



## International Research Journal of Public Health (ISSN:2573-380X)



# 2016 Deterministic Model Behind Zika Virus Infections in Brazil

Isack E. Kibona, Cuihong Yang, Shanshan Dong

College of Mathematics and Statistics, Central China Normal University, 152 Luoyu Avenue, Wuhan, Hubei 430079, P. R. China

### ABSTRACT

We formulated a deterministic model for simulation of zika virus (ZIKV) infections. This cooperates with WHO serious alert on February 1<sup>st</sup>, 2016 to contain ZIKV epidemic in the world, Brazil being the most hit. Accordingly, we have taken Brazil records on ZIKV cases as an example to justify the model. According to the model, simulations suggests that by 2020, ZIKV infections is no longer a threat in this country. In our analytic analysis we have included some brief simulations as specific cases. Finally, model simulation is all about Brazil.

In this model, besides a disease free equilibrium (DFE) point being globally stable, analysis of local DFE has two sets of eigenvalues, leading two different qualitative behavior. This follows due to variation in some parameters. In each of these two sets, none has backward bifurcation. That is the disease is controllable when  $R_0 < 1$ . Otherwise, when  $R_0 > 1$  the disease free is unstable. In the analytic analysis of either qualitative behavior, we have associated brief simulation. Only analytic analysis of endemic equilibrium has not been fully developed.

We have considered Brazil ZIKV cases from January 2016 onward to verify the model plus having some predictions about ZIKV infections to around 2020. The basic reproduction ( $R_0$ ) has been estimated as  $R_0 = 0.1922 < 1$ , since then ZIKV infections has been decreasing since highest peak in early 2016. Should this value of  $R_0 = 0.1922$  be stabilized or lowered, then ZIKV infections is no longer a threat in Brazil by 2020. Simulations for Brazil has been extended to understand the possible situation if  $R_0 > 1$ .

**Keywords:** Deterministic model of ZIKV infections; ZIKV simulation in Brazil; stability of DFE.

### \*Correspondence to Author:

Isack E. Kibona

College of Mathematics and Statistics, Central China Normal University, 152 Luoyu Avenue, Wuhan, Hubei 430079, P. R. China

### How to cite this article:

Isack E. Kibona, Cuihong Yang, Shanshan Dong. 2016 Deterministic Model Behind Zika Virus Infections in Brazil. International Research Journal of Public Health, 2018; 2:11.

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## 1 Introduction

On February 1st, 2016 the World Health Organization declared ZIKV epidemic in the Americas as a Public Health Emergency of International Concern gulland2016warns. The foremost reason was due to an emerging linkage of ZIKV infections with congenital birth anomalies such as microcephaly and Guillain-Barre syndrome rocklov2016assessing plus new mode of transmission (sexual-transmission) which had not known by the time freour2016sexual,turmel2016late. Recent studies report that ZIKV is transmitted not only via mosquito bite but also via sexual contacts, blood contamination and mother-to-child-transmission (MTCT)gao2016prevention, manrique2016simulation. Prenatal or perinatal complications of ZIKV infections have been noted. There is some evidence that perinatal transmission may occur, most probably trans-placental or during the delivery of a viraemic mother corsica2015zika.

### 1.1 Theoretical Framework in Mathematical Perspective

Basing on the nature of epidemic, though with a relatively long history since its knowledge in 1947, few researches have been conducted compared to related epidemics like HIV infections. Probably, the main reason is that its effects were not vividly clear to human being compared to recent studies. However, this does not rule out the fact that in the past people were not affected by zika virus disease (ZVD). Recently, a number of researches have been working to explore the disease down so as to come up with some means to control it. According to Rojas DP *et al.* rojas2016epidemiology all age groups are assumed vulnerable to ZIKV infections, but the most affected age group is 20 to 49 years of age due to its new known mode of transmission, that is sexual transmission turmel2016late. A similar study previously published outbreaks in Yap Island, Micronesia, El Salvador, and Brazil

cardoso2015outbreak. Since the population was fully susceptible to ZIKV transmission before the outbreaks, it was expected that all age groups would be affected. Joacim Rocklov *et al.* rocklov2016assessing, studied seasons in the year which are more risk to ZIKV transmission. There are as well more researches in medicine and other discipline miner2016zika.

This paper is about a more insight concerning with mathematical models exploring the interpersonal spread of the epidemic. One of the model was done by Adam J. Kucharski *et al.* in early 2016 kucharski2016transmission. The model provided understanding ZVD in mathematical perspective, basing on some assumptions the model did not include sexual transmission. Khalid *et al.* in the late of 2016, have formulated the mathematical model by including sexual transmission khalidstability. On one hand this article is an improvement of Kucharski's model, modified to include sexual-transmission. On the other hand this model includes infections to newborns through mother-to-child-transmission (MTCT) manrique2016simulation.

## 2 Model Formulation

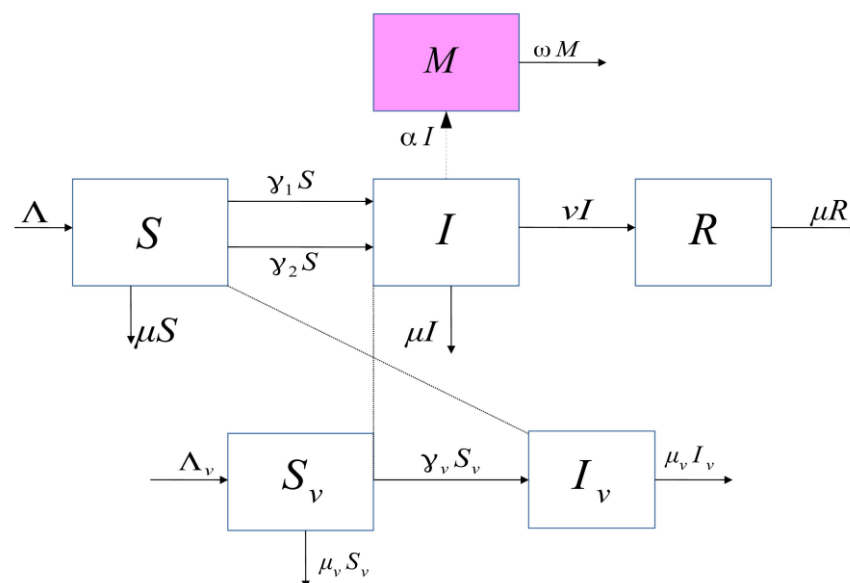
The model consists of two categories, the humans and mosquitoes with total population  $N_T$  and  $N_v$  respectively. Presumably, the humans have four classes, the susceptible ( $S$ ), infectious ( $I$ ), newborns infected with ZIKV-linked microcephaly ( $M$ ) and recovered ( $R$ ). Susceptible is an individual potential to infections. Infectious ( $I$ ) refer to individuals who are exposed or already full blown with ZVD symptoms. Recovered are individuals no longer infectious after survival against ZVD. It is assumed that individuals in the recovered class have built immune against the ZIKV infection. Mosquitoes category have only susceptible ( $S_v$ ) and infectious ( $I_v$ ) classes. The reason is that the life span of mosquitoes is short enough to ignore the recovery period.

**Table 1: Definition of Parameters**

| Parameter            | Definition   |
|----------------------|--|
| $\Lambda, \Lambda_v$ | constant rate of incoming susceptible                              |
| $\mu, \mu_v$         | natural death rates  |
| $\alpha$             | birth rate of infected newborns                                    |
| $\nu$                | rate of transfer of $I$ individuals to $R$                         |
| $\gamma_1$           | rate of infection by mosquitoes                                    |
| $\gamma_2$           | rate of infections through sexual transmission                     |
| $\gamma_v$           | rate of mosquitoes infected by humans                              |
| $\beta_v$            | effective bites between infected mosquitoes and susceptible humans |
| $\beta_h$            | effective contacts from humans to humans                           |
| $n$                  | average number of sexual partners                                  |
| $\beta$              | effective bites between infected humans to susceptible mosquitoes  |

Susceptible individual moves into the infectious class after effective interaction with infected mosquitoes, or sexual contact with and individual in the infectious class. Newborns with ZIKV infection through MTCT enters  $M$  class. The mosquitoes moves from the susceptible to their infectious-class after infection through biting an infectious human.

In this context, in all cases the subscript  $v$  signifies a transmission vector, the mosquitoes. System (1) and Fig.1 is the model and its compartments indicating inter flow of individuals in classes. Tab.1 above is definitions of parameters.

