frac{(\mu_h + \gamma_h + \phi_2) I_h^*}{\frac{\beta_{hv}\beta_{vh} N_v I_h^*}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h I_h^*}\Big) = 0.$$

This equation, after some algebra, yields a quadratic equation

$$A_1 I_h^{*2} + B_1 I_h^* + C_1 = 0, \tag{12}$$

where

$$\begin{aligned} A_1 &= -\beta_h\beta_{hv} a N_h, \\ B_1 &= \beta_h\mu_h\beta_{hv} N_h^2 - \mu_h a N_h \beta_{hv} - \beta_{vh}\beta_{hv} N_v a \\ &\quad - \beta_h a N_h^2 \mu_v - \beta_h a\phi_3 N_h^2 - \phi_1 a N_h \beta_{hv}, \\ C_1 &= \mu_h N_h \beta_{vh}\beta_{hv} N_v + \beta_h\mu_h\mu_v N_h^3 + \beta_h\mu_h N_h^3\phi_3 \\ &\quad - \mu_h\mu_v a N_h^2 - \mu_h a\phi_3 N_h^2 \\ &\quad - \phi_1 a N_h^2\mu_v - a\phi_1\phi_3 N_h^2, \end{aligned}$$

and where $a = \mu_h + \gamma_h + \phi_2$.

The roots of Eq. (12) have to satisfy

$$I_{h1}^* I_{h2}^* = \frac{C_1}{A_1} \quad \text{and} \quad I_{h1}^* + I_{h2}^* = -\frac{B_1}{A_1}.$$

It is obvious that $A_1 < 0$. Meanwhile we have

$$\begin{aligned} C_1 &= \mu_h N_h \beta_{vh}\beta_{hv} N_v + \beta_h\mu_h\mu_v N_h^3 + \beta_h\mu_h N_h^3\phi_3 \\ &\quad - \mu_h\mu_v a N_h^2 - \mu_h a\phi_3 N_h^2 \\ &\quad - \phi_1 a N_h^2\mu_v - a\phi_1\phi_3 N_h^2 \\ &= \mu_h N_h \beta_{vh}\beta_{hv} N_v + \Big(\beta_h\mu_h\mu_v N_h^3 - (\mu_h + \phi_1) a N_h^2\mu_v\Big) \\ &\quad + \Big(\beta_h\mu_h N_h^3\phi_3 - (\mu_h + \phi_1) a\phi_3 N_h^2\Big) \\ &= \mu_h N_h \beta_{vh}\beta_{hv} N_v + (\mu_h + \phi_1) a N_h^2\mu_v\Big(\frac{\beta_h\mu_h N_h}{(\mu_h + \phi_1) a} - 1\Big) \\ &\quad + (\mu_h + \phi_1) a\phi_3 N_h^2\Big(\frac{\beta_h\mu_h N_h}{(\mu_h + \phi_1) a} - 1\Big) \\ &= \mu_h N_h \beta_{vh}\beta_{hv} N_v + (\mu_h + \phi_1) a N_h^2\mu_v (R_0 - 1) \\ &\quad + (\mu_h + \phi_1) a\phi_3 N_h^2 (R_0 - 1). \end{aligned}$$

It can be clearly seen that $C_1 > 0$ when $R_0 > 1$. Thus $I_{h1}^* I_{h2}^* < 0$ and since the two roots of Eq. (12) are both real, hence, one must be positive and the other must be negative. Consequently, we have the result below:

Theorem 3 *The positive endemic equilibrium ϵ^* of the system* (1)–(5) *exists and is unique when $R_0 > 1$.*

Also, we note that if $I_v^* = 0$ (i.e., no infection persistent in mosquitoes, and thus no disease contributed to the humans from infectious mosquitoes and vice versa), then $\beta_{vh} = \beta_{hv} = 0$, and thus

$$\begin{aligned} C_1 &= (\mu_h + \phi_1) a N_h^2\mu_v (R_0 - 1) \\ &\quad + (\mu_h + \phi_1) a\phi_3 N_h^2 (R_0 - 1). \end{aligned}$$

It is obvious that $C_1 < 0$ when $R_0 < 1$ and $C_1 > 0$ when $R_0 > 1$. Since A_1 is always negative, thus $I_{h1}^* I_{h2}^* > 0$ when $R_0 < 1$; that is, the two roots of Eq. (12) can be either both negative or both positive real numbers. Meanwhile we have

$$B_1 = -\beta_h a N_h^2\mu_v - \beta_h a\phi_3 N_h^2 \le 0.$$

Consequently, Eq. (12) has only one biologically meaningful root $I_{h1}^* = I_{h2}^* = 0$ since $I_{h1}^* + I_{h2}^* \le 0$. These analytical findings show that in the absence of mosquitoes, the human subsystem (3)–(5) is reduced to a normal SIR model. We observe that the infected mosquitoes directly contribute to the positive growth of infectious humans in our model. Hence, using personal protection and insecticide through source would be important control measures to protect humans against the infection and to contain the disease outbreak.

4.2 Local stability

We proceed to analyze the stability properties of the endemic equilibrium. First, we establish the following result regarding local stability.

Theorem 4 *When $R_0 > 1$ and $I_v^* > 0$, the endemic equilibrium ϵ^* is locally asymptotically stable.*

Proof The Jacobian of the system (3)- (4) at ϵ^* is given by

$$J(\epsilon^*) = \begin{bmatrix} J_{11} & -\beta_h S_h \\ \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* & \beta_h S_h - (\mu_h + \gamma_h + \phi_2) \end{bmatrix}$$

where $J_{11} = -\mu_h - \frac{\beta_{vh}}{N_h} I_v^* - \beta_h I_h^* - \phi_1$.

