#### Dynamics of Zika virus epidemic in random environment and its numerical simulation

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## **1** Introduction

Zika virus has been known as a mosquito-borne disease, that is transmitted to humans by the bites of infected mosquitoes [1]. Evidence indicates that Zika can also be transmitted by sexual contact, yet the role of sexual transmission is not well-understood. Recently Gao *et al.* introduced a deterministic mathematical model that considered Zika as a mosquito-borne and sexually transmitted disease, and investigated the spread and control of Zika by analyzing the proposed model [3]. The analysis done in [3] provided the crucial information that prevention and control efforts against Zika should target not only mosquito-borne but also sexual transmission routes. Concerning the spread and transmission of Zika virus involve uncertainties, the goal of this work is to develop and study a mathematical model of Zika virus epidemic taking into account randomness due to fluctuations of environments.

Since the zika virus can be transmitted between humans, from humans to mosquitoes, and from mosquitoes to humans during the incubation period, we consider an SIR type of structure for humans and an SI type of structure for mosquitoes by combining their respective exposed and infected groups. In addition, since sexual transmission of zika from asymptomatically infected humans has not been documented and mosquitoes are not infected by biting them, we consider both the asymptomatically infected humans and the recovered humans as the removed.

Let  $x_1(t)$ ,  $x_2(t)$  and  $x_3(t)$  be the population of susceptible, symptomatically infected and removed humans, respectively, and let  $y_1(t)$ ,  $y_2(t)$  be the population of susceptible and infectious mosquitoes, respectively. Then a simplified version of the model proposed in [3] reads

$$\frac{\mathrm{d}x_1}{\mathrm{d}t} = -\alpha p x_1 y_2 - \kappa x_1 x_2, \tag{1}$$

$$\frac{\mathrm{d}x_2}{\mathrm{d}t} = \delta\left(\alpha p x_1 y_2 + \kappa x_1 x_2\right) - \gamma x_2,\tag{2}$$

$$\frac{\mathrm{d}x_3}{\mathrm{d}t} = (1-\delta)(\alpha p x_1 y_2 + \kappa x_1 x_2) + \gamma x_2, \tag{3}$$

$$\frac{\mathrm{d}y_1}{\mathrm{d}t} = \beta(y_1 + y_2) - \alpha q y_1 x_2 - \beta y_1, \tag{4}$$

$$\frac{\mathrm{d}y_2}{\mathrm{d}t} = \alpha q y_1 x_2 - \beta y_2. \tag{5}$$

The parameter values are  $\alpha \ge 0$ : mosquito biting rate per human,  $p \in [0, 1]$ : transmission probability from an infectious mosquito to a susceptible human per bite,  $q \in [0, 1]$ : transmission probability from a symptomatically infected human to a susceptible mosquito per bite,  $\kappa \ge 0$ : average transmission rate from symptomatically infected humans to susceptible humans,  $\gamma \ge 0$ : the recovery rate of infected humans,  $\delta \in [0, 1]$ : the proportion of symptomatic infections and  $\beta \ge 0$ : the production and the death rate of mosquitoes.

In the above model the total numbers of humans and mosquitoes are both assumed to be constant over time. While such an assumption is acceptable for humans, it is less well-justified for mosquitoes as the population of mosquitoes is more sensitive to the season and the environment (e.g., weather changes, mosquito treatments) and thus clearly varies with respect to time. In this work we assume that both the reproduction rate and loss rate of mosquitoes vary randomly and can be different, modeled by two random processes  $\beta(\theta_t \omega)$  and  $\nu(\theta_t \omega)$ , respectively. Note that here  $\nu(\theta_t \omega)$ stands for the collective loss rate of mosquitoes including natural death, mosquito treatments, migration out from the region, etc. In addition we include random external forces  $g_1(\theta_t \omega)$  and  $g_2(\theta_t \omega)$  to incorporate all non-reproduction type increase in the mosquito population, such as migration into the region. Furthermore, we assume that  $\beta(\theta_t \omega)$ ,  $\nu(\theta_t \omega)$  and  $g_j(\theta_t \omega)$  (j = 1,2) are continuous, non-negative, and essentially bounded, i.e., there exist non-negative constants  $m_{\beta}$ ,  $M_{\beta}$ ,  $m_{\nu}$ ,  $M_{\nu}$ ,  $m_{g}$  and  $M_{g}$  such that

$$m_{\beta} \leq \beta(\theta_t \omega) \leq M_{\beta}, \quad m_{\nu} \leq \nu(\theta_t \omega) \leq M_{\nu}, \quad m_g \leq g_j(\theta_t \omega) \leq M_g \ (j=1,2).$$
 (6)

