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Numerical Simulation of the Impact of Delay on Yellow Fever and Its Implication

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Abstract: *We formulated a discrete time delay mathematical model to investigate the yellow fever disease's transmission pattern. We established the stability of the delay system by identifying the equilibrium point that is both endemic and free of yellow fever through analytical investigations. Stability was also determined by computing the basic reproduction number using the next generation matrix method. We then conducted numerical simulation and results show that time delay plays a significant role in the case of stability of the endemic equilibrium point as equilibrium is quickly achieved for smaller time delays and vice versa. The basic reproduction number obtained using the model parameter is 0.68876; which shows that the yellow fever free equilibrium point is locally asymptotically stable. The implication of the boundedness is that the disease is controllable.*
Keywords: Yellow fever, discrete time delay, epidemiology

INTRODUCTION

Yellow fever (YF), a hemorrhagic fever caused by a Flavivirus, of the Flaviviridae family [26]. The virus was first isolated in 1927 in a male patient. Transmission is primarily by mosquitoes with an incubation period of 3 to 6 days. Yellow fever can cause the onset of clinical features which is characterized by fever, chills, loss of appetite, nausea, muscle pains particularly in the back and (Jaundice or Hemorrhagic symptom). It is characterized by fever, chills, loss of appetite, nausea, muscle pains particularly in the back, and headaches [33]. There are more than 200,000 infections and 30,000 deaths every year [33]. About 90% of YF cases occur in Africa (Tolle, 2009), and a billion people live in an area of the world where the disease is common. It also affects tropical areas of South America, but not Asia [2]. The number of cases of yellow fever has been increasing in the last 30 years [33,4], probably due to fewer people being immune, more people living in cities, people moving frequently, and changing climate. The origin of the disease is Africa, from where it spread in South America through the slave trade in the17th century [29]. The yellow fever virus was one of the first human virus discovered [21], and its family comprises approximately 70 viruses, most of which are transmitted by arthropod insects (hence the name arthropod borne

viruses or arboviruses). A safe and effective vaccine against yellow fever exists and some countries require vaccinations for travelers [33]. In rare cases (less than one in 200,000 to 300,000 doses), the vaccination can cause yellow fever vaccine-associated viscerotropic disease (YEL-AVD), which is fatal in 60% of cases, probably due to the genetic morphology of the immune system. Another possible side effect is an infection of the nervous system, which occurs in one in 200,000 to 300,000 cases, causing yellow fever vaccine-associated neurotropic disease (YEL-AND), which can lead to meningoencephalitis, fatal in less than 5% of cases. The control of Yellow fever has been achieved through various methods, including vector control (using insecticide-treated bed nets and indoor residual spraying), chemoprevention, and case management (early diagnosis and prompt treatment).

Mathematical modelling has proven to be essential in understanding the dynamics of infectious diseases. A direct application of mathematical models to data has been of enormous help in having more knowledge about the infection and control of diseases [30]. In recent times, there has been much concern about vector-borne transmission such as malaria and yellow fever, which spread rapidly with high cases of infection still recorded across nations [34].

[28] modelled the impact of information transmission on epidemic outbreak. Results from their study unveil some crucial threshold parameters which should be considered (for proper attention) in the design of YF control measures and vaccinations schedules in order to halt the spread of the disease, particularly in its endemic areas. Also, [36] modelled the recent YF outbreak in Luanda, Angola. Their model prediction fitted very well with weekly reported incidence and mortality resulting from the epidemic. One outstanding contribution from their work is that it gives a guideline for assessing future outbreaks while also equipping the decision makers with likely action to take in order to minimize the attendant casualties. In addition, their findings provide criteria for evaluating future vaccination program.

The use of mathematical and computational models to help vaccine development is not new. In fact, several works use computational tools to aid vaccine design. For example, epitope-mapping algorithms have been used for vaccine design since the 1980s [9]. Since then, new computational tools have been used for selection of vaccine targets. Most works focus on using mathematical and computational tools to predict epitopes [19] or to develop virtual screening approaches (i.e, the identification of relevant antigens) [15]. This traditional use of computational vaccinology is related to pre-clinical development.