The characteristic equation of the matrix $J(\epsilon^*)$ is

$$\begin{aligned} 0 &= \det[\lambda I - J(\epsilon^*)] \\ &= \Big(\lambda + \Big(\mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1\Big)\Big) \\ &\quad \times \Big(\lambda - \Big(\beta_h S_h^* - (\mu_h + \gamma_h + \phi_2)\Big)\Big) \\ &\quad + \beta_h S_h^*\Big(\frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^*\Big) \end{aligned}$$

The above equation can be put into a quadratic equation of the form

$$a_2\lambda^2 + a_1\lambda + a_0 = 0, \tag{13}$$

where

$$\begin{aligned}
a_2 &= 1,\\
a_1 &= \mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1 + a - \beta_h S_h^*,\\
a_0 &= -(\mu_h + \phi_1)\beta_h S_h^* + (\mu_h + \phi_1)a\\
&\quad + \Big(\frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^*\Big)a.
\end{aligned}$$

The Routh-Hurwitz criterion requires

$$a_1 > 0,\ a_2 > 0,\ \text{and}\ a_3 > 0$$

as the necessary and sufficient conditions for the locally asymptotical stability; i.e., all roots of the polynomial (13) have negative real parts. Meanwhile, we have

$$\begin{aligned}
a_1 &= \mu_h + \frac{\beta_{vh} I_v^*}{N_h} + \beta_h I_h^* + \phi_1 + a - \beta_h S_h^*,\\
&= \mu_h + \frac{\beta_{vh}\beta_{hv} I_h^* N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h I_h^* + \phi_1\\
&\quad + a\Big(1 - \frac{\beta_h}{\frac{\beta_{vh}\beta_{hv} N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h}\Big)
\end{aligned}$$

From Eq. (3) we observe that

$$\frac{dS_h^*}{dt} \le \mu_h N_h - (\mu_h + \phi_1)S_h^*,$$

which yields $S_h^* \le \frac{\mu_h N_h}{\mu_h + \phi_1}$. Next we proceed to show that $a_0 > 0$. We can write a_0 as

$$\begin{aligned}
a_0 &= \mu_h N_h\Big(\frac{\beta_{vh}\beta_{hv} N_v}{N_h(N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h)} + \beta_h\Big)\\
&\quad - (\mu_h + \phi_1)\beta_h S_h^*\\
&= \frac{\mu_h \beta_{vh}\beta_{hv} N_v}{N_h\mu_v + \beta_{hv} I_h^* + \phi_3 N_h}\\
&\quad + \beta_h(\mu_h + \phi_1)\Big(\frac{\mu_h N_h}{\mu_h + \phi_1} - S_h^*\Big).
\end{aligned}$$

It can be clearly seen that $a_0 > 0$. This completes the proof. □

5 Zika virus model with spatial movement

5.1 Model framework

As mentioned before, vectors and humans can be a key factor in the spread of the Zika virus. Thus, in this section, we will extend our model to a PDE system to investigate the spatial dynamics of Zika virus. We consider a one-dimensional spatial domain, $x \in [0, 1]$ and we assume that both the human population and the virus undergo a diffusion process. Let $D_i > 0$ $(0 \le i \le 5)$ is the diffusion coefficient of $S_v(x,t)$,$I_v(x,t)$, $S_h(x,t)$,$I_h(x,t)$, and $R(x,t)$, respectively. Then the Zika model (1)–(5) with the inclusion of diffusion takes the form :

$$\frac{\partial S_v}{\partial t} = \mu_v N_v - \Big(\mu_v + \frac{\beta_{hv} I_h}{N_h} + \phi_3\Big) S_v + D_1\frac{\partial^2 S_v}{\partial x^2}, \tag{14}$$

$$\frac{\partial I_v}{\partial t} = \frac{\beta_{hv} I_h}{N_h} S_v - \mu_v I_v + D_2\frac{\partial^2 I_v}{\partial x^2}, \tag{15}$$

$$\begin{aligned}
\frac{\partial S_h}{\partial t} &= \mu_h N_h - \Big(\mu_h + \frac{\beta_{vh} I_v}{N_h} + \beta_h I_h\Big) S_h - \phi_1 S_h\\
&\quad + D_3\frac{\partial^2 S_h}{\partial x^2},
\end{aligned} \tag{16}$$

$$\begin{aligned}
\frac{\partial I_h}{\partial t} &= \frac{\beta_{vh} I_v}{N_h} S_h + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2) I_h\\
&\quad + D_4\frac{\partial^2 I_h}{\partial x^2},
\end{aligned} \tag{17}$$

$$\frac{\partial R}{\partial t} = \gamma_h I_h - \mu_h R + \phi_1 S_h + \phi_2 I_h + D_5\frac{\partial^2 R}{\partial x^2}. \tag{18}$$

Meanwhile, we assume the entire domain represents a closed community of our interest with an assumption; that is, no individual would cross the boundary. Hence, we impose the Neumann (no-flux) boundary conditions for $x \in [0, 1], t > 0$:

$$\frac{\partial S_i}{\partial x} = \frac{\partial I_i}{\partial x} = \frac{\partial R}{\partial x} = 0, \qquad i = v, h. \tag{19}$$