The equations (1) - (5) then become the following system of random ordinary differential equations (RODEs) [2]:

$$\frac{\mathrm{d}x_1(t,\omega)}{\mathrm{d}t} = -\alpha p x_1 y_2 - \kappa x_1 x_2, \tag{7}$$

$$\frac{\mathrm{d}x_2(t,\omega)}{\mathrm{d}t} = \delta\left(\alpha p x_1 y_2 + \kappa x_1 x_2\right) - \gamma x_2,\tag{8}$$

$$\frac{dt}{dt} = (1-\delta)(\alpha px_1y_2 + \kappa x_1x_2) + \gamma x_2, \qquad (9)$$

$$\frac{dy_1(t,\omega)}{dt} = \beta(\theta,\omega)(y_1 + y_2) - \alpha \alpha y_1x_2 - y(\theta,\omega)y_1 + g_1(\theta,\omega) \qquad (10)$$

$$\frac{\mathrm{i}y_1(t,\omega)}{\mathrm{d}t} = \beta(\theta_t\omega)(y_1+y_2) - \alpha q y_1 x_2 - \mathbf{v}(\theta_t\omega)y_1 + g_1(\theta_t\omega), \tag{10}$$

$$\frac{\mathrm{d}y_2(t,\omega)}{\mathrm{d}t} = \alpha q y_1 x_2 - \mathbf{v}(\theta_t \omega) y_2 + g_2(\theta_t \omega). \tag{11}$$

#### **Basic properties of solutions** 2

For the above RODE system (7)–(11), the following theorem is obtained.

**Theorem 2.1** *For any*  $\omega \in \Omega$ *, t*<sup>0</sup>  $\in \mathbb{R}$  *and initial data* 

$$(x_1(t_0), x_2(t_0), x_3(t_0), y_1(t_0), y_2(t_0))^T = (x_1^0, x_2^0, x_3^0, y_1^0, y_2^0)^T := \boldsymbol{u}_0 \in \mathbb{R}^5_+,$$

the RODE system (7)–(11) admits a unique non-negative global solution  $\mathbf{u}(\cdot;t_0,\omega,\mathbf{u}_0) \in \mathscr{C}([t_0,\infty),\mathbb{R}^5_+)$  with  $\mathbf{u}(t_0;t_0,\omega,\mathbf{u}_0)$  $= u_0.$ 

#### 3 Long term dynamics of Zika virus

It is straightforward to check that the unique solution  $u(t;t_0,\omega,u_0)$  proved in Section 2 satisfies

$$\boldsymbol{u}(t+t_0;t_0,\boldsymbol{\omega},\boldsymbol{u}_0)=\boldsymbol{u}(t;0,\boldsymbol{\theta}_{t_0}\boldsymbol{\omega},\boldsymbol{u}_0)$$

for all  $t_0 \in \mathbb{R}, t \ge t_0, \omega \in \Omega$  and  $u_0 \in \mathbb{R}^5_+$ . This allows us to define a mapping  $\varphi(t, \omega, \cdot)$ , which is a random dynamical system (RDS), as

$$\varphi(t, \omega, u_0) = u(t; 0, \omega, u_0), \quad \forall t \ge 0, \ u_0 \in \mathbb{R}^5_+, \ \omega \in \Omega.$$

From now on, we will simply write  $\boldsymbol{u}(t; \boldsymbol{\omega}, \boldsymbol{u}_0)$  instead of  $\boldsymbol{u}(t; 0, \boldsymbol{\omega}, \boldsymbol{u}_0)$ .

Throughout this section, denote by H be the total population (susceptible, symptomatically infected, removed) of human beings in the region of zika virus prevalence under consideration. To simplify notations, let

$$\mu := \alpha q H + m_{\nu}, \quad y_1(t) + y_2(t) = Y(t), \quad y_1^0 + y_2^0 = Y_0.$$

To investigate the long term dynamics of the solution, we introduce next theorem.

**Theorem 3.1** The RDS  $\{\varphi(t, \omega)\}_{t>0, \omega \in \Omega}$  possesses a random attractor  $\mathscr{A}_H = \{A_H(\omega) : \omega \in \Omega\}$  provided  $M_\beta < m_\nu$ .

The above theorem proves the existence of a random attractor for the full RODE system (7) - (11) under the assumption  $m_V > M_B$ . In the subsections below we will discuss detailed dynamics of mosquito and human being populations, respectively.