**Figure 1: Model compartments flow diagram**

$$\begin{cases} S'(t) = \Lambda - (\gamma_1 + \gamma_2)S + \mu S; & S'_v(t) = \Lambda_v - (\mu_v + \gamma_v)S_v; \\ I'(t) = (\gamma_1 + \gamma_2)S - (\nu + \mu)I; & I'_v(t) = \gamma_v S_v - \mu_v I_v; \\ M'(t) = \alpha I - \omega M; \\ R'(t) = \nu I - \mu R. \end{cases} \quad (1)$$

$$\gamma_1 = \beta_v \frac{I_v}{N}; \quad \gamma_2 = n\beta_h \frac{I}{N}; \quad \gamma_v = \beta \frac{I}{N}; \quad N = S + I + R; \quad N_T = S + I + M + R; \quad N_v = S_v + I_v.$$

Assign  $\gamma = \gamma_1 + \gamma_2$  then the system (1) may be considered as model (2).

$$\begin{cases} S'(t) = \Lambda - \gamma S + \mu S; & S'_v(t) = \Lambda_v - (\mu_v + \gamma_v)S_v; \\ I'(t) = \gamma S - (\nu + \mu)I; & I'_v(t) = \gamma_v S_v - \mu_v I_v; \\ M'(t) = \alpha I - \omega M; \\ R'(t) = \nu I - \mu R. \end{cases} \quad (2)$$

$S_{t=0} = S(0)$ ,  $I_{t=0} = I(0)$ ,  $M_{t=0} = M_0$ ,  $T_{t=0} = T(0)$ ,  $R_{t=0} = R(0)$ ,  $S_v t = 0 = S_v(0)$  and  $I_v t = 0 = I_v(0)$  are initial values notations.  $\gamma$  is an expression in  $I$ ,  $I_v$  and  $N$ .

### 3 Model Analysis

Substitution of expression for  $\gamma$  and  $\gamma_v$  in the model (1), corresponds to the system

$$\begin{cases} S'(t) = \Lambda - \left(\frac{\beta_v I_v + n\beta_h I}{S+I+R} + \mu\right)S & S'_v(t) = \Lambda_v - \left(\frac{\beta I}{S+I+R} + \mu_v\right)S_v; \\ I'(t) = \left(\frac{\beta_v I_v + n\beta_h I}{S+I+R} + \mu\right)S - (\nu + \mu)I & I'_v(t) = \frac{\beta I S_v}{S+I+R} - \mu_v I_v; \\ M'(t) = \alpha I - \omega M; \\ R'(t) = \nu I - \mu R; \end{cases} \quad (3)$$

#### 3.1 Equilibrium Point and Basic Reproduction Number

The next generation method has been used to evaluate the basic reproduction number of the model. Basic reproduction number,  $R_0 = \frac{1}{2}(c_1 + \sqrt{c_1^2 + 4c_0})$ , where  $c_1 = \frac{n\beta_h}{\nu + \mu}$ ,  $c_0 = \frac{\beta_v \beta \Lambda_v \mu}{(\nu + \mu) \mu_v^2 \Lambda}$ .

Since  $N = S + I + R$ ,  $N_v = S_v + I_v$ , then the following can be deduced from the model (3):

The system (4) of differential equations implies that the model (3) is in  $R_+^6$  and from the latter  $D$  is a subset of  $R_+^6$  such that

$$D = \left\{ (S, I, M, R, S_v, I_v) \in R_+^6 \mid S + I + R \leq \frac{\Lambda}{\mu}, S_v + I_v \leq \frac{\Lambda_v}{\mu_v}, M \geq 0 \right\}.$$

Therefore, the condition to be considered is only that the model (3) is in  $D$ . That the system (3) in  $D$  is bounded in non-negative region. In order to obtain the equilibrium point, LHS of every equation in system (3) is set to zero, thus reducing the system to

$$\begin{cases} \Lambda = \left(\frac{\beta_v I_v + n\beta_h I}{S+I+R} + \mu\right)S & \dots (i); \\ (\nu + \mu)I = \left(\frac{\beta_v I_v + n\beta_h I}{S+I+R}\right)S & \dots (ii); \\ \alpha I = \omega M & \dots (iii); \\ \nu I = \mu R & \dots (iv); \\ \Lambda_v = \left(\frac{\beta I}{S+I+R} + \mu_v\right)S_v & \dots (v); \\ \frac{\beta I S_v}{S+I+R} = \mu_v I_v & \dots (vi). \end{cases}$$

Express  $I, M, R, S_v, I_v$  in terms of  $S$  and substitute in equation (ii), along side that include  $N = S + I + R = \frac{\Lambda}{\mu}$ . Thus, the equation in terms of  $S$  becomes

$$\begin{aligned} \beta_v \beta \Lambda_v (\Lambda - \mu S) S + \frac{n\beta_h \beta \mu_v S (\Lambda - \mu S)^2}{\mu + \nu} + n\beta_h \mu_v^2 R S (\Lambda - \mu S) \\ = \beta \mu_v R (\Lambda - \mu S)^2 + (\mu + \nu) R^2 \mu_v^2 (\Lambda - \mu S) \end{aligned}$$

On one hand the equation have  $\Lambda - \mu S = 0$  which leads to  $S = \frac{\Lambda}{\mu}$ , suggesting the disease free equilibrium for system of equations (i) - (vi); which is obtained as  $E_0\left(\frac{\Lambda}{\mu}, 0, 0, 0, \frac{\Lambda_v}{\mu_v}, 0\right)$ .

Table 2: Sensitivity Indices of  $R_0$

| Rank (Highest Sensitivity First) | Parameter  | Sensitivity Index |
|----------------------------------|------------|-------------------|
| 1                                | $\nu$      | -0.8856           |
| 2                                | $n\beta_h$ | +0.8038           |
| 3                                | $\beta$    | +0.0001077        |
| 4                                | $\beta_v$  | +0.00003591       |

### 3.2 Sensitivity Analysis of Basic Reproduction number ( $R_0$ )

Sensitivity analyses allow us to measure the relative change in a state variable when a parameter changes. In our simulation, we consider that a change of the state variable parallels with a change in  $R_0$ . Since  $R_0$  is a function of the parameters, then we can evaluate the relative sensitivity of  $R_0$  for every parameter.

Definition: The normalized forward sensitivity index for a variable ( $x$ ) which depends on a parameter ( $p$ ), denote it as  $(\gamma_p^x)$  and define

$$\gamma_p^x = \frac{\partial x}{\partial p} \cdot \frac{p}{x}.$$

So for  $R_0 = \frac{1}{2} \left( \frac{n\beta_h}{v+\mu} + \sqrt{\left( \frac{n\beta_h}{v+\mu} \right)^2 + \frac{4\beta_v\beta\Lambda_v\mu}{(v+\mu)\mu_v^2\Lambda}} \right)$ , the sensitivity index of  $R_0$ ,

$$\gamma_p^{R_0} = \frac{\partial R_0}{\partial p} \cdot \frac{p}{R_0}. \quad (5)$$

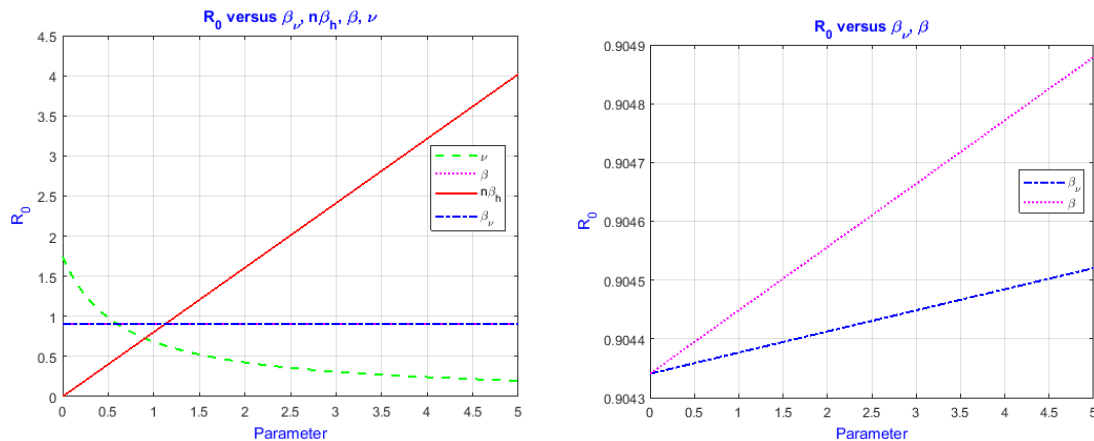


Figure 2: Graphs for Sensitivity Indices

#### 3.2.1 Sensitivity index of $R_0$

Tab.2 is a list of sensitivity indexes of  $R_0$  for the four parameters  $\beta_v$ ,  $\beta$ ,  $n\beta_h$  and  $\nu$ . Evaluation of the sensitivity indexes based on

The ranking in Tab.2,  $R_0$  is most sensitive to a parameter  $\nu$  and least sensitive for  $\beta_v$ . The signs on the sensitivity index indicate the directions of change. For instance,  $R_0$  increases with increase in  $n\beta_h$  and decreases with increase in  $\nu$  and so on.