5.2 Turing instabilty

It is known that in many reaction-diffusion systems with multiple components is the occurrence of Turing instability [15] ; that is, loss of stability due to inclusion of diffusion (i.e. there exist conditions under which the spatial uniform steady state in the absence of diffusion and can become unstable because of diffusion). We linearize system (12)–(16) at the DFE; $\epsilon^0 = (S_v^0, I_v^0, S_h^0, I_h^0, R^0)^T = (\frac{\mu_v N_v}{\mu_v + \phi_3}, 0, \frac{\mu_h N_h}{\mu_h + \phi_1}, 0, \frac{\phi_1 N_h}{\mu_h + \phi_1})^T$ of the system (1)–(5) in the absence of diffusion. Introducing the new coordinates $Y = (Y_1, Y_2, Y_3, Y_4, Y_5)^T = (S_v - S_v^0, I_v - I_v^0, S_h - S_h^0, I_h - I_h^0, R - R^0)^T$, we obtain the linear system as follows :

$$\frac{\partial Y}{\partial t} = D\frac{\partial^2 Y}{\partial x^2} + JY, \tag{20}$$

where J is the Jacobian matrix of the associated ODE system evaluated at the DFE;

$$J(\epsilon^0) = \begin{bmatrix} -(\mu_v+\phi_3) & 0 & 0 & -\frac{\beta_{hv}S_v^0}{N_h} & 0 \\ 0 & -\mu_v & 0 & \frac{\beta_{hv}S_v^0}{N_h} & 0 \\ 0 & -\frac{\beta_{vh}S_h^0}{N_h} & -(\mu_h+\phi_1) & -\beta_h S_h^0 & 0 \\ 0 & \frac{\beta_{vh}S_h^0}{N_h} & 0 & a_{22} & 0 \\ 0 & 0 & \phi_1 & \gamma_h+\phi_2 & -\mu_h \end{bmatrix},$$

where $a_{22} = \beta_h S_h^0 - (\mu_h + \gamma_h + \phi_2)$ and $D = \text{diag}\,[D_1, D_2, D_3, D_4, D_5]$. Consider the eigenvalue problem

$$\frac{\partial^2\psi(x)}{\partial x^2} = -\rho\psi(x), \qquad x \in (0,1),$$
$$\frac{\partial\psi(x)}{\partial x} = 0, \qquad x = 0, 1. \tag{21}$$

One can easily verify that the eigenvalues of the boundary value problem (21) are $\rho_k = (k\pi)^2 \geq 0$ and the corresponding eigenfunctions are $\psi_k(x) = cos(k\pi x)$. Now let us return to our system (20). Since the system is linear, the solution $Y(x,t)$ can be written as the sum of eigenfunctions

$$Y(x,t) = \sum_j a_j e^{\lambda t}\psi_j(x) \qquad (1 \leq j \leq 5) \tag{22}$$

where $\psi_j(x)$ is the solution of the eigenvalue problem (21), λ and a_j are constants. Substituting (22) into (20) yields

$$|J - \rho D - \lambda I_5| = 0, \tag{23}$$

where I_5 is a 5×5 identity matrix. We are interested in whether there exists λ such that $Re(\lambda) > 0$ at the DFE. Solving (23), we find that the associated eigenvalues are given by

$$|J - \rho D - \lambda I_5| = [-a_1 - \rho D_1 - \lambda][-\mu_h - \rho D_5 - \lambda] \times \begin{vmatrix} -\mu_v - \rho D_2 - \lambda & 0 & \frac{\beta_{hv}S_v^0}{N_h} \\ -\frac{\beta_{vh}S_h^0}{N_h} & -a_3 - \rho D_3 - \lambda & -\beta_h S_h^0 \\ \frac{\beta_{vh}S_h^0}{N_h} & 0 & \beta_h S_h^0 - a_4 - \rho D_4 - \lambda \end{vmatrix} = 0$$

where $a_1 = \mu_v + \phi_3$, $a_3 = \mu_h + \phi_1$, and $a_4 = \mu_h + \gamma_h + \phi_2$. This implies that

$$\lambda_1 = -\frac{k_1+k_4}{2} + \frac{\sqrt{(k_1-k_4)^2 + 4k_2k_3}}{2}, \tag{24}$$

$$\lambda_2 = -\frac{k_1+k_4}{2} - \frac{\sqrt{(k_1-k_4)^2 + 4k_2k_3}}{2}, \tag{25}$$

$$\lambda_3 = -(a_1 + \rho D_1), \tag{26}$$

$$\lambda_4 = -(a_3 + \rho D_3), \tag{27}$$

$$\lambda_5 = -(\mu_h + \rho D_5), \tag{28}$$

where

$$k_1 = \mu_v + \rho D_2,$$
$$k_2 = \frac{\beta_{vh}\mu_h}{(\mu_h+\phi_1)},$$
$$k_3 = \frac{\beta_{hv}\mu_v N_v}{(\mu_v+\phi_3)N_h},$$
$$k_4 = -\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)} + (\mu_h+\gamma_h+\phi_2) + \rho D_4. \tag{29}$$

Proposition 1 *If $R_0^{ODE} < 1$, inclusion of diffusion spatial spread into model (1)-(5) will not produce a Turing instability.*

Proof Suppose that $R_0^{ODE} < 1$. We obtain that

$$0 < (\mu_h+\gamma_h+\phi_2) - \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)}.$$

