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REPRODUCTION NUMBER FOR YELLOW FEVER DYNAMICS BETWEEN PRIMATES AND HUMAN BEINGS

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Abstract. Vector borne diseases are spreading very rapidly in the populations all over the World. Thus, there is need to mobilize people about transmission of the disease in order to eradicate it. In this paper we propose a deterministic mathematical model through non-linear ordinary differential equations in order to gain an insight into dynamics of yellow fever between primates, human beings and *Aedes* mosquito for the purpose of controlling the disease. In the analysis of the model we investigate the basic reproduction number, R_0 , between primates, vectors and human host. The disease threshold parameter is obtained using next generation matrix approach and is of the form $R_0^2 = R_h + R_m$, where R_h and R_m are the reproduction number of human-vector and vector-primate compartments respectively. It is proved that the global transmission dynamics of the disease are completely determined by the basic reproduction number. In order to study the effect of model parameters to R_0 , the sensitivity analysis of basic reproductive number, R_0 , with respect to epidemiological and parameters is performed. Results call attention to parameters regarding to daily biting rate of mosquitoes, birth rate of vectors, probability of transmission from infectious vector to susceptible human and vice versa, recruitment of human host which includes unvaccinated immigrants as well as the incubation period for both vector and humans. Thus, quick and focused interventions, like personal protection and destruction of breeding sites, may be effective for controlling the disease transmission.

Keywords: yellow fever; primates; humans; vector born infectious disease; sensitivity analysis.

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1. Introduction

Yellow Fever (YF) is among the vector-borne infectious diseases caused by viruses which is primarily transmitted by disease transmitting biological agents, called vectors. It is a viral hemorrhagic fever caused by yellow fever virus (YFV) and is transmitted through the bite of an infected female yellow fever mosquito [26]. It only infects humans, other primates and several species of mosquito [36]. The disease is endemic in tropical and subtropical areas of Africa and South America.

A dramatic resurgence of YF has occurred since 1980s in both sub-Saharan Africa and South America [27]. Increasing migration, accelerating urbanization, and improved travel infrastructure are global trends that increase the risk of YF spreading to parts of the world where the disease had disappeared. There are three epidemiologically different infectious cycles, in which the YFV is transmitted from mosquitoes to humans and/or other primates [2]: jungle (sylvatic), intermediate (savannah), and urban. In the 'urban cycle', only the yellow fever mosquito *Aedes aegypti* is involved.

Besides the urban cycle there is, both in Africa and South America, a sylvatic cycle (forest cycle or jungle cycle), where *Aedes africanus* (in Africa) or mosquitoes of the genus *Haemagogus* and *Sabethes* (in South America) serve as vectors. In the jungle, mosquitoes infect mainly non-human primates; and the disease is mostly asymptomatic in African primates. In South America, the sylvatic cycle is currently the only way humans can infect each other [2]. People who are bitten by *Aedes africanus* or *Haemagogus* in the jungle become infected and can carry the virus to urban centres, where *Aedes aegypti* acts as a vector. It is because of this sylvatic cycle that yellow fever cannot be eradicated [2].

In Africa the third infectious cycle, 'savannah cycle' or intermediate cycle, occurs between the jungle and urban cycle. Different mosquitoes of the genus *Aedes* are involved. In recent years, this has been the most common form of transmission of yellow fever in Africa [37]. In humans, yellow fever's incubation period is three to six days. During this time, there are generally no symptoms identifiable to the host [30]. After that time, a person infected begins with an abrupt onset of symptoms, including fever and chills, intense headache and lower backache, muscle aches, nausea and extreme exhaustion.

The World Health Organization estimated that YF causes 200,000 illnesses and 30,000 deaths every year in unvaccinated populations and today 90% of the infections occur in African continent [30].

Mathematical models have become an important tool in analysing the spread and control of infectious diseases. Thome *et al.* [31] conducted a study on optimal control of *Aedes aegypti* mosquitoes by the sterile insect technique (SIT) and insecticide. They presented a mathematical model to describe the dynamics of mosquito population when sterile male mosquitoes are introduced as a biological control, besides the application of insecticide. Their results showed that application of insecticide is needed at the beginning of the control in order to reduce the *Aedes aegypti* populations.

Monath and Cetron [22] conducted a study to address transmission and prevention of YF in persons traveling to the tropics. They argued that because YF is maintained in nature by transmission between monkeys and mosquitoes and because it cannot be eradicated, prevention and control of the disease requires continuous immunization of human populations at risk.

Another theoretical study was done by Amaku *et al.* [1] to address the question as to why dengue and yellow fever coexist in some areas of the world and not in others? They developed a theoretical model which includes humans and two mosquito species, *Aedes aegypti* (which transmits both infections: yellow fever and dengue) and *Aedes albopictus* (which transmits only dengue). Their results shows that in Asia, vaccination of the local community is virtually absent but travelers from endemic areas are demanded to produce a vaccination certificate at entrance of the countries of this region so as to reduce the probability of importation of the disease. They recommended on the role of vaccination of population in the endemic regions aiming to control yellow fever epidemic. Most of these papers, consider one host only.

In this paper, we propose a mathematical model of YF that assesses the dynamics of YF between two hosts (primates and human beings) with one vector. The developed model is of type SEIRV for human host and SEI for the vector and primates. The model is based on the basic model of Dengue transmission (the YF like disease) by Yang and Ferreira [35]. Modifications have been made to incorporate primates as another host, vaccination, treatment and immigration.

2. Materials and Methods

2.1 Model Formulation

We formulate a model for the spread of YF in the human, vector and primates populations with the total population sizes at time t given by $N_H(t)$, $N_V(t)$ and $N_M(t)$ respectively. The populations are further compartmentalized into epidemiological classes as shown in the model flow diagram in Figure 1. The vector and primate compartments of the model do not include the immune class as they never recover from the infection, that is their infective period ends with their death due to their relatively short life cycle.

As indicated in the compartmental diagram Figure 1, the model divides the human population into 5 classes: susceptible, S_H , vaccinated, V_H , exposed, E_H , infectious, I_H and recovered (immune), R_H . People enter susceptible class either through per capita birth at a constant rate b_H or through immigration (Λ) whereby proportion ρ of the immigrants enter to the vaccinated class. Susceptible individuals may choose to be vaccinated at the rate ε .