For values of  $n\beta_h$  below a 5 units, there is approximately a linear relationship between  $R_0$  and  $n\beta_h$ , fig.2. In this particular case of the plot, 5 units change in  $n\beta_h$  leads to 4 units change in  $R_0$ . On the other hand  $R_0$  has not only very small but also almost same sensitivity to  $\beta$  and  $\beta_v$ . fig.2 clearly indicates the graph for  $R_0$  versus  $\beta_v$ , that there is very small increase in  $R_0$  in 5 units change of  $\beta_v$ .

In contrary  $\nu$  has negative influence on  $R_0$ ,

the parameters estimated from the data recorded in Brazil kibona2017sir. The formula (5) has been used to evaluate the sensitivity indexes.

Fig.2 is a graphical illustration of the sensitivity of  $R_0$  for some selected interval of the parameters. Any increase in  $n\beta_h$ ,  $\beta$  or  $\beta_v$  leads to an increase in  $R_0$ , however,  $n\beta_h$  has the greatest positive influence of all on  $R_0$ .

fig.2. Increasing  $\nu$  from 0 to 1, decreases values of  $R_0$  from 1.75 to 1. This evidently suggests that increasing  $\nu$  lowers the value of  $R_0$ .

### 3.3 Local Stability of Disease Free Equilibrium

Below is the discussion considering the stability of the system at equilibrium point,  $E_0$  for  $R_0 < 1$ . Jacobian matrix,  $J$  of the system (3).

$$J = \begin{pmatrix} -\mu - \frac{(\beta_v I_v + n\beta_h I)(I + R)}{N^2} & \frac{\beta_v I_v S - n\beta_h S(I + R)}{N^2} & 0 & \frac{(\beta_v I_v + n\beta_h I)S}{N^2} & 0 & -\frac{\beta_v S}{N} \\ \frac{(\beta_v I_v + n\beta_h I)(I + R)}{N^2} & -\frac{\beta_v I_v S - n\beta_h S(I + R)}{N^2} & -(\nu + \mu) & 0 & -\frac{(\beta_v I_v + n\beta_h I)S}{N^2} & \frac{\beta_v S}{N} \\ 0 & \alpha & -\omega & 0 & 0 & 0 \\ 0 & \nu & 0 & -\mu & 0 & 0 \\ \frac{\beta S_v I}{N^2} & -\frac{\beta S_v (S + R)}{N^2} & 0 & \frac{\beta S_v I}{N^2} & -\frac{\beta I}{N} - \mu_\nu & 0 \\ -\frac{\beta S_v I}{N^2} & \frac{\beta S_v (S + R)}{N^2} & 0 & -\frac{\beta S_v I}{N^2} & \frac{\beta I}{N} & -\mu_\nu \end{pmatrix}$$

That is at the DFE, the Jacobian matrix ( $J_{E_0}$ ) becomes:

$$J_{E_0} = \begin{pmatrix} -\mu & -n\beta_h & 0 & 0 & 0 & -\beta_v \\ 0 & n\beta_h - (\nu + \mu) & 0 & 0 & 0 & \beta_v \\ 0 & \alpha & -\omega & 0 & 0 & 0 \\ 0 & \nu & 0 & -\mu & 0 & 0 \\ 0 & -\frac{\Lambda_v \mu \beta}{\mu_\nu \Lambda} & 0 & 0 & -\mu_\nu & 0 \\ 0 & \frac{\Lambda_v \mu \beta}{\Lambda \mu_\nu} & 0 & 0 & 0 & -\mu_\nu \end{pmatrix}$$

Clearly, the matrix  $J_{E_0}$  has eigenvalues

$$\lambda_{1,2} = -\mu, \lambda_3 = -\omega, \lambda_4 = -\mu_\nu$$

plus the eigenvalues  $\lambda_5$  and  $\lambda_6$  to be solved from the determinant equation

$$\begin{vmatrix} n\beta_h - (\nu + \mu) - \lambda & \beta_v \\ \frac{\Lambda_v \mu \beta}{\Lambda \mu_\nu} - \lambda & -\mu_\nu - \lambda \end{vmatrix} = 0$$

which leads to the characteristic equation

$$\lambda^2 + (\mu_\nu + \mu + \nu - n\beta_h)\lambda + \mu_\nu(\mu + \nu - n\beta_h) - \frac{\Lambda_v \mu \beta \beta_v}{\mu_\nu \Lambda} = 0. \quad (6)$$

By properties of roots of quadratic equation:

$$\lambda_5 + \lambda_6 = -(\mu_\nu + \mu + \nu - n\beta_h), \quad \lambda_5 \cdot \lambda_6 = \mu_\nu(\mu + \nu - n\beta_h) - \frac{\Lambda_v \mu \beta \beta_v}{\mu_\nu \Lambda}$$

When  $R_0 < 1$ , leads to  $c_1 = \frac{n\beta_h}{\mu + \nu} < 1$ , and  $\lambda_5 + \lambda_6 < 0$ , alongside with  $c_1 + c_0 < 1$ . So, accordingly  $\lambda_5 \cdot \lambda_6 > 0$  so then  $\lambda_5 < 0, \lambda_6 < 0$ . Therefore, the system's equilibrium point,  $E_0$  is locally asymptotically stable. When  $R_0 > 1$ , that means  $c_1 + c_0 > 1$  and  $\lambda_5 \cdot \lambda_6 < 0$  upholds, in this case there exists at least one positive

eigenvalue. This leads to unstable DFE point.

### 3.3.1 Simulation of a local DFE point

Consider equation (6):  $\lambda^2 + (\mu_\nu + \mu + \nu - n\beta_h)\lambda + \mu_\nu(\mu + \nu - n\beta_h) - A = 0$ , where  $A = A(\beta_v, \beta) = \frac{\Lambda_v \mu \beta \beta_v}{\Lambda \mu_\nu} \geq 0$ . That is  $A$  takes non-negative real constants. Consider the nature of stability of the DFE for  $A = 0$  and  $A > 0$  each at a time. From theorem (3.1) below point  $A = 0$  is simply a bouncing back point.

**Theorem 3.1** When  $A = 0$ ,  $\chi(\lambda_0) = 0$  results into four eigenvalues:  $\lambda_0 = -\mu, -\omega, -\mu_\nu, n\beta_h - (\nu + \mu)$ . The DFE is asymptotically stable provided that  $\frac{n\beta_h}{\nu + \mu} < 1$ , of which  $R_0 < 1$ .

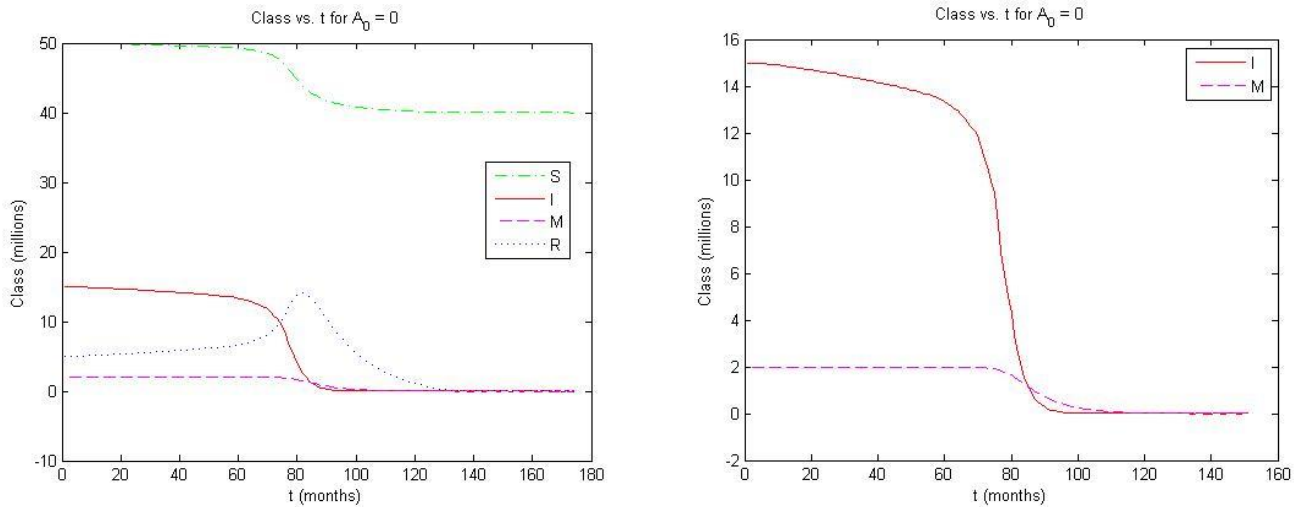
*Proof.* The for four eigenvalues follows as a solution from  $\chi(\lambda_0) = 0$ :  $(\mu + \lambda_0)^2(\omega + \lambda_0)(-\mu_\nu - \lambda_0)(\mu + \lambda_0)(n\beta_h - (\nu + \mu) - \lambda_0) = 0 \Leftrightarrow \lambda_0 = -\mu, -\omega, -\mu_\nu, n\beta_h - (\nu + \mu)$ . All eigenvalues are negative provided  $n\beta_h - (\nu + \mu) < 0 \Leftrightarrow \frac{n\beta_h}{\nu + \mu} < 1$  which is the condition for asymptotically stable DFE.