Thus $k_4 = -\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)} + (\mu_h+\gamma_h+\phi_2) + \rho D_4 > 0$. This implies that $k_i > 0$ for all $i = 1,2,3,4$. It follows that $\lambda_i < 0$, $(i = 2,3,4)$ and the only eigenvalue that could have a sign change is λ_1. We now demonstrate that $\lambda_1 < 0$. Notice that

$$\lambda_1\lambda_2 = \left(-\frac{k_1+k_4}{2}\right)^2 - \left(\frac{\sqrt{(k_1-k_4)^2+4k_2k_3}}{2}\right)^2 = \frac{k_1^2+2k_1k_4+k_4^2-k_1^2+2k_1k_4-k_4^2-4k_2k_3}{4} = k_1k_4 - k_2k_3$$

where

$$\begin{aligned} k_1k_4 - k_2k_3 &= -\mu_v\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)} + \mu_v(\mu_h+\gamma_h+\phi_2) \\ &\quad + \mu_v\rho D_4 \\ &\quad - \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)}\rho D_2 + (\mu_h+\gamma_h+\phi_2)\rho D_2 \\ &\quad + \rho^2 D_2 D_4 - \frac{\beta_{vh}\mu_h}{(\mu_h+\phi_1)}\frac{\beta_{hv}\mu_v N_v}{(\mu_v+\phi_3)N_h} \\ &= \mu_v\rho D_4 \\ &\quad + \left(-\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)} + (\mu_h+\gamma_h+\phi_2) + \rho D_4\right)\rho D_2 \\ &\quad + \left[\mu_v\left(-\frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)} + (\mu_h+\gamma_h+\phi_2)\right)\right. \\ &\quad \left. - \frac{\beta_{vh}\mu_h}{(\mu_h+\phi_1)}\frac{\beta_{hv}\mu_v N_v}{(\mu_v+\phi_3)N_h}\right]. \end{aligned}$$

$$= \mu_v \rho D_4 + k_4 \rho D_2 + \left[\mu_v \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) \right) - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h} \right]. \quad (30)$$

It is clear that the first two terms of Eq. (30) are the sum of two positive terms ($k_4 > 0$). Thus by Theorem 3, $\mu_v \left(-\frac{\beta_h \mu_h N_h}{(\mu_h + \phi_1)} + (\mu_h + \gamma_h + \phi_2) \right) + (\mu_h + \gamma_h + \phi_2) - \frac{\beta_{vh} \mu_h}{(\mu_h + \phi_1)} \frac{\beta_{hv} \mu_v N_v}{(\mu_v + \phi_3) N_h}$ is a product of two eigenvalues of $J(\epsilon^0)$ at the DFE, hence it is positive since the system (1)-(5) is stable at the DFE. This yields $\lambda_1 \lambda_2 > 0$ and it implies that $\lambda_1 < 0$ (since $\lambda_2 < 0$). Therefore, we obtain that all eigenvalues of the system (12)-(16) are negative real numbers and hence Turing instability will not occur. □

5.3 PDE model threshold dynamics

We now study the spatial threshold dynamics of the Zika virus by analyzing the basic reproduction number derived from the PDE model (12)–(16). We will use the ideas presented in [16–18], which the concept of the basic reproduction number is extended to the reaction-diffusion epidemic system with Neumann (no-flux) boundary conditions. Based on these studies, the basic reproduction number R_0 for a PDE epidemic system is defined as the spectral radius of the operator

$$L[\phi(x)] = \int_0^\infty F(x) T(t) \phi dt = F(x) \int_0^\infty T(t) \phi dt \quad (31)$$

and in [18] they showed that

$$\int_0^\infty T(t) \phi dt = -B^{-1} \phi, \quad (32)$$

where

$$L = -F B^{-1}, \quad (33)$$

for $B := \nabla \cdot (d_I \nabla) - \nabla - V$. Here F and V are analogues to the next-generation matrices associated with the corresponding ODE system (i.e. without diffusion terms); $T(t)$ denotes the solution semigroup for the linearized reaction-diffusion system for disease compartments; ϕ describes the distribution of the initial infection; and d_I is the diffusion coefficient vector. For our Zika virus model (12)-(16), we have

$$d_I = \text{diag}[D_2, D_4],$$
$$F = \left[\frac{\beta_h \mu_h N_h}{\mu_h + \phi_1} \right], \quad V = \left[\mu_h + \gamma_h + \phi_2 \right],$$

and

$$B = \left[D_4 \frac{\partial^2}{\partial x^2} - (\mu_h + \gamma_h + \phi_2) \right]. \quad (34)$$

To analyze the basic reproduction number of the PDE system (12)-(16) which is

$$R_0^{PDE} = \rho(L), \quad (35)$$

we proceed to calculate B^{-1} by solving $B(\phi_1) = y_1$ subject to homogeneous Neumann boundary conditions. First, let us consider the boundary value problem

$$B_1[\phi_1] := D_4 \frac{\partial^2 \phi_1}{\partial x^2} - (\mu_h + \gamma_h + \phi_2)\phi_1 = y_1,$$
$$\phi_1'(0) = 0, \quad \phi_1'(1) = 0, 0 \le x \le 1 \quad (36)$$

This problem can be easily solved by using the Laplace transform. We note that the Laplace transforms of $\phi_1(x)$ and $y_1(x)$ are represented by $\psi_1(s)$ and $Y_1(s)$, respectively. Consider

$$L[D_4 \phi_1'' - (\mu_h + \gamma_h + \phi_2)\phi_1] = L[y_1],$$
$$(D_4 s^2 - (\mu_h + \gamma_h + \phi_2))\psi_1(s) - D_4 s \psi_1(0) = Y_1(s). \quad (37)$$

It yields

$$\psi_1(s) = \frac{Y_1(s)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)} + \frac{s D_4 \psi_1(0)}{D_4 s^2 - (\mu_h + \gamma_h + \phi_2)}$$

where we have applied the first boundary condition of ψ_1. The inverse Laplace transform and the convolution integral then give

$$\psi_1(x) = \frac{1}{\sqrt{D_4(\mu_h + \gamma_h + \phi_2)}} \times \int_0^x \sinh\left[\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}} (x - \tau) \right] y_1(\tau) d\tau - \frac{\cosh\left(\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}} \right)}{\sqrt{D_4(\mu_h + \gamma_h + \phi_2)} \sinh\left(\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}} \right)} \times \int_0^1 \cosh\left[\sqrt{\frac{\mu_h + \gamma_h + \phi_2}{D_4}} (1 - \tau) \right] y_1(\tau) d\tau. \quad (38)$$