We divide the vector (mosquito) population into 3 classes: susceptible, S_V , exposed, E_V , and infectious, I_V . Female YF mosquitoes enter the susceptible class through birth then moves from the susceptible to the exposed class and later to the infectious class. The mosquito remains infectious for life [7] and leave the population through a per capita density-dependent natural death rate.

We also divide the primates population which is the source of infection [11] into 3 classes: susceptible, S_M , exposed, E_M , and infectious, I_M . When an infected primate is bitten by a tree-hole breeding mosquito, the mosquito acquires the virus and then the mosquito can pass the virus on to any number of other primates and humans it may bite when it comes across them. When human is bitten by an infected mosquito, the human may acquire the virus. The infected human returns to the city, where an urban mosquito (*Aedes aegypti*) serves as a viral vector spreading infection rapidly by biting other humans.

The developed model rely on the following assumptions, the new born babies do not have the disease, the efficacy of the vaccine is 100% effective for not more than ten years, the disease

Parameters of the model are as shown in Table 1:

TABLE 1. Description of parameters of the model system (4)

Symbol	Description
β_1	Transmission probability of vector to human
β_2	Transmission probability of human to vector
β_3	Transmission probability of primate to vector
β_4	Transmission probability of vector to primate
δ_h	Progression rate from e_h to i_h
δ_v	Progression rate from e_v to i_v
δ_m	Progression rate from e_m to i_m
b_h	Birth rate of human
b_v	Birth rate of vector
b_m	Birth rate of primates
a	Daily biting rate
γ	Recovery rate
α	Death rate due to disease for human
ω	rate of relapse of vaccinated and recovered human
ε	vaccination rate of susceptible human
ρ	proportion of immigrant who are vaccinated
σ	arrival rate of immigrant per individual per time
μ_h	natural death rate of human
μ_v	natural death rate of vector
μ_m	natural death rate of primates

has no epidemiological effect on the demographic dynamics of the vector (mosquito), we ignore bites of an infected female mosquito onto an infected human host.

However, we also assume that the rate of relapse of vaccinated individual back to susceptibility is the same as that of recovered individuals and no vertical transmission of the infection

in the vector population. Migration of primates was ignored, that is to say; mosquitoes that go to the primates habitats are the ones infected by the bites of infected primates and can infect susceptible primates.

2.2 Model Flow Diagram and Description

Basing on the above assumptions, the model for transmission dynamics of YF in human, vector and primates population is as shown in Figure 1.

When an infectious female *Aedes aegypt* mosquito bites a susceptible human, there is some

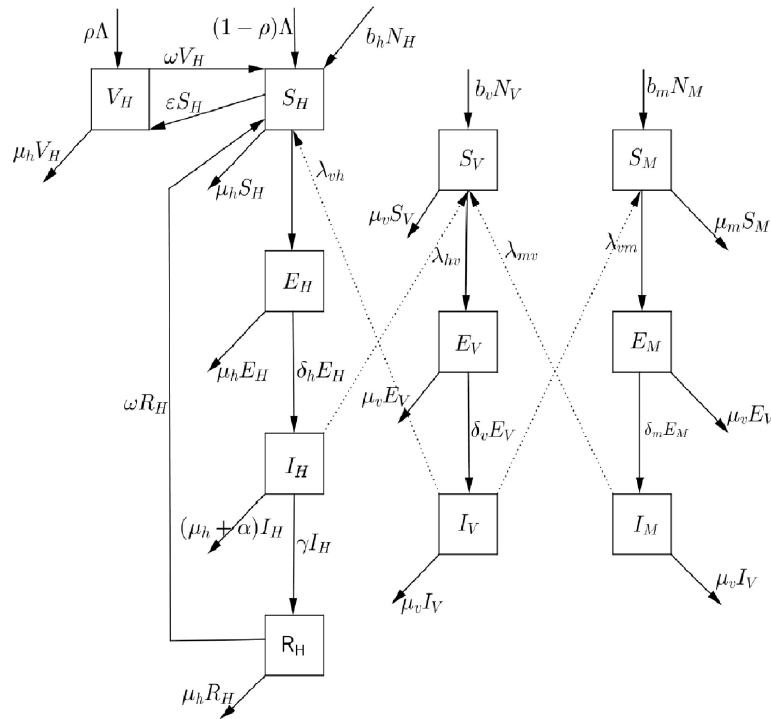


FIGURE 1. *model flow diagram for transmission dynamics of YF.*

finite probability that the parasite will be passed on to the human and the person will move to the exposed class. After a certain period of time, people from the exposed class enter the infectious class at a rate δ that is the reciprocal of the duration of the latent period.

After some time, the infectious humans undergo treatment and recover at the rate γ , hence move to the recovered class. The recovered humans have some immunity to the disease and do not get clinically ill, after some years, they lose their immunity and return to the susceptible class at the rate ω . Humans leave the population through natural death rate μ_H , and through a

per capita disease-induced death rate α , which is small in this case. However, like any other vector born diseases the YF disease induced death rate is very small in comparison with the recovery rate [31].

2.3 Model Equations

Applying the assumptions, definition of variables and parameters and description of terms above, the differential equations which describe the dynamics of YF in the human, vector and primates population are formulated as shown below:

Human:

$$(1) \quad \begin{aligned} \frac{dS_H(t)}{dt} &= b_h N_H + (1 - \rho)\Lambda + \omega(V_H + R_H) - \lambda_{vh} - \varepsilon S_H - \mu_h S_H, \\ \frac{dV_H(t)}{dt} &= \rho\Lambda + \varepsilon S_H - \omega V_H - \mu_h V_H, \\ \frac{dE_H(t)}{dt} &= \lambda_{vh} - \delta_h E_H - \mu_h E_H, \\ \frac{dI_H(t)}{dt} &= \delta_h E_H - (\mu_h + \alpha)I_H - \gamma I_H, \\ \frac{dR_H(t)}{dt} &= \gamma I_H - \mu_h R_H - \omega R_H, \end{aligned}$$

Vector:

$$(2) \quad \begin{aligned} \frac{dS_V(t)}{dt} &= b_v N_V - (\lambda_{hv} + \lambda_{mv}) - \mu_v S_V, \\ \frac{dE_V(t)}{dt} &= (\lambda_{hv} + \lambda_{mv}) - \delta_v E_V - \mu_v E_V, \\ \frac{dI_V(t)}{dt} &= \delta_v E_V - \mu_v I_V, \end{aligned}$$

Primates:

$$(3) \quad \begin{aligned} \frac{dS_M(t)}{dt} &= b_m N_M - \lambda_{vm} - \mu_m S_M, \\ \frac{dE_M(t)}{dt} &= \lambda_{vm} - \delta_m E_M - \mu_m E_M, \\ \frac{dI_M(t)}{dt} &= \delta_m E_M - \mu_m I_M. \end{aligned}$$

where; $\lambda_{vh} = \frac{a\beta_1 S_H I_V}{N_V}$, $\lambda_{hv} = \frac{a\beta_2 S_V I_H}{N_H}$, $\lambda_{mv} = \frac{a\beta_3 S_V I_M}{N_M}$ and $\lambda_{vm} = \frac{a\beta_4 S_M I_V}{N_V}$.