[6] tried to qualitatively validate a simplified mathematical-computational model of the immune response to the YF vaccine which is based on a live, attenuated viral strain. The model uses Ordinary Differential Equations (ODEs) to model the main cells and molecules related to adaptive immune response. Another work by [20] uses an ODE-based approach to model the human immune response to vaccination against both YF and smallpox using distinct data and equations sets, one for each disease. The aim of the authors was to primarily evaluate the dynamics of CD8+ T cells.

[8] modeled the immune response to the YF virus from infection of epithelial cells to secretion of antibodies, considering various populations of cells and molecules, in different stages and compartments. There were 19 ODEs divided into two compartments: one representing the tissue where the virus proliferates and the other the lymph nodes.

[18] have proposed transmission laws that include nonlinearity, such as the Holling typeII functional, Crowley–Martin functional, Beddington–DeAngelis functional, etc., to study the dynamics of infectious diseases. The general incidence rate was suggested by [22] and used by numerous authors in their models.

[10] formulated a mathematical model to study the effect of sterile insect technique to control the vectors *Aedes aegypti* responsible for yellow fever. This technique aims at displacing the wild insects from the habitat. The factors like mating competitiveness and spread of males that are sterilized by the technique were incorporated in model. Immigration of females was also considered. [27] studied yellow fever dynamics with vaccine as a control measure. [14] developed mathematical model for yellow fever epidemic. The effect of treatment of standing water on mosquito population was investigated. [35] formulated a deterministic model with multiple control measures for yellow fever outbreak. It was found that outbreak can be controlled if chemical and biological tools control mosquito population. Transmission parameters, travel rates, local evidence are a few important factors to know the probability or risk of yellow fever spread in an urban outbreak. In the finding of [36], it was found that the basic reproduction number lies between 2.6 and 3.4 in the period of December 2015 and August 2016 for outbreak of yellow fever in Angola. [29] estimated the number of Chinese workers who were unvaccinated in an outbreak in Angola. The same study was also done by [17] for an outbreak for Democratic Republic of the Congo 2015 − 16. Many researchers have studied yellow fever with effect of vaccine. [4] studied the availability of live attenuated vaccine 17D strain. It was suggested that occasional supply or insufficient supply of vaccine should be taken care of.

[1] formulated a model of yellow fever epidemics, which involves the interactions of two principal communities; hosts (humans) and Vectors (aedes aegypti mosquitoes). The host community was divided into three compartments of Susceptible S(t), Infected I(t) and Recovered R(t) while the vector community was partitioned into two compartments of Susceptible N(t) and Infective or virus carriers M (t) where $t \geq 0$ is the time. They analyzed the local stability of the model using Jacobian matrix and implicit function. [11] formulated a model and incorporated the biology of the urban vector of yellow fever, the mosquito *Aedes aegypti*, and the stages of the disease in the host (humans). From the epidemiological point of view, the mosquito follows a SEI sequence (Susceptible, Exposed, and Infective). In their, model the adult populations are subdivided according to their status with respect to the virus. They assumed that there is no vertical transmission of the virus and eggs, larvae, pupae and non-parous adults are always susceptible. The humans are subdivided in sub-populations according to their status with respect to the illness as susceptible (S), exposed (E), infective (I), in remission (r), toxic (T) and recovered (R). [32] considered an epidemic model of a vector-borne disease which has direct mode of transmission in addition to the vector-mediated transmission. The incidence term is assumed to be of the bilinear mass-action form. They include both a baseline ordinary differential equation (ODE) version of

the model, and, a differential-delay model with a discrete time delay. The delay in the differential-delay model accounts for the incubation time the vectors need to become infectious. They studied the effect of that delay on the stability of the equilibria.

A lot of work has been done on the epidemiology of yellow fever but to our knowledge, there is no model for yellow fever that has incorporated delay in infection into the model equations. In this paper, we have formulated a compartmental model for yellow fever to study the effect of delay in infection of the disease.