Indeed,

$$\psi_1(x) = L^{-1}[\psi_1(s)] = L^{-1}\left[\frac{Y_1(s)}{D_4 s^2 - (\mu_h+\gamma_h+\phi_2)}\right] + L^{-1}\left[\frac{sD_4\psi_1(0)}{D_4 s^2 - (\mu_h+\gamma_h+\phi_2)}\right]. \quad (39)$$

Consider,

$$L^{-1}\left[\frac{Y_1(s)}{D_4 s^2 - (\mu_h+\gamma_h+\phi_2)}\right] = L^{-1}\left[\frac{Y_1(s)\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}(\sqrt{D_4})^2 s^2 - (\mu_h+\gamma_h+\phi_2)}\right].$$

Setting

$$f(s) = \frac{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}{(\sqrt{D_4}s)^2 - (\sqrt{\mu_h+\gamma_h+\phi_2})^2} \quad (40)$$

and

$$g(s) = \frac{Y_1(s)}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}}. \quad (41)$$

We obtain

$$L^{-1}[f*g] = \frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}} \times \int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau.$$

Next, we consider

$$L^{-1}\left[\frac{sD_4\psi_1(0)}{D_4 s^2 - (\mu_h+\gamma_h+\phi_2)}\right] = \psi_1(0)L^{-1}\left[\frac{sD_4}{(\sqrt{D_4})^2 s^2 - (\sqrt{\mu_h+\gamma_h+\phi_2})^2}\right] = \psi_1(0)\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right). \quad (42)$$

Consequently, we have

$$\psi_1(x) = \frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}} \times \int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau + \psi_1(0)\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right). \quad (43)$$

We differentiate ψ_1 and applying the boundary condition $\psi_1'(1) = 0$, we obtain that

$$\psi_1'(x) = \frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}} \times \frac{d}{dx}\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau + \psi_1(0)\frac{d}{dx}\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)$$
$$= \frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}} \times \int_0^x \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau + \frac{\psi_1(0)}{\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right). \quad (44)$$

Hence

$$\psi_1(0) = -\frac{1}{\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)} \times \int_0^1 \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(1-\tau)\right] y_1(\tau)d\tau.$$

Now let us focus on the eigenvalue problem $L[\phi] = \lambda\phi$; that is,

$$-FB^{-1}\phi = \lambda\phi = L[\phi] = R_0. \quad (45)$$

With some algebraic manipulation, the eigenvalue problem can be put into the form

$$k_{i1}\int_0^x \sinh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(x-\tau)\right] y_1(\tau)d\tau + k_{i2}\cosh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right) \times \int_0^1 \cosh\left[\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}(1-\tau)\right] y_1(\tau)d\tau \quad (i=1) \quad (46)$$

where

$$k_{11} = \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}},$$
$$k_{12} = \frac{\beta_h\mu_h N_h}{(\mu_h+\phi_1)\sqrt{D_4(\mu_h+\gamma_h+\phi_2)}\sinh\left(\sqrt{\frac{\mu_h+\gamma_h+\phi_2}{D_4}}\right)}.$$

6 Optimal control

Now we turn to the more general model (1)–(5) with time-dependent control profiles $\phi_1(t)$, $\phi_2(t)$ and $\phi_3(t)$, and conduct an optimal control study [19]. We consider the system on a time interval $[0, T]$. The functions $\phi_1(t)$, $\phi_2(t)$ and $\phi_3(t)$ are assumed to be at least Lebesgue measurable on $[0, T]$. The control set is defined as

$$\begin{aligned}\Gamma = \{&(\phi_1(t), \phi_2(t), \phi_3(t) | 0 \le \phi_1(t) \le \phi_{1max},\\ &0 \le \phi_2(t) \le \phi_{2max},\\ &0 \le \phi_3(t) \le \phi_{3max}\}\end{aligned}$$

where ϕ_{1max}, ϕ_{2max} and ϕ_{3max} are the upper bounds for the control rates. The bound reflects a practical limitation on the maximum rate of controls in a given time.

Our optimal control study aims to minimize the total numbers of infectious people and the cost of controls over the time interval $[0, T]$; i.e.,

$$\begin{aligned}\min_{\phi_1,\phi_2,\phi_3 \in \Omega} \int_0^T &[I_h(t) + I_v(t) + c_1\phi_1(t)S_h(t)\\ &+ c_2\phi_2(t)I_h(t) + c_3(t)\phi_3(t)S_v(t)\\ &c_4\phi_1^2(t) + c_5\phi_2^2(t) + c_6\phi_3^2(t)\Big] dt \end{aligned} \tag{47}$$

where c_1, c_2, c_3, c_4, c_5 and c_6 are appropriate units defined the appropriate costs associated with the controls.

Let us first define the adjoint functions λ_{S_v}, λ_{S_h}, λ_{I_h} and λ_{I_v} associated with the state equations for S_v, S_h, I_h and I_v, respectively. We then form Hamiltonian, H, by multiplying each adjoint function with the right-hand side of its corresponding state equation and adding each of these products to the integrand of the objective functional.