In the model the term $\lambda_{vh} = \frac{a\beta_1 S_H I_V}{N_V}$ denotes the rate at which susceptible human hosts S_H get infected from the infected vector I_V (force of infection from vector to human), $\lambda_{hv} = \frac{a\beta_2 S_V I_H}{N_H}$ denotes the rate at which susceptible vector S_V get infected from the infected human host I_H

(infection force from human host to vector), $\lambda_{mv} = \frac{a\beta_3 S_V I_M}{N_M}$ denotes the rate at which the susceptible vector S_V get infected from the infected primate I_M (force of infection from primate to vector) and the term $\lambda_{vm} = \frac{a\beta_4 S_M I_V}{N_V}$ denotes the rate at which the susceptible primates S_M get infected from the infected vector I_V . However, it is observed that the infected vector I_V can transmit the infection to both the human hosts and the primates.

The total population sizes $N_H(t)$, $N_V(t)$ and $N_M(t)$ can be determined by:

$$\begin{aligned} N_H(t) &= S_H(t) + V_H(t) + E_H(t) + I_H(t) + R_H(t), \\ N_V(t) &= S_V(t) + E_V(t) + I_V(t), \\ N_M(t) &= S_M(t) + E_M(t) + I_M(t). \end{aligned}$$

Also, adding from the differential equations, of the model system (1), (2), and (3) for the human host population, vector population and primates population, we have;

$$\begin{aligned} \frac{dN_H(t)}{dt} &= \Lambda + (b_h - \mu_h)N_H - \alpha I_H, \\ \frac{dN_V(t)}{dt} &= (b_v - \mu_v)N_V, \\ \frac{dN_M(t)}{dt} &= (b_m - \mu_m)N_M. \end{aligned}$$

The total population sizes of female mosquitos and primates, N_V and N_M is stationary for $b_v = \mu_v$ and $b_m = \mu_m$, declines for $b_v < \mu_v$ and $b_m < \mu_m$ and grows exponentially for $b_v > \mu_v$ and $b_m > \mu_m$ respectively.

2.4 Dimensionless Transformation

We transform our model equations into normalized quantities such that the total population for the normalized model is equal to 1. This can be done by scaling the population of each class by the total species population. We make the following transformation:

$$\begin{aligned} s_h &= \frac{S_H}{N_H}, \quad v_h = \frac{V_H}{N_H}, \quad e_h = \frac{E_H}{N_H}, \quad i_h = \frac{I_H}{N_H}, \quad r_h = \frac{R_H}{N_H}, \quad s_v = \frac{S_V}{N_V}, \quad e_v = \frac{E_V}{N_V}, \quad i_v = \frac{I_V}{N_V}, \\ s_m &= \frac{S_M}{N_M}, \quad e_m = \frac{E_M}{N_M} \quad \text{and} \quad i_m = \frac{I_M}{N_M}. \end{aligned}$$

in the classes S_H , V_H , E_H , I_H , R_H , S_V , E_V , I_V , S_M , E_M and I_M of the populations respectively. Also, we define $\sigma = \frac{\Lambda}{N_H}$ as the arrival rate of immigrants per individual per unit time.

Differentiating the scaling equations and solving for the derivatives of the scaled variables, system (1), (2), (3) becomes the normalised model as:

$$\begin{aligned}
(4) \quad \frac{ds_h}{dt} &= b_h + \sigma(1 - \rho) + \omega v_h + \omega r_h - a\beta_1 s_h i_v - s_h(\varepsilon + b_h + \sigma) + \alpha s_h i_h, \\
\frac{dv_h}{dt} &= \rho\sigma + \varepsilon s_h - v_h(\omega + b_h + \sigma) + \alpha v_h i_h, \\
\frac{de_h}{dt} &= a\beta_1 s_h i_v - e_h(\delta_h + b_h + \sigma) + \alpha e_h i_h, \\
\frac{di_h}{dt} &= \delta_h e_h - i_h(\gamma + \alpha + b_h + \sigma) + \alpha i_h^2, \\
\frac{dr_h}{dt} &= \gamma i_h - r_h(\omega + b_h + \sigma) + \alpha r_h i_h, \\
\frac{ds_v}{dt} &= b_v - (a\beta_2 s_v i_h + a\beta_3 s_v i_m) - s_v b_v, \\
\frac{de_v}{dt} &= a\beta_2 s_v i_h + a\beta_3 s_v i_m - e_v(\delta_v + b_v), \\
\frac{di_v}{dt} &= \delta_v e_v - i_v b_v, \\
\frac{ds_m}{dt} &= b_m - a\beta_4 s_m i_v - s_m b_m, \\
\frac{de_m}{dt} &= a\beta_4 s_m i_v - e_m(\delta_m + b_m), \\
\frac{di_m}{dt} &= \delta_m e_m - i_m b_m.
\end{aligned}$$

However, it is easy to show that $\frac{dn_h}{dt} = 0$, $\frac{dn_v}{dt} = 0$ and $\frac{dn_m}{dt} = 0$ for the humans, vector and primates respectively. Where solutions are restricted to the hyperplanes $s_h + v_h + e_h + i_h + r_h = 1$, $s_v + e_v + i_v = 1$ and $s_m + e_m + i_m = 1$.