$R_0 = \frac{1}{2}(\frac{n\beta_h}{\nu + \mu} + \sqrt{(\frac{n\beta_h}{\nu + \mu})^2 + \frac{4\beta_v \beta \Lambda_v \mu}{(\nu + \mu)\mu_\nu^2 \Lambda}})$ . Since  $A = \frac{\Lambda_v \mu \beta \beta_v}{\Lambda \mu_\nu} = 0$  then either  $\beta_v = 0$  or  $\beta = 0$ . Not that whenever  $\beta_v = 0$  so does  $\beta$ , and the converse is true. That is either  $\beta_v = 0$  or  $\beta = 0$ , meaning that there is no ZVD transmission due to mosquito. Thus,  $R_0 = \frac{1}{2}(\frac{n\beta_h}{\nu + \mu} + \sqrt{(\frac{n\beta_h}{\nu + \mu})^2 + 0}) = \frac{\beta_h}{\nu + \mu} < 1$ , this completes the proof.

Fig.3 illustrates typical dynamics for  $A = 0$  at

DFE for some initial state due to introduction of ZIKV infectious when  $R_0 = 0.4553 < 1$ . The system at  $R_0 = 0.4553 < 1$  stabilizes to the DFE. Fig.3 depicts the diminishing behavior of

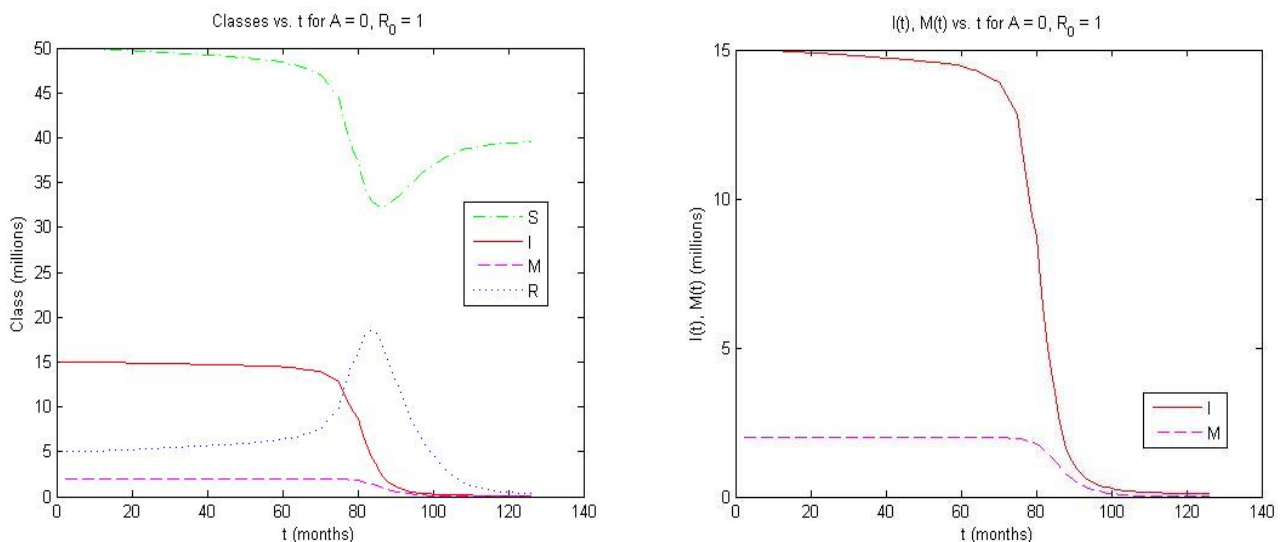
ZIKV infections. For clarity purpose Fig.3 bears the  $I$  and  $M$  time series achieving the endemic equilibrium.



**Figure 3: Dynamics of DFE point when  $A = A_0 = 0$ ,  $R_0 = 0.4553 < 1$**

Well, it is difficult to practically get  $R_0 = 1$ . However, for the sake of understanding this is simulated in Fig.4. For  $R_0 = 1$  the epidemic is prevalent at endemic equilibrium (Fig.4). Time series for  $I(t)$  and  $M(t)$  are shown again in Fig.4 in large scale so as to see their

prevalence. On the other hand when  $R_0 > 1$  the epidemic does not diminish with time rather remains. Fig.5 is an example of unstable DFE ( $R_0 = 1.6667 > 1$ ) with some initial state of the epidemic.

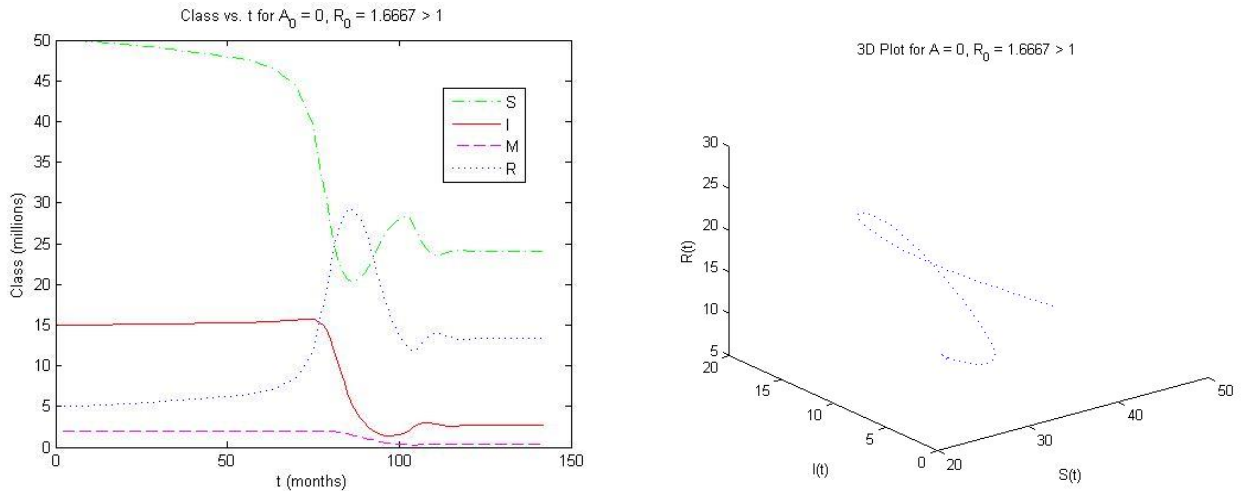


**Figure 4: Ideally the endemic is stable if  $R_0 = 1$**

Invasion by the epidemic lead to endemic equilibrium because for  $R_0 = 1.6667 > 1$  the DFE is unstable. Fig.5 is an illustration for all

classes. Fig.5 is a 3D plot for selected three classes. It appears that the initial state spirals toward the equilibrium point.





**Figure 5: For  $A_0 = 0$ ,  $R_0 = 1.6667 > 1$  DFE switches into Endemic equilibrium**

However, any small change of  $\beta_v$  or  $\beta$  enough to be  $\approx 0$  at  $A = 0$  takes it to a positive constant,  $A > 0$  which calls for new set of eigenvalues in  $\chi(\lambda_0) = 0$ . New set of eigenvalues definitely results to new qualitative behavior of DFE. Conventionally,  $A = 0$  does not define a bifurcation point, since there is no crossing at  $A = 0$  from  $A > 0$  to  $A < 0$  rather it is just a bounce back point to  $A > 0$ .

**Theorem 3.2** When  $A > 0$ ,  $\chi(\lambda_0) = 0$  has five eigenvalues  $\lambda_0 = -\mu$ ,  $-\omega$ ,  $-\mu_v$ ,  $\frac{1}{2}[-(2\mu + \nu - n\beta_h) \pm \sqrt{D}]$ . Provided that  $\frac{n\beta_h}{\nu + \mu} < 1$  then,  $R_0 < 1$  and DFE is asymptotically stable.