As a result, we obtain

$$\begin{aligned}H = &I_h(t) + I_v(t) + c_1\phi_1(t)S_h(t) + c_2\phi_2(t)I_h(t)\\ &+ c_3\phi_3(t)S_v(t) + c_4\phi_1^2(t) + c_5\phi_2^2(t) + c_6\phi_3^2(t)\\ &+ \lambda_{S_h}\Big(\mu_h N_h - \Big(\mu_h + \frac{\beta_{vh}I_v}{N_h} + \beta_h I_h\Big)S_h - \phi_1(t)S_h\Big)\\ &+ \lambda_{I_h}\Big(\frac{\beta_{vh}I_v}{N_h}S_h + \beta_h I_h S_h - (\mu_h + \gamma_h + \phi_2(t))I_h\Big)\\ &+ \lambda_{S_v}\Big(\mu_v N_v - (\mu_v + \frac{\beta_{hv}I_h}{N_h})S_v - \phi_3(t)S_v\Big)\\ &+ \lambda_{I_v}\Big(\frac{\beta_{hv}I_h S_v}{N_h} - \mu_v I_v\Big)\end{aligned}$$

To achieve the optimal control, the adjoint functions must satisfy $\frac{d\lambda_{S_h}}{dt} = -\frac{\partial H}{\partial S_h}$, $\frac{d\lambda_{S_v}}{dt} = -\frac{\partial H}{\partial S_v}$, $\frac{d\lambda_{I_h}}{dt} = -\frac{\partial H}{\partial I_h}$, and $\frac{d\lambda_{I_v}}{dt} = -\frac{\partial H}{\partial I_v}$. Thus, we have

$$\begin{aligned}\frac{d\lambda_{S_h}}{dt} &= -c_1\phi_1(t) + \lambda_{S_h}\Big(\mu_h + \frac{\beta_{vh}I_v}{N_h} + \beta_h I_h + \phi_1\Big)\\ &\quad - \lambda_{I_h}\Big(\frac{\beta_{vh}I_v}{N_h} + \beta_h I_h\Big),\\ \frac{\lambda_{I_h}}{dt} &= -1 - c_2\phi_2(t) + \lambda_{S_h}\beta_h S_h - \lambda_{I_h}(\beta_h S_h\\ &\quad - (\mu_h + \gamma_h + \phi_2(t))) + \lambda_{S_v}\frac{\beta_{hv}S_v}{N_h} - \lambda_{I_v}\frac{\beta_{hv}S_v}{N_h},\\ \frac{d\lambda_{S_v}}{dt} &= -c_3\phi_3(t) + \lambda_{S_v}\Big(\mu_v + \frac{\beta_{hv}I_h}{N_h} + \phi_3(t)\Big)\\ &\quad - \lambda_{I_v}\frac{\beta_{hv}I_h}{N_h},\\ \frac{d\lambda_{I_v}}{dt} &= -1 + \lambda_{S_h}\frac{\beta_{vh}S_h}{N_h} - \lambda_{I_h}\frac{\beta_{vh}S_h}{N_h} + \lambda_{I_v}\mu_v\end{aligned}$$

with the final-time conditions $\lambda_{S_h}(T) = 0, \lambda_{S_v}(T) = 0, \lambda_{I_h}(T) = 0$, and $\lambda_{I_v}(T) = 0$. The characterizations of the optimal controls $\phi_1(t)$, $\phi_2(t)$ and $\phi_3(t)$ are then based on the conditions

$$\frac{\partial H}{\partial \phi_1} = 0, \quad \frac{\partial H}{\partial \phi_2} = 0, \text{ and } \quad \frac{\partial H}{\partial \phi_3} = 0 \tag{48}$$

respectively, subject to the constraints $0 \le \phi_1(t) \le \phi_{1max}$, $0 \le \phi_2(t) \le \phi_{2max}$ and $0 \le \phi_3(t) \le \phi_{3max}$. Thus we have

$$\begin{aligned}\phi_1^*(t) &= \max[0, \min(\phi_1(t), \phi_{1\max})],\\ \phi_2^*(t) &= \max[0, \min(\phi_2(t), \phi_{2\max})],\\ \phi_3^*(t) &= \max[0, \min(\phi_3(t), \phi_{3\max})],\end{aligned}$$

where

$$\begin{aligned}\phi_1(t) &= \frac{(\lambda_{S_h} - c_1)S_h}{2c_4},\\ \phi_2(t) &= \frac{(\lambda_{I_h} - c_2)I_h}{2c_5},\\ \phi_3(t) &= \frac{(\lambda_{S_v} - c_3)S_v}{2c_6}\end{aligned}$$

7 Numerical results

The optimal control system, consisting of the state equations, the adjoint equations, and the optimality conditions, has to be solved numerically. We have conducted numerical simulation using various choices of cost parameters and time intervals, and have observed a unique solution in each case. The numerical results demonstrate that optimal control strategies can significantly bring down the number of infectious individuals and infectious mosquitoes.

In the simulation for our diffusion model, we assume that a Zika virus disease outbreak first appears on day 1 of the first