The YF model system (4) monitors human, mosquito (vector) and primates populations, we assume that all state variables and parameters of the model are non-negative $\forall t \geq 0$. Thus, the model will be analysed in a suitable feasible region where it makes biological sense. This region will be obtained as follows:

Lemma 1. *Solutions of the normalised model system (4) are contained in the region $\Phi = \Phi_H \cup \Phi_V \cup \Phi_M \subset \Gamma_+^5 \times \Gamma_+^3 \times \Gamma_+^3$.*

Proof. We split the model system into three parts; namely the human component (n_h), vector (mosquito) component (n_v) and the primates component (n_m), given respectively by,

$$n_h = s_h + v_h + e_h + i_h + r_h, \quad n_v = s_v + e_v + i_v \quad \text{and} \quad n_m = s_m + e_m + i_m. \text{ Such that}$$

$$\Phi_H = \{(s_h, v_h, e_h, i_h, r_h) \in \Gamma_+^5 : 0 < s_h + v_h + e_h + i_h + r_h \leq 1\}$$

$$\Phi_V = \{(s_v, e_v, i_v) \in \Gamma_+^3 : 0 < s_v + e_v + i_v \leq 1\}$$

$$\Phi_M = \{(s_m, e_m, i_m) \in \Gamma_+^3 : 0 < s_m + e_m + i_m \leq 1\}.$$

Thus,

$$\Phi = \Phi_H \cup \Phi_V \cup \Phi_M \subset \Gamma_+^5 \times \Gamma_+^3 \times \Gamma_+^3.$$

that can be shown to be positively invariant with respect to the model system (4). From this lemma, we conclude that it is sufficient to consider the dynamics of model system (4) in Φ . In this region, the model can be considered as being epidemiologically and mathematically well-posed [13].

3. Model Analysis

We now investigate the existence of disease-free equilibrium (E_0) and basic reproduction number. E_0 is obtained by setting the derivatives with respect to time of the model system (4), equal to zero. On computations, the following E_0 is obtained as:

$$(5) \quad E_0 = \left(\frac{b_h + (1 - \rho)\sigma + \omega}{\omega + \varepsilon + b_h + \sigma}, \frac{\rho\sigma + \varepsilon}{\omega + \varepsilon + b_h + \sigma}, 0, 0, 0, 1, 0, 0, 1, 0, 0 \right).$$

3.1 The Basic Reproduction Number, R_0

One of the most important concerns in the analysis of epidemiological models is the determination of the asymptotic behaviour of their solutions which is usually based on the stability of the associated equilibria [21]. These models typically consist of a disease-free equilibrium and at least one endemic equilibrium. The local stability of the disease-free equilibrium is determined based on a threshold parameter, known as the basic reproductive number.

An easy way to theoretically compute R_0 is to follow the approach described by Van den Driessche and Watmough [34]. In model system (4), we consider only the terms in which the infection is in progression, i.e e_h, i_h, e_v, i_v, e_m and i_m .

The corresponding equations can be re-written in the following way

$$(6) \quad x'_i = f_i(x) = \mathcal{F}_i(x) - (\mathcal{V}_i^-(x) - \mathcal{V}_i^+), i = 1, \dots, 6.$$

where $\mathcal{F}_i(x)$ represents the rate of appearance of new infections in compartment i , $\mathcal{V}_i^+(x)$ represents the rate of transfer of individuals into compartment i by all other means, other than the epidemic and $\mathcal{V}_i^-(x)$ represents the transfer of individuals out of the compartment i .

Hence, the following system is obtained:

$$(7) \quad \begin{aligned} \frac{de_h}{dt} &= a\beta_1 s_h i_v - e_h(\delta_h + b_h + \sigma) + \alpha e_h i_h, \\ \frac{di_h}{dt} &= \delta_h e_h - i_h(\gamma + \alpha + b_h + \sigma) + \alpha i_h^2, \\ \frac{de_v}{dt} &= a\beta_2 s_v i_h + a\beta_3 s_v i_m - e_v(\delta_v + b_v), \\ \frac{di_v}{dt} &= \delta_v e_v - i_v b_v, \\ \frac{de_m}{dt} &= a\beta_4 s_m i_v - e_m(\delta_m + b_m), \\ \frac{di_m}{dt} &= \delta_m e_m - i_m b_m. \end{aligned}$$

From (7), we derive \mathcal{F}_i and \mathcal{V}_i as

$$(8) \quad \mathcal{F}_i = \begin{bmatrix} a\beta_1 s_h i_v \\ 0 \\ a\beta_2 s_v i_h + a\beta_3 s_v i_m \\ 0 \\ a\beta_4 s_m i_v \\ 0 \end{bmatrix}$$

and

$$(9) \quad \mathcal{V}_i = \begin{bmatrix} e_h(\delta_h + b_h + \sigma) - \alpha e_h i_h \\ i_h(\gamma + \alpha + b_h + \sigma) - \delta_h e_h - \alpha i_h^2 \\ e_v(\delta_v + b_v) \\ i_v b_v - \delta_v e_v \\ e_m(\delta_m + b_m) \\ i_m b_m - \delta_m e_m \end{bmatrix}$$

Thus, to obtain R_0 , we compute matrices F and V which are $m \times m$ matrices, where m represents the infected classes, defined by

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j} (E_0) \right]$$

and

$$V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j} (E_0) \right] \text{ with } 1 \leq i, j \leq m.$$

We then compute matrix FV^{-1} , defined as the next generation matrix [6]. The R_0 is then defined as

$$(10) \quad R_0 = \rho(FV^{-1}),$$

where $\rho(FV^{-1})$ is the spectral radius of matrix FV^{-1} . Thus,

$$(11) \quad R_0 = \sqrt{\frac{a^2 \beta_1 \beta_2 \delta_h \delta_v s_h^\circ}{(\delta_h + b_h + \sigma)(\gamma + \alpha + b_h + \sigma) b_v (\delta_v + b_v)} + \frac{a^2 \beta_3 \beta_4 \delta_v \delta_m}{b_m (\delta_m + b_m) b_v (\delta_v + b_v)}},$$

where $s_h^\circ = \frac{b_h + (1 - \rho)\sigma + \omega}{\omega + \varepsilon + b_h + \sigma}$ from the first component of E_0 in (5).

In our model we have two hosts and one vector, and it is indicated in the model that the vector can transmit the infection to both the human host and the primates. Thus, for easy understanding, we can represent the reproduction number as, $R_0 = \sqrt{R_h + R_m}$, such that

$$(12) \quad R_h = \frac{(b_h + \sigma(1 - \rho) + \omega) a^2 \beta_1 \beta_2 \delta_h \delta_v}{(\omega + \varepsilon + b_h + \sigma)(\delta_h + b_h + \sigma)(\gamma + \alpha + b_h + \sigma) b_v (\delta_v + b_v)},$$

which is the reproduction number of human host and vector compartments. It represents the infection from vector to human and human to vector. Again, we can represent it as $R_h = R_{vh} \times R_{hv}$. Thus,

$$R_{vh} = \frac{a \beta_1 s_h^\circ \delta_h}{(\gamma + \alpha + b_h + \sigma)(\delta_h + b_h + \sigma)}$$

for

$$s_h^o = \frac{(b_h + \sigma(1 - \rho) + \omega)}{(\omega + \varepsilon + b_h + \sigma)}.$$

It represents the product between transmission probability of the infection from vector to human and the number of susceptible human host per vector. Also

$$R_{hv} = \frac{a\beta_2\delta_v}{(\delta_v + b_v)}.$$

This represents the product between transmission probability of the infection from human host to vector and the proportion of vectors that survive the incubation period.