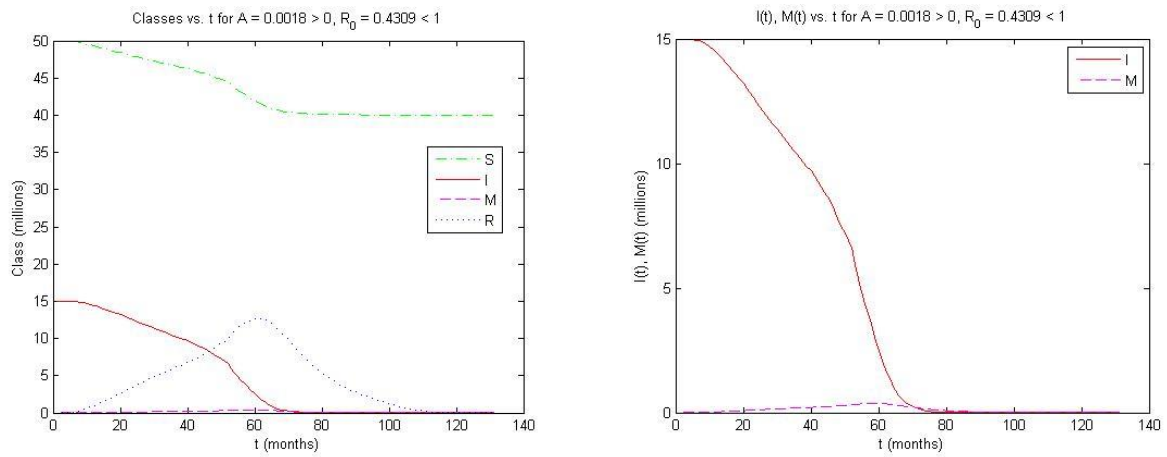
*Proof.* For  $A > 0$ , the characteristic equation ( $\chi(\lambda_0) = 0$ ) has three negative eigenvalues  $\lambda_0 = -\mu$ ,  $-\omega$ ,  $-\mu_v$  plus two roots from quadratic equation  $\lambda_0^2 + \lambda_0(\mu - [n\beta_h - (\nu + \mu)]) + [(v + \mu - n\beta_h)\mu - A] = 0$ . Thus eigenvalues includes  $\lambda_0 = \frac{1}{2}[-(2\mu + \nu - n\beta_h) \pm \sqrt{D}]$ . The roots from the quadratic equation has non positive real roots if  $D < [(2\mu + \nu) - n\beta_h]^2$ . That is  $D < [(2\mu + \nu) - n\beta_h]^2 \Leftrightarrow A < [(v + \mu) - n\beta_h]\mu$ . It follows that  $\frac{A}{(v + \mu)\mu} < 1 \Leftrightarrow \frac{\beta_v \beta \Lambda_v \mu}{(v + \mu)\mu_v \mu \Lambda} < 1$ . Easy to see that  $\frac{\beta_v \beta \Lambda_v \mu}{(v + \mu)\mu_v^2 \Lambda} < \frac{\beta_v \beta \Lambda_v \mu}{(v + \mu)\mu_v \mu \Lambda}$ , since  $\mu_v > \mu > 0$ . Thus  $\frac{\beta_v \beta \Lambda_v \mu}{(v + \mu)\mu_v^2 \Lambda} < \frac{\beta_v \beta \Lambda_v \mu}{(v + \mu)\mu_v \mu \Lambda} < 1$ .

$$\begin{aligned} R_0 &= \frac{1}{2} \left( \frac{n\beta_h}{\nu + \mu} + \sqrt{\left( \frac{n\beta_h}{\nu + \mu} \right)^2 + \frac{4\beta_v \beta \Lambda_v \mu}{(\nu + \mu)\mu_v^2 \Lambda}} \right) \\ &= \frac{n\beta_h}{2(\nu + \mu)} + \sqrt{\left( \frac{n\beta_h}{2(\nu + \mu)} \right)^2 + \frac{\beta_v \beta \Lambda_v \mu}{(\nu + \mu)\mu_v^2 \Lambda}} \\ &< \frac{n\beta_h}{2(\nu + \mu)} + \sqrt{\left( \frac{n\beta_h}{2(\nu + \mu)} \right)^2 + \frac{\beta_v \beta \Lambda_v \mu}{(\nu + \mu)\mu_v \mu \Lambda}} \\ &< \frac{1}{2} + \sqrt{\left( \frac{1}{2} \right)^2 + 0 + 0} = 1 \end{aligned}$$

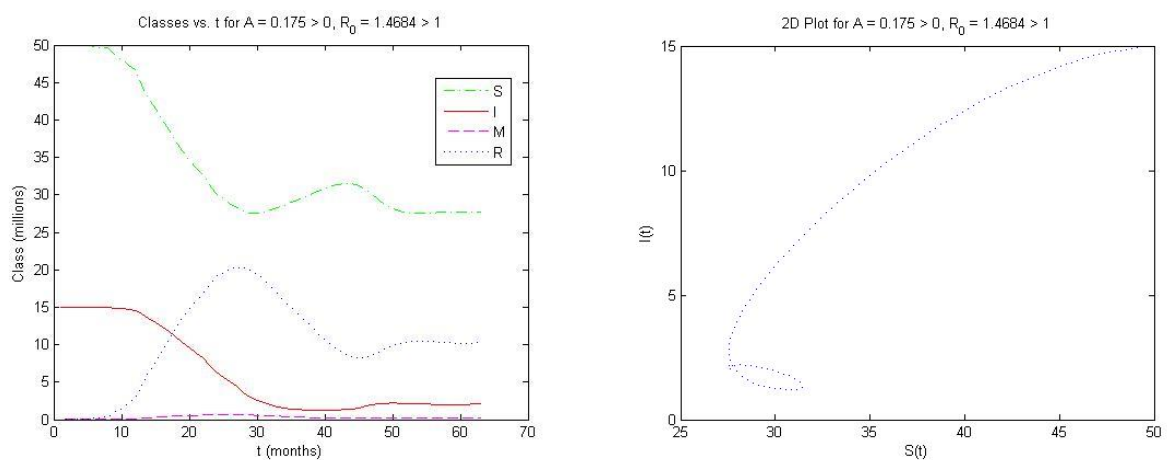
Some simulations for theorem 3.2 are shown below. Fig.6 illustrates DFE for some initial state of ZIKV infectious when  $A = 0.0018 > 0$  and  $R_0 = 0.4309 < 1$ . The system at DFE combats successfully to eliminate the epidemic, eventually stabilizes to the DFE. Fig.5 demonstrates a the diminishing behavior of ZIKV infectious classes. Fig.5 portrays in large scale the dynamics of  $I$  and  $M$ .

So when  $A = 0$ , the quadratic equation  $\lambda_0^2 + \lambda_0(\mu - [n\beta_h - (\nu + \mu)]) + [(v + \mu - n\beta_h)\mu - A] = 0$  has two roots  $-\mu$  and  $n\beta_h - (\nu + \mu)$  of which  $-\mu$  becomes a root of multiplicity of three in total. Therefore, two eigenvalues from the quadratic equation (theorem 3.2) degenerate to a single eigenvalue  $n\beta_h - (\nu + \mu)$  (theorem 3.1) when  $A$  reduces to zero of which there are four eigenvalues.





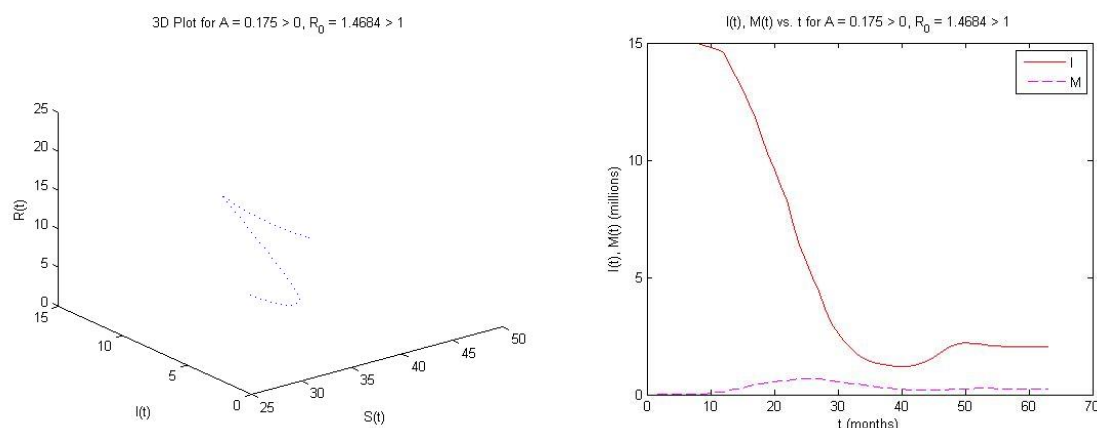
**Figure 6:** Dynamics of DFE point when  $A_1 = 0.0018 > 0$ ,  $R_0 = 0.4309 < 1$



**Figure 7:** DFE is replaced by Endemic equilibrium  $A > 0$ ,  $R_0 = 1.3078 > 1$

However, when  $R_0 > 1$ , the DFE is unstable. An incidence of the epidemic (Fig.7) escalates to endemic equilibrium. For instance, when  $R_0 = 1.3078 > 1$ , DFE is unstable and the

epidemic persists in the society. Fig.7 demonstrates the scenario. On one hand Fig.7 is a 2D plot for  $S(t)$  and  $I(t)$ .