### 3.1 Dynamics of mosquito population

In this subsection we will discuss dynamics of mosquito population, in particular, population of infected mosquitoes  $y_2(t, \omega)$ , in two scenarios: (1)  $m_v > M_\beta$ ; and (2)  $m_\beta > M_v$ .

**Theorem 3.2** Assume that  $m_V > M_\beta$ . Then the population of infected mosquitoes satisfies

$$\frac{m_g}{M_{\mathbf{v}}} \leq \lim_{t \to \infty} y_2(t, \omega) \leq \frac{2\alpha q H M_g}{\mu(m_{\mathbf{v}} - M_{\beta})} + \frac{M_g}{\mu}$$

**Corollary 3.1** Assume that  $m_v > M_\beta$ . Then the attractor  $\mathscr{A}_H$  for the RDS generated by solutions to (7)–(11) consists of nontrivial component sets provided

$$\frac{m_g}{M_\nu} < \frac{2\alpha q H M_g}{\mu (m_\nu - M_\beta)} + \frac{M_g}{\mu}.$$
(12)

**Theorem 3.3** Assume that for every  $\omega \in \Omega$  there exist  $\sigma > 0$  and  $I_g > 0$  such that

$$e^{\int_0^t (\beta(\theta_s \omega) - \nu(\theta_s \omega)) ds} \le \sigma, \qquad \int_0^t g(\theta_s \omega) ds \le I_g \qquad \forall t \ge 0.$$
(13)

Then the population of infected mosquitoes satisfies

$$\frac{m_g}{M_\nu} - \varepsilon \leq y_2(t) \leq \frac{\alpha q H \sigma}{\mu} \left( Y_0 + I_g \right) + \frac{M_g}{\mu} + \varepsilon, \quad \forall t \geq T_\varepsilon.$$

In summary we have the following corollary on the population of infected mosquitoes.

**Corollary 3.2** For any  $t \ge 0$  and  $\omega \in \Omega$ , the following bounds for  $y_2(t, \omega)$  hold:

$$y_2(t,\boldsymbol{\omega}) \geq \left(y_2^0 - \frac{m_g}{M_v}\right) e^{-M_v t} + \frac{m_g}{M_v},\tag{14}$$

$$y_2(t,\omega) \leq Y_0 + \frac{2M_g}{m_v - M_\beta}, \quad \text{if } M_\beta < m_v \tag{15}$$

$$y_2(t,\omega) \leq y_2^0 + \frac{\alpha q H \sigma(Y_0 + I_g)}{\mu}, \quad if \begin{cases} \int_0^t g(\theta_s \omega) ds \leq I_g \text{ and} \\ e^{\int_0^t (\beta(\theta_s \omega) - v(\theta_s \omega)) ds} \leq \sigma \end{cases}.$$
(16)

### 3.2 Dynamics of human being populations

In this subsection we investigate the long term dynamics for human beings. For simplicity, let

$$\hat{x}_{1}^{0} = x_{1}^{0} e^{\left|\frac{\alpha p}{M_{V}}(y_{2}^{0} - \frac{m_{g}}{M_{V}})\right|}.$$
(17)

Lemma 3.1 The population of susceptible human beings satisfies

$$x_1(t,\omega) \le \hat{x}_1^0 \cdot e^{-\alpha p \frac{m_0}{M_V} t}, \quad \forall \ \omega \in \Omega.$$
(18)

The above Lemma states that the populations of susceptible human beings will exponentially decay to zero. This will be used to investigate the sufficient conditions under which population of infected human beings decreases monotonically to zero. To simplify notations, let

$$\hat{y}_2 = \max\left\{Y_0 + \frac{2M_g}{m_v - M_\beta}, y_2^0 + \frac{\alpha q H \sigma(Y_0 + I_g)}{\mu}\right\}.$$
(19)

Throughout the rest of this subsection it is assumed that either

- (I)  $m_{\nu} > M_{\beta}$ , or
- (II) there exist  $\sigma > 0$  and  $I_g > 0$  such that the assumption (13) holds.

**Theorem 3.4** The population of infected human beings  $x_2(t, \omega)$  always decays to zero as  $t \to \infty$ . In particular  $x_2(t, \omega) \to 0$  monotonically provided

$$\delta \hat{x}_1^0 \left( \kappa + \frac{\alpha p \hat{y}_2}{x_2^0} \right) \le \gamma < \alpha p \frac{m_g}{M_\nu}.$$
(20)

The theorem above states that when  $m_v > M_\beta$ , or the assumption (13) holds for some  $\sigma > 0$  and  $I_g > 0$ , the Zika virus will always die out given a long enough time. Moreover if Assumption (20) holds, the prevalence of virus decreases monotonically to zero, i.e., the Zika virus is controlled. In the theorem below we construct conditions under which there is an outbreak or epidemic of Zika virus, in the sense that infected human beings increase for a certain period of time before eventually decaying to zero.