1. **Mathematical Model Formulation**

The mathematical model described below addresses the transmission dynamics of an infectious agent in a homogeneous population. We consider a nonlinear system of ordinary differential equations involving the human and the vector- mosquitoes and their eggs populations. The term "eggs" also includes the intermediate stages, such as larvae and pupae. It is also worth highlighting that the model proposed here is based on previous paper [3] and we updated the model originally developed by [23] to include time delay in infection.

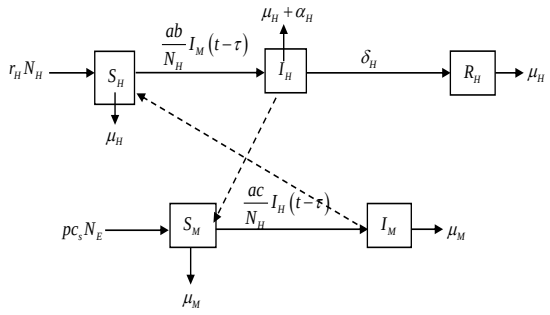

Figure 1: Flow diagram of model

All variables and parameters in the human system will carry the subscript H, while those in the vector system will carry one of the subscripts M (mosquitoes) or E (eggs). In our model the total human population, denoted by N_H, is split into four subclasses which are susceptible humans S_H, infected humans I_H, and recovered (and immune) humans R_H, so that $N_H = S_H + I_H + R_H$. The total vector population, which is formed by both total mosquito population, denoted by N_M, and the total eggs population, denoted is by N_E, infected and infectious mosquitoes I_M, and non-infected eggs S_E, so that $N_M = S_M + I_M$ and $N_E \supset S_E$. A flow diagram of the model is depicted in

Figure 1, and the associated variables and parameters are described in Table below, where some values are realistic assumptions and the rest taken from [23]. The model supposes a homogeneous mixing of human and mosquito population based on the idea that the mosquito has a human biting habit, so that each mosquito bite has an equal probability of transmitting the virus to the susceptible human in the population or acquiring infection from an infected human. The equations are derived based on the fact that, the presence of yellow fever in the population, both mosquitoes and humans can infect each other upon contact. While an infected mosquito remains infected until death, it is assumed that infected humans can recover from the disease [25]. We define a logistic recruitment rate of humans, mosquitoes, and eggs, and all new born humans and newly emerged mosquitoes are susceptible with no vertical transmission [25]. Susceptible humans become infected through the bite by an infected mosquito and the susceptible mosquitoes become latent infected as result of biting infectious humans. Upon acquiring infection, the susceptible individuals move into the infected compartment. The incidence of new infections is given by the standard incidence [12]. Deaths can occur amongst the human population, mosquitoes, and eggs, naturally. In contrast, in the presence of the yellow fever, the human population can either die due to the additional effects of the disease or recover. It is also assumed that recovered human individuals acquire immunity against reinfection, so that they do not acquire yellow fever for a second time. We will introduce the delay in the transmission. We will use the assumption that a susceptible after contact with an infective takes the delay time to become infective itself [16, 13]. That is, a newly exposed susceptible stays as a susceptible until a time equal to the delay elapses and only then it turns into an infective. Combining the above formulation and assumption, it follows that the model for the transmission dynamics of the yellow fever disease is given by the following system of nonlinear ordinary differential equations:

$$\frac{dS_H(t)}{dt} = r_H N_H - \frac{ab}{N_H} I_M(t-\tau) S_H(t-\tau) - \mu_H S_H(t) \qquad \frac{dI_H(t)}{dt} = \frac{ab}{N_H} I_M(t-\tau) S_H(t-\tau) - (\mu_H + \alpha_H + \delta_H) I_H \quad (1)$$

$$\frac{dR_H(t)}{dt} = \delta_H I_H(t) - \mu_H R_H(t) \quad (2)$$

$$\frac{dS_M(t)}{dt} = pc_s N_E - \frac{ac}{N_H} I_H(t-\tau) S_M(t-\tau) - \mu_M S_M(t) \quad (3)$$

$$\frac{dI_M(t)}{dt} = \frac{ac}{N_H} I_H(t-\tau) S_M(t-\tau) - \mu_M I_M(t) \quad (5)$$

where the time lag $\tau>0$ represents the incubation period of the disease, defined as a fixed time during which the infectious agent develops in the vector; only after this time can the infected vector infect a susceptible individual.