**Figure 8:** DFE is replaced by Endemic equilibrium  $A > 0$ ,  $R_0 = 1.3078 > 1$

On the other hand Fig.8 is a 3D plot for  $S$ ,  $I$  and  $R$ , where as Fig.8 is time series for  $I(t)$  and  $M(t)$  in which the endemic equilibrium is maintained.

### 3.3.2 Global Stability of Disease Free Equilibrium

Global stability of disease free equilibrium point,  $E_0$  such that  $D$  is a global attraction. Consider the differential equations:

$$\begin{cases} I'(t) = \left( \frac{\beta_v I_v + n\beta_h I}{S+I+R} + \mu \right) S - (v + \mu) I; \\ I'_v(t) = \frac{\beta I S_v}{S+I+R} - \mu_v I_v. \end{cases} \quad (7)$$

$$\begin{aligned} I'(t) &\leq \left( \frac{\beta_v I_v + n\beta_h I}{S} \right) S - (v + \mu) I \\ &= \beta_v I_v + n\beta_h I - (v + \mu) I \quad \dots (i) \end{aligned}$$

$$\begin{aligned} I'_v(t) &\leq \frac{\beta I \frac{\Lambda_v}{\mu_v}}{I} - \mu_v I_v \\ &= \beta I \frac{\Lambda_v}{\mu_v} - \mu_v I_v \quad \dots (ii) \end{aligned}$$

Now that, (i) and (ii) are approximates the differential equations in system (7) as linear.

$$\begin{cases} I'(t) = \beta_v I_v + n\beta_h I - (v + \mu) I; \\ I'_v(t) = \beta I \frac{\Lambda_v}{\mu_v} - \mu_v I_v. \end{cases} \quad (8)$$

The system (8) has two eigenvalues:  $\lambda_1 = n\beta_h - (\mu + v)$ ,  $\lambda_2 = -\mu_v$ . When  $R_0 < 1$ ,  $c_1 = \frac{n\beta_h}{\mu+v} < 1$  and so then  $\lambda_1 = n\beta_h - (\mu + v) < 0$ ,  $\lambda_2 = -\mu_v < 0$ . Therefore, when  $t \rightarrow \infty$ ,  $I \rightarrow 0$ ,  $I_v \rightarrow 0$ . Conclusively, since the system (7) has  $M \rightarrow 0$ ,  $R \rightarrow 0$ ,  $S \rightarrow \frac{\Lambda}{\mu}$ ,  $S_v \rightarrow \frac{\Lambda_v}{\mu_v}$  as  $t \rightarrow \infty$  it is deduced that for  $R_0 < 1$  the disease free equilibrium point,  $E_0$  in  $D$  is a global

attraction.

### 3.4 Local Stability of the Endemic Equilibrium

For endemic equilibrium,  $E^*(S^*, I^*, M^*, R^*, S_v^*, I_v^*)$ ,  $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dM}{dt} = \frac{dR}{dt} = \frac{dS_v}{dt} = \frac{dI_v}{dt} = 0$ . The system of equations (3) reduces to

$$\begin{aligned} 0 &= \Lambda - (\gamma + \mu)S & \dots i; & 0 = \nu I - \mu R & \dots iv; \\ 0 &= \gamma S - (\nu + \mu)I & \dots ii; & 0 = \Lambda_v - (\mu_v + \gamma_v)S_v & \dots v; \\ 0 &= \alpha I - \omega M & \dots iii; & 0 = \gamma_v S_v - \mu_v I_v & \dots vi. \end{aligned}$$

Solving this simultaneously, the endemic equilibrium point,  $E^*$  is:

$$\begin{aligned} S^* &= \frac{\Lambda}{\gamma + \mu}, \quad I^* = \frac{\Lambda \gamma}{(\gamma + \mu)(\nu + \mu)}, \quad M^* = \frac{\Lambda \gamma \alpha}{(\gamma + \mu)(\nu + \mu)\omega}, \quad R^* = \frac{\Lambda \gamma \nu}{(\gamma + \mu)(\nu + \mu)\mu} \\ S_v^* &= \frac{\Lambda_v(\mu + \nu)(\gamma + \nu)}{\mu_v(\gamma + \mu)(\nu + \mu) + \mu \beta \gamma}, \quad I_v^* = \frac{\Lambda_v \mu \beta \gamma}{\mu_v[\mu_v(\gamma + \mu)(\nu + \mu) + \mu \beta \gamma]}. \end{aligned}$$

Assign  $c_2 = \frac{\mu_v}{\nu}$ ,  $c_3 = \frac{\nu + \mu + \beta}{(\nu + \mu)\nu}$ ,  $c_4 = \frac{1}{\mu}$ .  $\gamma$  is a positive value from the equation:

$$\gamma = \frac{c_0 c_2}{1 + \gamma c_3} + \frac{c_1 \gamma}{1 + c_4 \gamma}. \quad (10)$$

Equation (10) is simply a cubic equation:  $c_3 c_4 \gamma^3 + (c_3 - c_1 c_3 + c_4) \gamma^2 + (1 - c_1 - c_0 c_2 c_4) \gamma - c_0 c_2 = 0$ . Since  $c_3 c_4 > 0$  and  $-c_0 c_2 < 0$ , according to Descartes's rule of signs, equation (10) has at least one positive root. Thus, the system (3) has at least one endemic equilibrium. On the other hand, if  $c_3 - c_1 c_3 + c_4 < 0$  and  $1 - c_1 c_2 c_4 > 0$  there exist one or three positive roots. From Jacobian matrix, characteristic polynomial  $\chi(\lambda)$ :

$$\chi(\lambda) = \begin{vmatrix} -\mu - k_0 - \lambda & k - k_1 & 0 & 0 & 0 & 0 \\ k_0 & -(k - k_1) - (\nu + \mu) - \lambda & 0 & k_2 & 0 & -k_3 \\ 0 & \alpha & -\omega - \lambda & 0 & 0 & k_3 \\ 0 & \nu & 0 & -\mu - \lambda & 0 & 0 \\ k_4 & -k_5 & 0 & k_4 & -k_6 - \mu_v - \lambda & 0 \\ -k_4 & k_5 & 0 & -k_4 & k_6 & -\mu_v - \lambda \end{vmatrix} = 0$$

for endemic equilibrium; where:

$$\begin{aligned} k_0 &= \frac{(\beta_v I_v^* + n\beta_h I^*)(I^* + R^*)}{(N^*)^2} & k &= \frac{\beta_v I_v^* S^*}{(N^*)^2} & k_1 &= \frac{n\beta_h S^*(I^* + R^*)}{(N^*)^2} & k_2 &= \frac{(\beta_v I_v^* + n\beta_h I^*) S^*}{(N^*)^2} \\ k_3 &= \frac{\beta_v S^*}{N^*} & k_4 &= \frac{\beta S_v^* I^*}{(N^*)^2} & k_5 &= \frac{\beta S_v^*(S^* + R^*)}{(N^*)^2} & k_6 &= \frac{\beta I^*}{N^*} \end{aligned}$$

Note that  $k, k_0, k_1, k_2, k_3, k_4, k_5, k_6 > 0$

The roots ( $\lambda$ ) in  $\chi(\lambda) = 0$  are the eigenvalues which equivalently evaluated from

$$a_0\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 =$$

$$a_0 = \mu + \nu$$

$$a_1 = \nu k_3 + (\mu + \nu)[k_1 - (k - 4\mu + 2k_0)]$$

$$a_2 = \nu k_2(3\mu + k_0) + k_6(k_4 - k_3k_5) + (\mu + \nu)[(\mu + k_0)k_1 - [(\mu + k_0)k_1 + 3\mu^2 + 4k_0\mu + k_0^2]]$$