We also have,

$$(13) \quad R_m = \frac{a^2\beta_3\beta_4\delta_v\delta_m}{b_m(\delta_m + b_m)b_v(\delta_v + b_v)}$$

as the reproduction number of primate to vector and vector to primate compartments. Again, it can be represented as $R_m = R_{mv} \times R_{vm}$ into which

$$R_{mv} = \frac{a\beta_3\delta_v}{b_v(\delta_v + b_v)}$$

represents the product between transmission probability of the infection from primate to vector and the proportion of the vector that survive the incubation period.

$$R_{vm} = \frac{a\beta_4\delta_m}{b_m(\delta_m + b_m)}$$

represents the product between transmission probability of the infection from vector to primate and the proportion of primate that survive the incubation period.

3.2 Sensitivity Analysis of R_0

In order to determine how best to reduce mortality and morbidity due to YF infection, it is necessary to study the relative importance of different factors responsible for its transmission and prevalence [3]. Thus, we perform sensitivity analysis of the basic reproduction number with respect to model parameters.

The sensitivity analysis will assist in curtailing the transmission of the disease by using appropriate intervention strategies. According to Humby [12] there are more ways of conducting

sensitivity analysis, all resulting in a slightly different sensitivity ranking. Following the approaches by [17], [3] and [25], we use the normalized forward sensitivity index which is the backbone of nearly all other sensitivity analysis techniques and is computationally efficient.

Definition 1. The normalized forward sensitivity index of a variable, h , that depends differentially on a parameter, l , is defined as:

$$(14) \quad \Upsilon_l^h = \frac{\partial h}{\partial l} \times \frac{l}{h}.$$

We therefore evaluate the sensitivity indices of R_0 at the baseline parameter values given in Table 2 to each of the seventeen parameters described in Table 1 using Maple software. The sensitivity index of R_0 with respect to a , for example is,

$$(15) \quad \Upsilon_a^{R_0} = \frac{\partial R_0}{\partial a} \times \frac{a}{R_0} = 1.$$

The detail sensitivity indices of R_0 , resulting from the evaluation to the seventeen different parameters of the model are shown in Table 2.

By analyzing the sensitivity indices we observe that, the most sensitive parameter is the mosquito biting rate, a . Other important parameters include the probability of disease transmission from infectious mosquitoes to susceptible humans, β_1 , progression rate of exposed vector, δ_v , progression rate of exposed human, δ_h , human to mosquito disease transmission probability, β_2 , and mosquitoes birth rate.

The reproductive number R_0 is directly related to the biting rate of mosquito, transmission probabilities of vector to human as well as the progression rate of exposed vector, human and primates and inversely related to birth rate of vector, human and primate and disease induced death rate of human host.

Since $\Upsilon_a^{R_0} = 1$ increasing (or decreasing) a by 10% increases (or decreases) R_0 by 10%. In the same way, increasing (or decreasing) δ_v , β_1 and β_2 by 10% increases (or decreases) R_0 by 5%. Similarly, increasing (or decreasing) b_v by 10% decreases (or increases) R_0 by 20%.

Reducing the number of contacts between humans and mosquitoes, through a reduction in either or both, the probability (frequency) of transmitting the infection, and the daily mosquitoes biting rate, would have the largest effect on disease transmission. Also, as the latent period of vector is about the same as the lifespan of mosquitoes, controlling the birth rate of vectors and

TABLE 2. Sensitivity indices of model parameters to R_0

Parameter	Description	Sensitivity index
a	Mosquito daily biting rate	1
δ_v	Progression rate of exposed vector	0.4999200128
β_1	Transmission probability of vector to human	0.4994664012
β_2	Transmission probability of human to vector	0.4994664003
δ_h	Progression rate of exposed human	0.4912808422
β_3	Transmission probability of primate to vector	0.0005335993926
β_4	Transmission probability of vector to primate	0.0005335993926
δ_m	Progression rate of exposed primate	0.0005335980587
ω	rate of relapse of vaccinated and recovered human	0.0001434728868
b_v	Birth rate of vector	-0.9999200135
b_h	Birth rate of human	-0.7511775104
b_m	Birth rate of primates	-0.001067197451
α	Death rate due to disease for human	-0.1302751918
σ	arrival rate of immigrant per individual per time	-0.0002276878858
γ	Recovery rate	-0.001833
ε	vaccination rate of susceptible human	-0.0006476651371
ρ	proportion of immigrant who are vaccinated	-0.000002334632744

shortening the lifespan of the mosquitoes reduces the basic reproductive number because more infected mosquitoes will die before they become infectious [3], [17].

This suggests that strategies that can be applied in controlling the disease transmission are to target the mosquito biting rate and death rate such as the use of mosquito treated bed-nets, insect repellents, indoor residual spraying, insecticides and larvacides.

4. Numerical Results and Discussions

In this section we present some numerical results for the model. The values of parameters are given in Table 3. Most of these values are according to the *A. aegypti* mosquitoes in vector borne diseases reported in the literature. At first we investigate the effects of the threshold pa-

TABLE 3. Description of parameters values of model system (4)

Parameter	Range of values	Source
β_1	[0.5-0.8]	[7], [1]
β_2	[0.37-0.8]	[24], [28]
β_3	[0.5]	estimate
β_4	[0.37]	estimate
δ_h	[0.05-1] day ⁻¹	[10], [8]
δ_v	[0.05-1] day ⁻¹	[1], [10]
δ_m	[1] day ⁻¹	estimate
b_h	[3] day ⁻¹	[8]
b_v	[5000] day ⁻¹	[5], [8]
b_m	[2] day ⁻¹	estimate
a	[0.5-1]	[7], [1]
γ	[0.05-0.1] day ⁻¹	[26], [4]
α	[10 ⁻³]	[10]
ω	[0.35] day ⁻¹	[10]
ε	[0.5]	estimate
ρ	[0.8]	[28]
σ	0.05	estimate
μ_h	[0.0143-0.0167] day ⁻¹	[26]
μ_v	[0.25,0.5] day ⁻¹	[20]
μ_m	[0.08] day ⁻¹	estimate

parameter, that is the basic reproductive number, R_0 , governing the dynamics of populations and

the proportion of individuals in each class. We have seen earlier, that R_0 obtained was expressed in the form of $R_0^2 = R_h + R_m$, this is because in our model, we have three different populations: human host, primates and vector. So the expected basic reproduction number reflects the infection between vector-human and human-vector as well as primate-vector and vector-primate respectively since the vector is capable of transmitting the infection to both human hosts and primates.