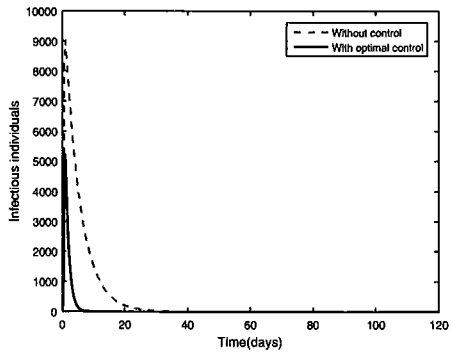

Fig. 2 Infectious humans of the ODE model

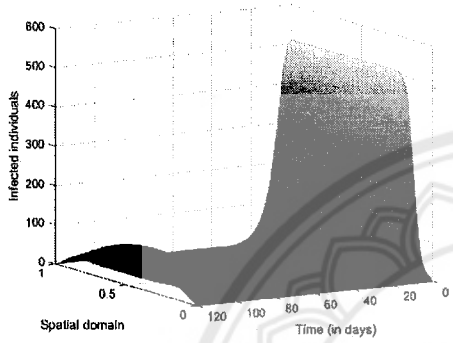

Fig. 3 Infected humans in diffusion model

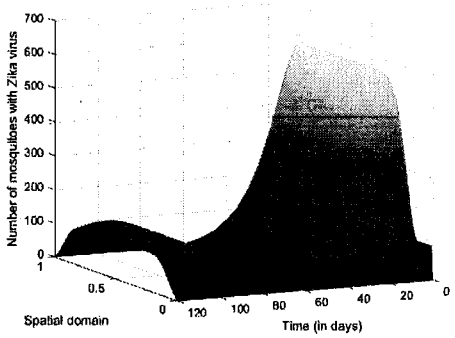

Fig. 4 Mosquitoes with the Zika virus in each spatial location versus time

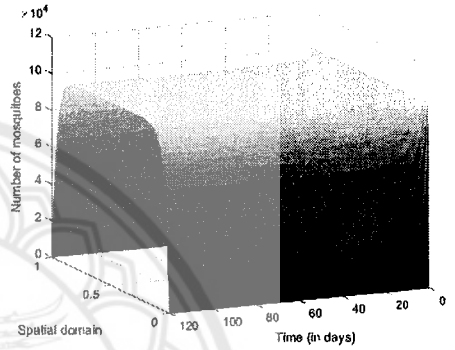

Fig. 5 Susceptible mosquitoes in each spatial location versus time

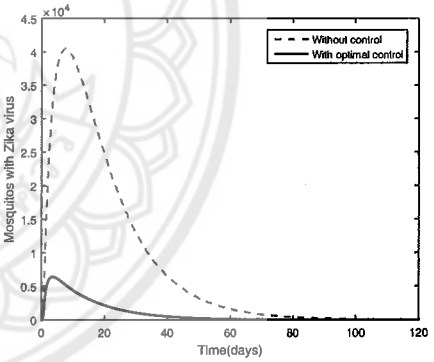

Fig. 6 Infectious mosquitoes

month, then it spreads to the neighboring cities (in diffusion way) and reaches its peak of the outbreak in about two months and a half (average mosquitoes' life-span). Also, for each location (in the spatial domain), we assume that the initial number of infected mosquitoes is the same (from reproduction). We further assume that cities in our simulation are about the same size, therefore, in each spatial location, the initial condition for infected humans is also the same. We also extend our numerical study to investigate the time-dependent bitting rate that is based on seasonality by assuming that the biting rate of mosquitoes starts small and increases over time. It will reach its maximum value about seventy days and decrease to almost zero at the end of the fourth month.

Figure 2 shows the number of infectious humans, which without control curve is shown in the dashed line and that with optimal control is shown in the solid line. The controls included in the study are personal protection, medical treatment, and insecticide. As the graph presented, the reductions in both the infection level and the outbreak period are significant. To further understand the effects of social connection among humans, we also present the human infectious diffusion curve in Fig. 3. As demonstrated, we observe that if an outbreak starts at location $x = 0.5$, it will spread further out to the neighboring cities (the closer to the starting point, the number of infected individuals stays high). From our numerical simulations, the total number of mosquitoes (infected and susceptible as shown in Figs. 4 and 5, respectively) near the starting point of the outbreak is high and decreases farther out over time. Thus, the simulations suggest that if we can control the disease to stay close to the starting point, it will not transfer to other neighboring cities, and as a result, it reduces the number of infections in humans in total.

The infection level in humans will not reduce if the population of infected mosquitoes is still high. Figure 6 represents that the infection level of mosquitoes has been significantly reduced due to the incorporation of the three types of controls. Also, the peak of I_v, infectious mosquitoes, without control curve reaches its highest value at $t \approx 5$ - 8 days,

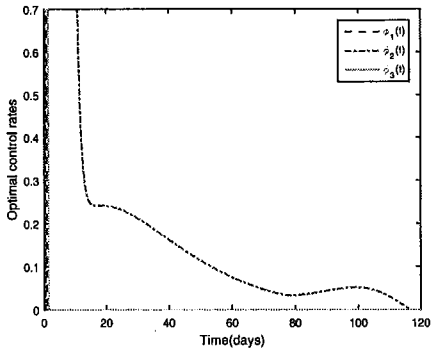

Fig. 7 Rates of controls with $\phi_{1\max} = 0.7$, $\phi_{2\max} = 0.7$ and $\phi_{3\max} = 0.7$. The result shows that medical treatment is needed at its maximum rate for about 7 days to reduce the number of infectious individuals

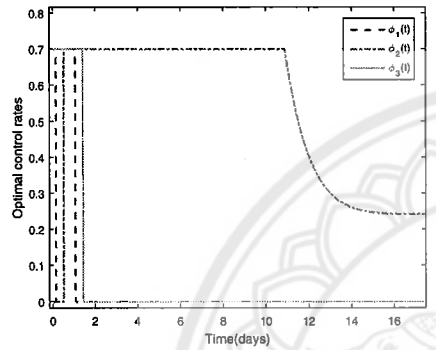

Fig. 8 Zoomed-in rates of controls with $\phi_{1\max} = 0.7$, $\phi_{2\max} = 0.7$ and $\phi_{3\max} = 0.7$. It is seen that the insecticide and personal protection control measures are very important to control Zika virus outbreaks. Also, they should be implemented immediately after the onset of a Zika virus outbreak

however, the peak of I_v with controls reaches its peak at $t \approx 2$ days and its value is much lower than that without control. Figure 7 shows the optimal control rates and their zoom-in versions are presented in Fig. 8.