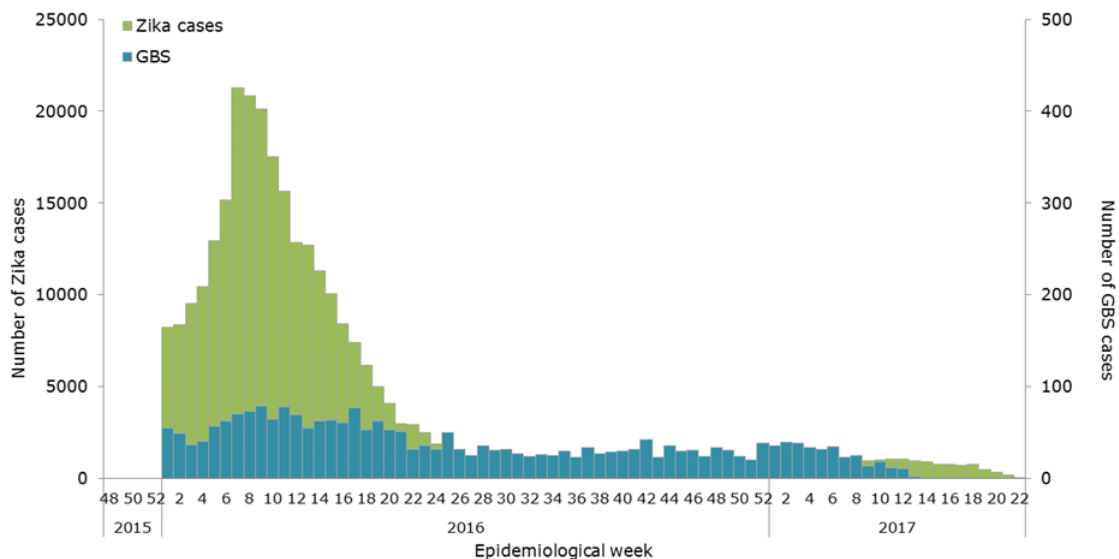
$$a_3 = (\nu + \mu)[k_3k_4 + 2\mu k_1 - k_3(k_5 - (2\mu + \nu)k_0 - (3\mu + 2\nu)\mu) + k_0[(\mu\nu - k_2\nu)k_0 + 2\mu^2\nu] + \mu\nu(\mu^2 + \nu k_2) + k_6[k_4(\mu + 1) - k_3k_5\mu - k_3k_5(1 + 2\mu)]$$

$$a_4 = k_3k_5[k_0(2\nu + \mu + \mu^2) - \mu^2 - \mu\nu] + (\nu + \mu)[k_1 - k - (k_0 + \mu)^2(2\mu + \nu) - \mu k_3k_4] - \mu^2k_0k_3k_4$$

Although the characteristic polynomial  $\chi(\lambda)$  is not evidently justified as Hurwitz, numerical simulations are evident from previous figures Fig.7 and Fig.5 demonstrating that when  $R_0 > 1$  endemic equilibrium is stable and it is unstable when  $R_0 < 1$ . On the other hand the disease is controllable provided  $R_0 < 1$ .

#### 4 Simulation of Spread of ZIKV Infections in Brazil

Faria, N.R. et al., found that ZIKV in Brazil occurred as early as May 2013 [faria2016zika](#). For some reasons our simulation is based on ZIKV cases since January 2016. These records are available from PAHO/WHO 2017 ([paho.org](#)) [faria2017establishment](#). For the purpose of simulating the recorded ZIKV cases we used Matlab built-in implementation of the Levenberg-Marquardt algorithm called `nlinfit`.

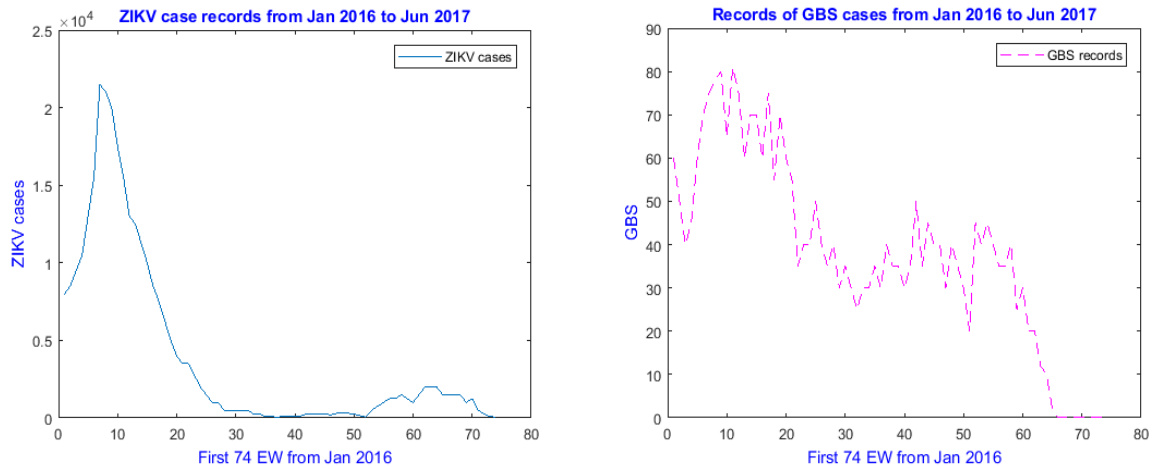


**Figure 9: Total cases of ZIKV and GBS, EW1 of 2016 to EW22 of 2017 [faria2017establishment](#), [faria2016zika](#)**

In order to estimate suitable parameters for the model, required initial guess of parameters plus some recorded cases of the epidemic. Initial guess from a Kibona et al., [kibona2017sir](#) were used, and recorded cases were estimated from Fig.9. We found it necessary to split the set of parameters into two. It appears that before WHO declaration that ZIKV need attention by

the whole world the trend to the epidemic had different set of parameters, so is thereafter. Thus, one set of parameters which is an extension before WHO declaration has  $R_0 = 5.8316$ . On the other set of parameters the value of  $R_0 = 0.1970$  which is inline with the epidemic being under control [nishiura2016preliminary](#). The histogram, Fig.9

for ZIKV cases and GBS records has been used to draw the information and later plotted by MaTLab as in Fig.10.