Indeed, Figures 2, ..., 10 in simulation part indicates proportion of susceptible and infectious as varies with time. Proportion of susceptible human increases up to a certain level but does not reach 1, indicating that some of them are affected and might die of the disease as time goes, as compared to the proportions of susceptible primates and vector as their number reaches a maximum value, indicating that they are not affected as much as humans.

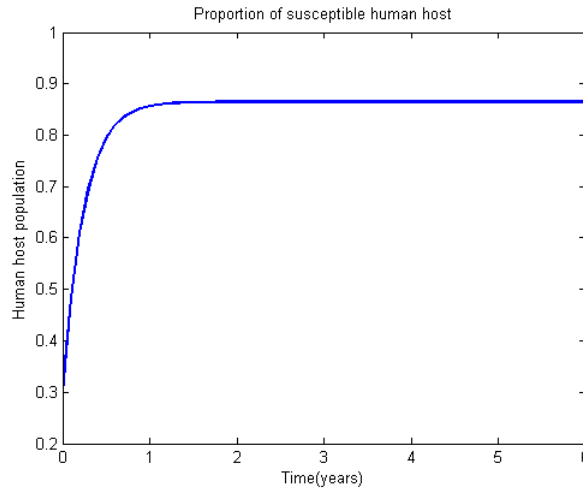
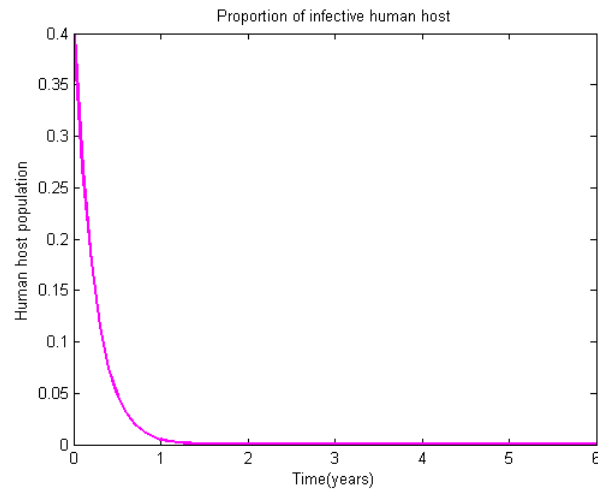
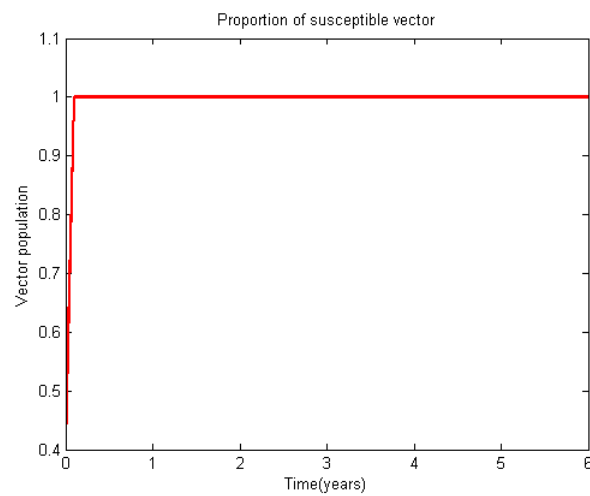


FIGURE 2. *Proportion of susceptible human host.*

Again, proportion of vector population (transmitters of the infection) can be controlled easily so long as they go to extinction very rapidly compared to other proportions of populations (Figure 5 and 9). Also, simulation indicates that the disease prevalence reduces to about zero in a years time, this means that it is possible to eradicate the infection in human population if we can have controls such as continuous vaccination to susceptible population. However, we can not eradicate the disease in the primates.

FIGURE 3. *Proportion of infectious human host.*FIGURE 4. *Proportion of susceptible vector.*

5. Conclusion

A deterministic mathematical model for YF has been formulated using ordinary differential equations. The model considers two hosts (humans and primates) and one vector. The reproduction number, R_0 , as a threshold of the epidemic is discussed through sensitivity analysis and simulation with different parameter settings giving an illustration of the dynamics of the epidemic.