We have also run the numerical simulation for this model with various parameter values and initial conditions, and the results are consistent with our analytical predictions: when $R_0 < 1$, the disease dies out; when $R_0 > 1$, the disease persists and all solutions converge to the endemic equilibrium. In particular, using the parameter values given in Table 1 (with $R_0 > 1$), we show a set of results in Figs. 9, 10 and 11. We observe that all three curves approach the endemic equilibrium over time, indicating the global asymptotic stability of the endemic equilibrium. We also investigate the reproduction number of our optimal control problem as shown in Fig. 12 and it shows that the reproduction number decreases in the first few days due to the implementation of controls and starts increasing after day 2 or 3. The result indicates that controls can help to reduce the number of newly infected patients.

To investigate our diffusion model, we have used simple finite difference schemes for our PDE systems to facilitate numerical implementation while maintaining good numerical stability. Parameter values used in this numerical simulation are presented in Table 1.

Table 1 Parameter values and symbols

Parameter	Symbol	Value
Human birth rate	μ_h	0.0000391/day
Mosquito birth rate	μ_v	0.0714/day
Vector-human contact rate	β_{vh}	0.3/day
Human-vector contact rate	β_{hv}	0.09/day
Human-human contact rate	β_h	0.1/day
The recovery rate	γ_h	0.2
Death rate due to disease	α	0.03

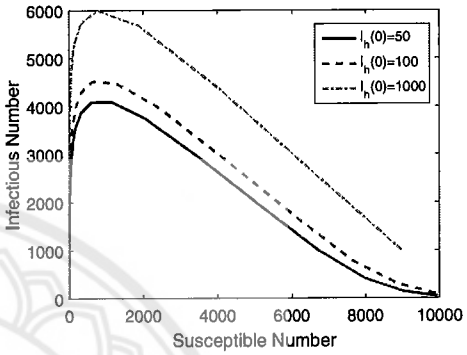

Fig. 9 Phase portraits for the Zika virus model (without controls) with different initial conditions, and $R_0 > 1$. All the curves converge to the endemic equilibrium

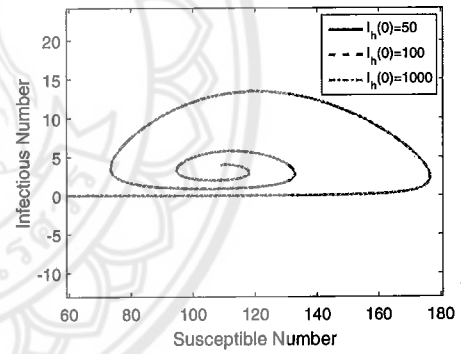

Fig. 10 Phase portraits (zoomed-in) for the Zika virus model (without controls) with different initial conditions, and $R_0 > 1$. All the curves converge to the endemic equilibrium

8 Conclusion

We have presented a mathematical model for the Zika virus disease that incorporates the control measures; personal protection, medical treatment, and insecticide. The model exhibits two feasible points of equilibrium, namely, the

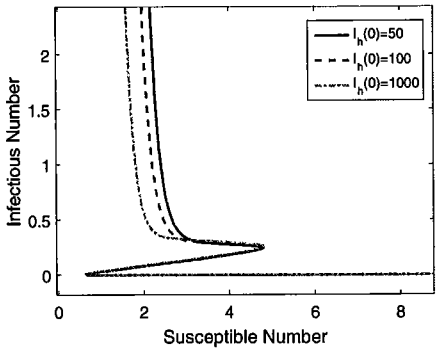

Fig. 11 The zoomed-in phrase plots of infectious individuals with control. All the curves converge to almost zero

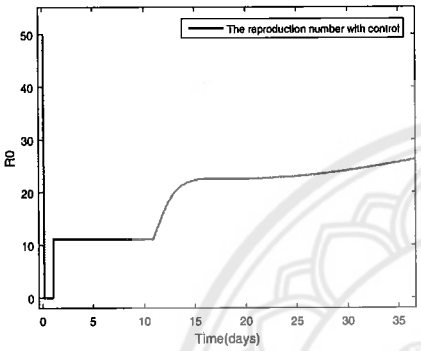

Fig. 12 The reproduction number with control

disease-free equilibrium and the endemic equilibrium. The stability of these two feasible points of equilibrium is controlled by the threshold number R_0. If R_0 is less than one, then the disease dies out and the disease-free equilibrium stable. If R_0 is greater than one, then the disease persists and the disease-free equilibrium is unstable. The analytical predictions are verified by our numerical simulation results for our model. We further have extended our work to a diffusion model to study the spatial movement of both mosquitoes and humans via a PDE model to better understand the time-space model for the Zika virus.

We have also performed an optimal control study by investigating three types of controls: personal protection, medical treatment, and insecticide, to seek the optimal control strategy to contain the disease outbreak in humans. Our results show that personal protection and insecticide, when strategically deployed, are very important control measures to reduce the numbers of human and mosquito infectious and to help eradicate the disease outbreak. Also, we have conducted a numerical simulation to investigate the reproduction number under an optimal control problem to gain guidelines for preventing the spread of the Zika virus disease.

The diffusion model also represents that to stop the virus from spreading to other nearby cities or places, we need to additionally implement other control strategies such as social distancing or quarantine. The numerical simulations suggest that if the center of an outbreak is contained, the disease will not spread to other places and it results in stopping the outbreak.

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