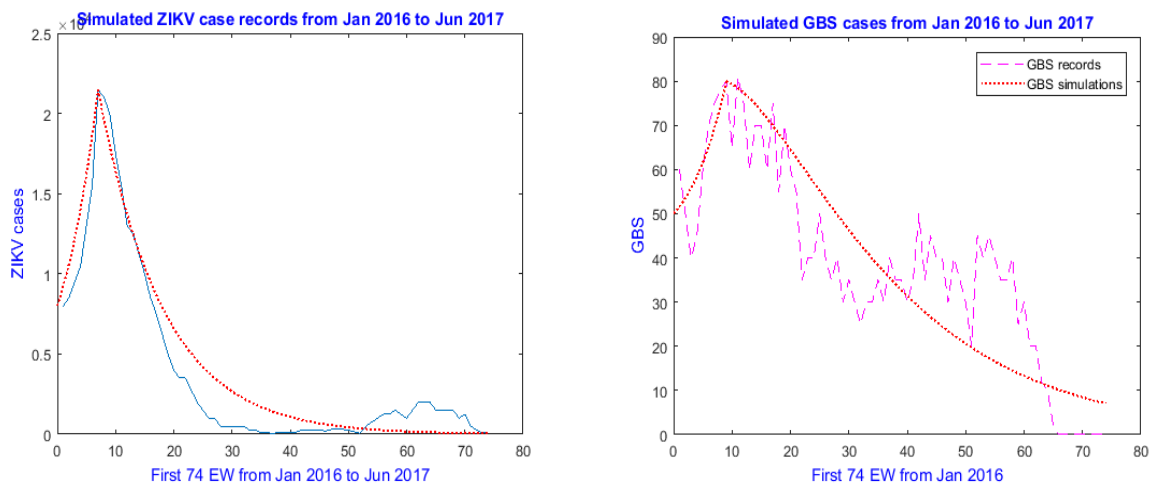


**Figure 10: Source: PAHO/WHO 2017, Zika-Epidemiological Report, Brazil favoretto2016first.**

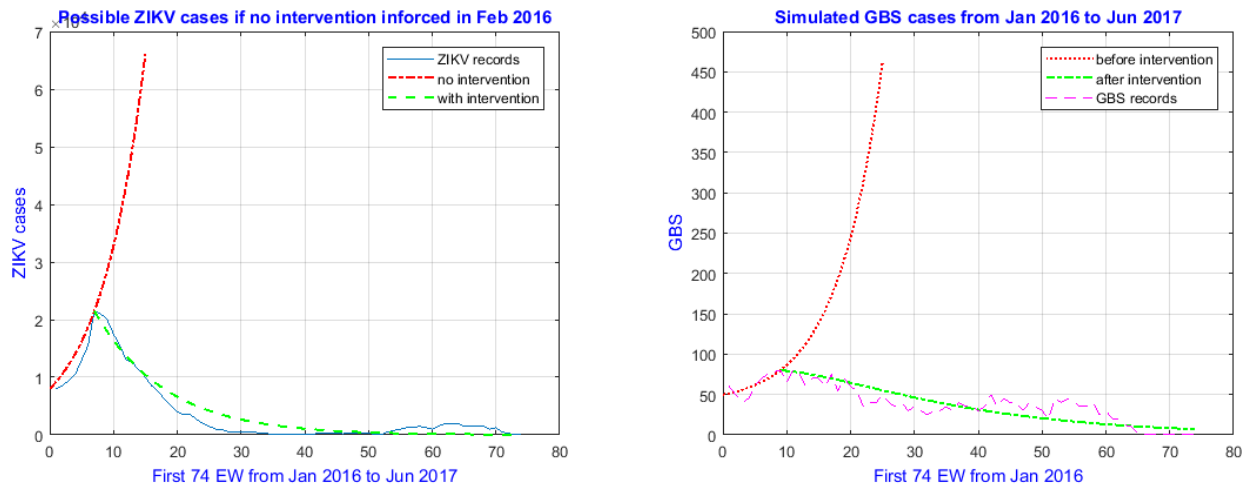
The estimated parameter by nlinfit then were used in the model to plot the graphs as depicted in Fig.11. ZIKV information in Fig.11, that is Zika cases and GBS are separated into two figures Fig.11 and Fig.11 for clarity. In addition, plots in Fig.9 look similar in modelling ZIKV obtained by J Ikejezie et al jamboos2017simulation, ikejezie2017zika.

Should it be the case that no intervention were made against the epidemic in February 2016, then  $R_0 = 5.8316 > 1$  would have been the

case for sometime. The ZIKV infections could have taken a no intervention path. In this case ZIKV infections spread could be catastrophic as in Fig.12. That we believe that some intervention have shifted the model from one set of parameters with no intervention in which  $R_0 = 5.8316$ , Fig.12 to another set of parameters with intervention, Fig.12 in which  $R_0 = 0.1970$ . The later is what prevails in Brazil.



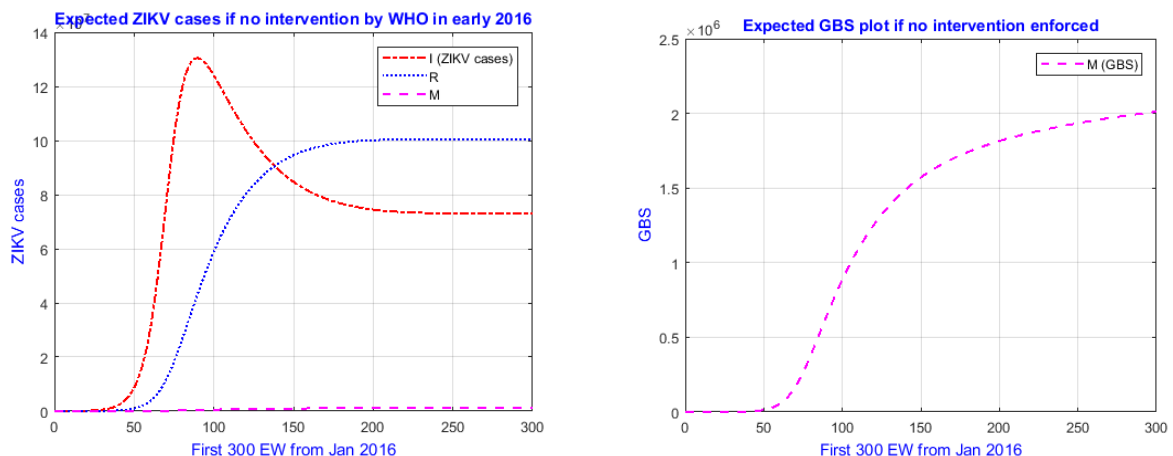
**Figure 11: Model simulation of recorded ZIKV cases and GBS**



**Figure 12: Intervention against the epidemic bridges set of Parameters for the model**

The model includes an assumption that individuals recovered from ZIKV are resistant to reinfection dejnirattisai2016dengue. So a no intervention model would take the path to

endemic equilibrium Fig.13. On the other hand, with intervention; number of ZIKV infections decreases toward disease free equilibrium, Fig.12.



**Figure 13: Possibility of the Endemic Equilibrium**

In addition to deliberate efforts against the epidemic; an increase in number of recovered individual do not favour spread of the epidemic. This is one important aspect of ZIKV infections Fig.13. The latter as well explains as to why countries ever infected by ZIKV are not prone to the epidemic. Evidently, basing on the estimated value of  $R_0 = 0.1970 < 1$  along with plots of ZIKV cases we expect that in the near future after 2017 ZIKV infections can no longer be threat to Brazil.

#### 4.1 Conclusion

In epidemiological concern the dynamics of the model at the DFE points poses no threats since the epidemic appears to be controllable if  $R_0 < 1$ . That is, maximizing recovery rate, and minimizing both unsafe sexual contacts and mosquito bites to the extent of  $R_0 < 1$  the epidemic can be eliminated. The reason is that no backward bifurcation has been justified. On the other hand, only forward bifurcation exists; that is when  $R_0 > 1$  DFE point is unstable in

which case the endemic equilibrium prevails. Brazil has been taken as an example for simulation, found with  $R_0 = 0.1970 < 1$ . Accordingly, simulation comply to the fact that the epidemic is dying in this country.

The analytic study of the disease free equilibrium (DFE) justifies two different sets of eigenvalues from the characteristic equation at DFE point. These sets of eigenvalues are functions of variation in some parameters. Each set of eigenvalues determines its own qualitative behavior of DFE point. One of the two sets of eigenvalues simply occurs at one point on the varying parameter. Therefore, practically there is only one qualitative behavior of the DFE in which the local DFE point has five eigenvalues. Analysis justifies that DFE point is locally asymptotically stable provided that  $R_0 < 1$ . On the other hand if  $R_0 > 1$  the the DFE is locally unstable and for any given initial state of the epidemic the endemic equilibrium becomes stable.

Not only that the DFE point is locally asymptotically stable but also has been found to be globally stable. This is interesting and offers more room for ability to control the epidemic when  $R < 1$ . Simulations on specific case in the analytic analysis have been done on  $R_0$  for values around  $R_0 = 1$  and some relatively away from this. Numerically the

results from simulations is that epidemic grows only when  $R_0 > 1$ . That means there is no backward bifurcation.

There is great hope that for  $R_0 = 0.1970 < 1$  as estimated from Brazil ZIKV case records, beyond 2020 there can be no more threat of the epidemic in this nation. It is strongly recommended that current efforts against the epidemic have to be strengthened. One important finding in this model is that  $R_0$  is most sensitive to recovery rate followed by sexual sexual transmission (Tab.2). Therefore, although no specific treatment is known about ZVD knowing the status of any suspected individual is still important. That can help to take necessary precautions plus treating the patient from available treatment.

## 5 Acknowledgments

This research is on going in China at Central China Normal University (CCNU), school of mathematics and statistics. Special thanks to CCNU for offering an opportunity in this emerging area of research at this era. Research work as well is partially supported by the National Nature Science Foundation of China (No. 11371161, 11471133) and the Foundation Research Funds for the Central Universities, Central China Normal University (No. CCNU15A02055). The two are greatly appreciated for their contribution.

Note the acronyms from Tab. 3 below available in the whole article.

**Table 3: Acronyms**

|       |                                  |
|-------|----------------------------------|
| DFE   | Disease Free Equilibrium         |
| EW    | Epidemiological Week             |
| GBS   | Guillain-Barre syndrome          |
| MTCT  | Mother-to-child-transmission     |
| PAHO  | Pan American Health Organization |
| $R_0$ | Basic Reproduction Number        |
| WHO   | World Health Organization        |
| ZIKV  | Zika virus                       |
| ZVD   | Zika virus disease               |

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- Title: International Research Journal of Public Health
  - ISSN: 2573-380X
  - DOI: 10.28933/IRJPH
  - IF: 1.36 (citefactor)
  - Email: IRJPH@escipub.com
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