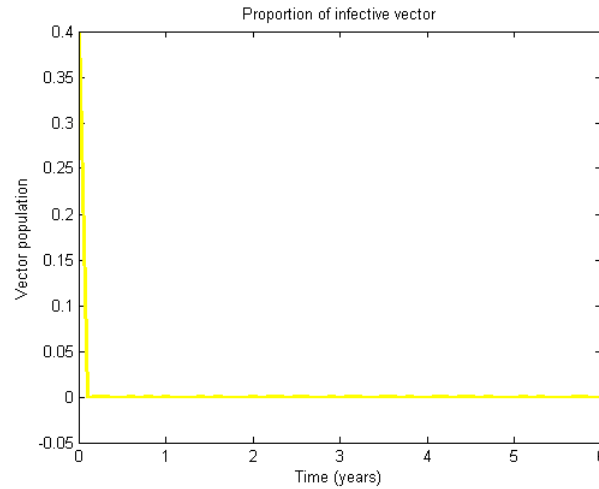


FIGURE 5. *Proportion of infectious vector.*

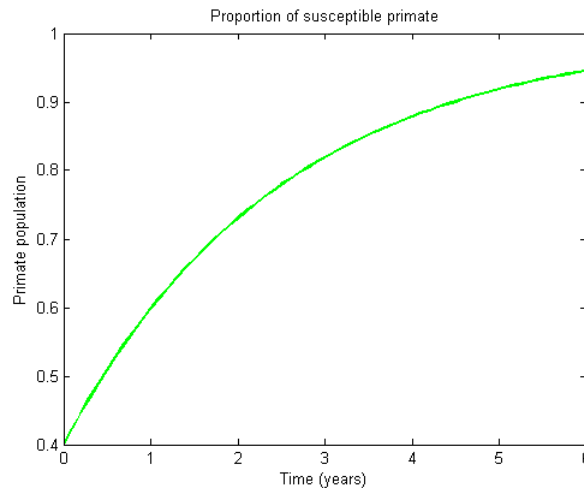


FIGURE 6. *Proportion of susceptible primates.*

Results call for attention to parameters regarding daily biting rate of mosquitoes, recruitment rate of vectors, incubation period for vectors and human hosts, probability of contact between susceptible humans and infectious vectors as well as the recruitment of human host which includes unvaccinated immigrants. Also, numerical results (Fig 9) revealed that in a years time eradication of the disease is possible to human host but not possible to the primates may be because the origin of the virus is the primate dead body. Again an increase in the proportion of infected vector and biting rate of vector to human will contribute greatly to an increase in YF transmission dynamics.

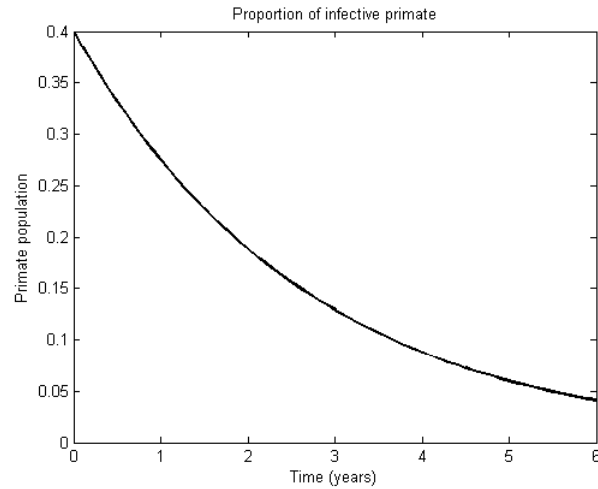


FIGURE 7. *Proportion of infectious primates.*

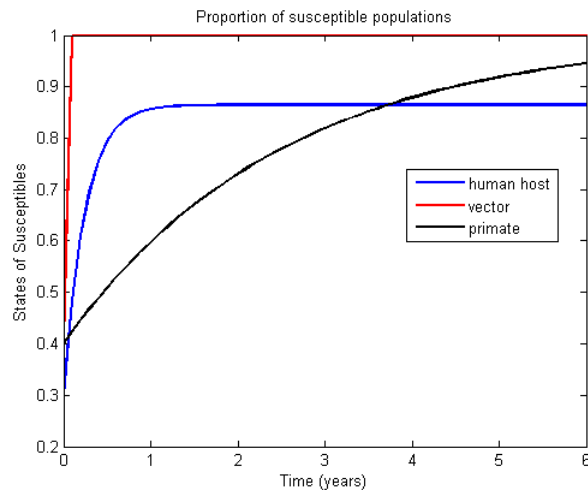


FIGURE 8. *Proportion of susceptible populations.*

However, human migration plays an important role in the transmission and spread of YF. They contribute to the sustainability of the YF epidemic either directly (infected immigrants) or indirectly (health immigrants susceptible to infection by locals). Thus, transmission factors must closely be monitored to ensure health and well being of everyone in the community.

To provide further insights in planning and assessing the impact of current and future control strategies, numerous additions in the model will be required to help suggest the best mitigation strategy, for example thinking of vector control to minimize breeding of mosquito, personal protection which includes the use of mosquito repellents and treated bed-nets that can reduce the

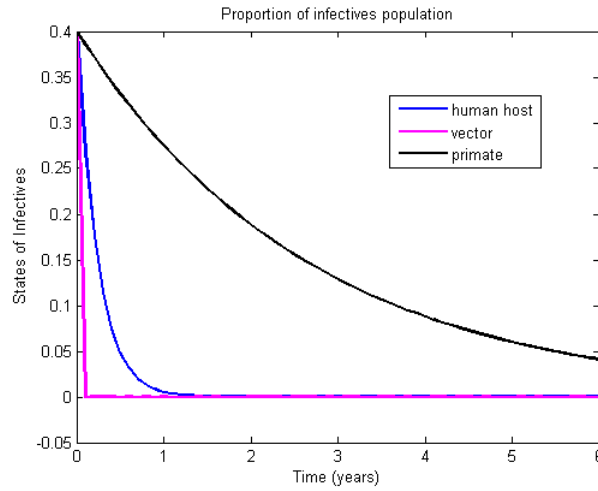


FIGURE 9. *Proportion of infectious populations.*

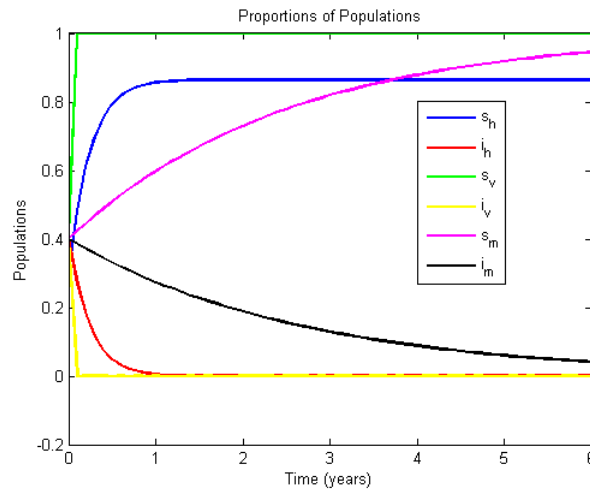


FIGURE 10. *Proportion of populations.*

probability of contact between vectors and humans as well as vertical transmission of the disease to *Aedes aegypti*. Therefore, to ensure minimization of the outbreak human population should be educated regarding YF, its transmissions and control for the management of the epidemic.

Conflict of Interests

The authors declare that there is no conflict of interests.