**Theorem 3.5** The population of infected human beings  $x_2(t, \omega)$  keeps increasing for at least up to some  $T_M > 0$ , provided

$$\gamma < \delta x_1^0 \left( \kappa + \frac{\alpha p}{H} y_2^0 \right). \tag{21}$$

# 4 Numerical experiments

In this section, we will simulate the system (7) – (11) numerically and verify that the long term dynamics of infected mosquitoes satisfy Corollary 3.2 and the population of susceptible human being satisfies Lemma 3.1. In addition, we confirm that the population of infected humans  $x_2(t, \omega)$  decreases monotonically under the condition (20) and increases for a while before decreases under the condition (21).

To this end we transform the system (7) – (11) with four independent Ornstein–Uhlenbeck (OU) processes  $Z_j(t)$  into a system of RODE–SODE pair [2]:

$$\mathbf{d} \begin{pmatrix} x_{1}(t) \\ x_{2}(t) \\ x_{3}(t) \\ y_{1}(t) \\ y_{2}(t) \\ Z_{j}(t) \end{pmatrix} = \begin{pmatrix} -\alpha \rho x_{1}y_{2} - \kappa x_{1}x_{2} \\ \delta(\alpha x_{1}y_{2} + \kappa x_{1}x_{2}) - \gamma x_{2} \\ (1 - \delta)\delta(\alpha x_{1}y_{2} + \kappa x_{1}x_{2}) + \gamma x_{2} \\ \beta(Z_{2})(y_{1} + y_{2}) - \alpha qy_{1}x_{2} - v(Z_{1})y_{1} + g_{1}(Z_{3}) \\ \alpha qy_{1}x_{2} - v(Z_{1})y_{2} + g_{2}(Z_{4}) \\ \theta_{j,1} - \theta_{j,2}Z_{j} \end{pmatrix} \mathbf{d}t + \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \theta_{j,3} \end{pmatrix} \mathbf{d}W_{t}$$

where j = 1, 2, 3, 4. The loss and the production rates of mosquitoes  $v(Z_1)$  and  $\beta(Z_2)$  and the external forces modelling random environments  $g_1(Z_3)$  and  $g_2(Z_4)$  are assumed to distribute in a finite interval or have switching effect.

The following figures illustrate theoretical results under scenario (I) and (II).



Scenario (I) With parameters  $\alpha = 0.1$ , p = 0.2, q = 0.3,  $\kappa = 0.05$ ,  $\delta = 0.01$ ,  $\gamma = 0.16$ ,  $\bar{\nu} = 0.3$ ,  $r_1 = 0.1$ ,  $\bar{a} = 0.1$ ,  $r_2 = 0.1$ ,  $\bar{g}_1 = 3.5$ ,  $r_3 = 0.2$ ,  $\bar{g}_2 = 3.5$  and  $r_4 = 0.2$  satisfying Assumption (20), the population of infected human beings decreases monotonically.



Scenario (II) With parameters  $\alpha = 0.3$ , p = 0.2, q = 0.3,  $\kappa = 0.00005$ ,  $\delta = 0.9$  and  $\gamma = 0.08$ ,  $\bar{\nu} = 0.9$ ,  $r_1 = 0.1$ ,  $\bar{\beta} = 0.1$ ,  $r_2 = 0.1$ ,  $\bar{g}_1 = 3$ ,  $r_3 = 0.9$ ,  $\bar{g}_2 = 5$  and  $r_4 = 0.9$  satisfying Assumptions  $M_\beta < m_\nu$  and (21), the population of infected human beings first increases before it decreases.

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## References

- [1] A. S. Fauci and D. M. Morens, *Zika Virus in the Americas yet another arbovirus threat*, New England Journal of Medicine **374** (2016), 601–604.
- [2] X. Han and P. E. Kloeden, Random Ordinary Differential Equations and their Numerical Solution, Springer Nature, Singapore (2017).
- [3] D. Gao, Y. Lou, D. He, T. C. Porco, Y. Kuang, G. Chowell and S. Ruan, *Prevention and control of Zika as a mosquito-borne and sexually transmitted disease: a mathematical modeling analysis*, Scientific Reports 6, Article number: 28070 (2016).

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