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REFERENCES

- [1] M. Amaku, F. A. B. Coutinho and E. Massad, Why dengue and yellow fever coexist in some areas of the world and not in others?, *BioSystems*. 106 (2011), 111-120
- [2] A. Barrett, S. Higgs, Yellow fever: a disease that has yet to be conquered, *Annu. Rev. Entomol.* 52 (2007), 209-229.
- [3] N. Chitnis, J. Hyman, J. Cushing, Determining important parameters in the spread of malaria through the sensitivity analysis of a malaria model, *Bull. Math. Biology.* 70 (2008), 1272-1296.
- [4] C. Codeco, P. Luz, F. Coelho, A. Galvani and C. Struchiner, Vaccinating in Disease-Free Regions: a Vaccine Model with Application to Yellow Fever, *J. Royal Soc. Interface.* 4 (2007), 1119-1125
- [5] F. A. B. Coutinho, M. N. Burattini, L. F. Lopez, E. Massad E, Threshold conditions for a non-autonomous epidemic system describing the population dynamics of dengue, *Bull Math Biol.* 68 (2006), 2263-2282
- [6] O. Diekmann, J. A. P. Heesterbeek, J. A. J. Metz, On the definition and the computation of the basic reproduction ratio in models for infectious diseases in heterogeneous populations, *J. Math. Biol.* 28 (1990), 365-382
- [7] Y. Dumont, F. Chiroleu, C. Domerg, On a temporal model for the Chikungunya disease, *Modeling theory and numerics, Math. Biosciences.* 213 (2008), 1-12.
- [8] L. Esteva, C. Vargas, Analysis of dengue disease transmission model, *Math. Biosciences.* 150 (1998), 131-151
- [9] A. Fall, G. Sallet, A. Iggidr and J. Tewa, Epidemiological Models and Lyapunov Functions, *Math. Modelling of Natural Phenomena.* 2 (2007), 55-63.
- [10] S. M. Garba, A. B. Gumel, M. R. Abu Bakar, Backward bifurcations in dengue transmissions dynamics (2008)
- [11] E. Gould, X. de Lamballerie, P. Zanotto, E. Holmes, Origins, evolution, coadaptations within the genus *Flavivirus*, *Adv. in Virus Research.* 59 (2003), 277-314
- [12] D. Hamby, A review of techniques for parameter sensitivity analysis of environmental models, *Environmental Monitoring and Assessment* 32 (1994), 135-154
- [13] H. Hethcote, (2000), The mathematics of infectious diseases *SIAM Review.* 42 (2000), 599-653
- [14] J. Kamgang, G. Sallet, Computational of threshold conditions for epidemiological models and global stability of the disease-free equilibrium (DFE), *Math. Biosciences.* 313 (2008), 80-91

- [15] A. Korobeinikov, Global properties of basic virus dynamics models, *Bull. Math. Biol.* 66 (2004), 879-883
- [16] J. LaSalle, *The Stability of dynamical systems*, CBMS-NSF regional conference series in applied Mathematics 25. SIAM Philadelphia. (1976)
- [17] O. Makinde, K. Okoson, Impact of chemo-therapy on optimal control of malaria disease with infected immigrants, *BioSystems* 104 (2011), 32-41.
- [18] A. Markos, F. Antonio, B. Coutinho, E. Massad, Why dengue and yellow fever coexist in some areas of the world and not in others?, *Biosystems*. 106 (2011), 111-120
- [19] A. Misra, A. Sharma, J. Li, A mathematical model for control of vector born diseases through media campaigns, *Discrete Continuous Dyn. Sys.* 18 (2013), 1909-1927.
- [20] D. Moulay, M. Aziz-Alaoui, H. Kwon, Optimal control of Chikungunya disease, Larvae reduction, treatment and prevention. 9 (2012), 369-393.
- [21] S. Moghadas, Analysis of an epidemic model with bistable equilibria using the Poincare index, *Appl. Math. Comput.* 149 (2004), 689-702.
- [22] T. Monath, M. Cetron, Prevention of Yellow Fever in Persons Traveling to the Tropics, *Clinical Infectious Diseases of America* 34 (2002) 69-78
- [23] Z. Mukandavire, W. Garira and J. Tchuenche, Modelling effects of public health educational campaigns on HIV/AIDS transmission dynamics, *Appl. Math. Model.* 33 (2009), 2084-2095.
- [24] H. Nishiura, *Mathematical and statistical analyses of the spread of dengue*, Research center for tropical infectious disease, Nagasaki University Institute of Tropical medicine, (2006)
- [25] D. J. Pannell, Sensitivity analysis of normative economic models: Theoretical framework and practical strategies, *Agricultural Economics*. 16 (1997), 139-152.
- [26] S. Pinho, C. Ferreira, L. Esteva, F. Barreto, V. Morato, M. Teixeira, Modelling the dynamics of dengue real epidemics, *Philosophical Transactions of the Royal society A.* (2010), 5679-5693
- [27] S. Robertson, B. Hull, O. Tomori, Yellow Fever: A Decade of Re-emergence, *J. Appl. Math. Appl.* 276 (1996), 1157-1162.
- [28] H. S. Rodrigues, M. Teresa, T. Monteiro, F. Delfim, M. Torres, Vaccination models and optimal control strategies to dengue (2010)
- [29] B. Sylvie, A. Beresniak, T. Nguyen, T. Yonli, G. Duru, C. Kambire, W. Perea, The Yellow Fever Risk Assessment Group-YF RAG (2009) Assessment of Yellow Fever Epidemic Risk, An Original Multi-Criteria Modelling Approach. (2009)
- [30] M. Tolle, Mosquito-Borne Diseases, *Current Probabl Prediatr Adolescence Health Care.* (2009) 97-104
- [31] J. Tumwiine, J. Mugisha, L. S. Luboobi, A host vector model for malaria with infective immigrants, *J. Math. Anal. Appl.* 361 (2010), 139-149

- [32] Y. Thome, C. Roberto, L. Esteva, Optimal Control of *Aedes aegypti* Mosquitoes by the Sterile Insect Technique and Insecticide, *Math. Biosciences*. (2009), 12-23
- [33] R. Ullah, G. Zaman, S. Islam, Stability Analysis of the Endemic Equilibrium of Multigroup SIR Epidemic Models, *VFast Transactions on Mathematics*. 1 (2013)
- [34] P. Van der Driessche and J. Watmough, Reproduction numbers and sub threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosciences*. 180 (2002), 29-48.
- [35] H. Yang and C. Ferreira, Assessing the effects of vector control on dengue transmission, *Appl. Math. Comput.* 198 (2008), 401-413.
- [36] Yellow fever Fact sheet N00, World Health Organization, May 2013. Retrieved 23 February 2014
- [37] Yellow fever fact sheet, World Health Organization, 2006. Retrieved 18 April 2013.