Parameter description	
	Description
a	Average daily biting rate
b	Fraction of actually infective bites
μ_H	Human natural mortality rate
α_H	Yellow fever mortality rate in humans
r_H	Birth rate of humans
δ_H	Human recovery rate
p	Susceptible egg hatching rate
μ_M	Mosquitoes natural mortality rate
c	*A. aegypti* susceptibility to yellow fever
c_s	Climatic factor

Let $C=\left(\left[-\tau,0\right],\square^3\right)$ denote the Banach space of continuous functions, mapping the interval [−τ, 0] to $\square^3$ with the topology of uniform convergence. It is well known from the fundamental theory of functional differential equations that the model described by Equations (1) – (5) admits a unique solution $\left(S_H,I_H,R_H,S_M,I_M\right)$ with initial data $\left(S_{H0},I_{H0},R_{H0},S_{M0},I_{M0}\right)\in C$. For biological reasons, the initial conditions of the model described by Equations (1) – (5) are nonnegative continuous functions,

$$S_{H0}(\varphi)\geq 0,\ I_{H0}(\varphi)\geq 0,$$
$$R_{H0}(\varphi)\geq 0,\ S_{M0}(\varphi)\geq 0, \qquad (6)$$
$$I_{M0}(\varphi)\geq 0,\ \varphi\in\left[-\tau,0\right]$$

For ecological reasons, it is assumed that all the parameters in table 1 are positive. It is therefore important to show that all state variables with nonnegative initial data will remain nonnegative and bounded for all time. Thus, we prove the following theorem:

Theorem 1: All state variables of the system of Equations (1) – (5), subject to the condition (6) remain nonnegative and bounded for all t ≥0.

Proof: We define

$$\frac{dN_H}{dt}=r_HN_H-\frac{ab}{N_H}I_M(t-\tau)S_H(t-\tau)$$

$N_H=S_H+I_H+R_H$ and $N_M=S_M+I_M$

$$-\mu_HS_H(t)+\frac{ab}{N_H}I_M(t-\tau)S_H(t-\tau)$$
$$-(\mu_H+\alpha_H+\delta_H)I_H(t)+\delta_HI_H(t)-\mu_HR_H(t)$$

$$\frac{dN_H}{dt} = r_H N_H - \mu_H N_H - \alpha_H I_H(t) \le (r_H - \mu_H) N_H$$

$$\frac{dN_M}{dt} = pc_s N_E - \frac{ac}{N_H} I_H(t-\tau) S_M(t-\tau)$$

$$-\mu_M S_M(t) + \frac{ac}{N_H} I_H(t-\tau) S_M(t-\tau) - \mu_M I_M(t)$$

$$\frac{dN_M}{dt} = pc_s N_E - \mu_M N_M \le pc_s N_E$$

Therefore, bounded and nonnegative.

2. Analytical Solution (Equilibria and Stability)

The model system of Equations (1)– (5) has two equilibria, which are obtained from the system of equations. We shall categorize the equilibrium points as the yellow fever free equilibrium point (YFEP) and the yellow fever endemic equilibrium point (YEEP) which are denoted by E^0 and E^1 respectively. It is well known that a system has a stable equilibrium if its neighborhood trajectory approaches the point asymptotically at $t \to \infty$ and same is applicable to a system with a time delay. Thus, we obtain the equilibrium for the system (1)–(5) by setting $\frac{dS_H(t)}{dt} = 0$, $\frac{dI_H(t)}{dt} = 0$, $\frac{dR_H(t)}{dt} = 0$, $\frac{dS_M(t)}{dt} = 0$ and $\frac{dI_M(t)}{dt} = 0$.

A. Yellow Fever – Free Equilibrium Point and stability analysis

The YFEP occur when we set $I_H = 0$, $R_H = 0$ and $I_M = 0$ in the system (1)–(5), we get

$$S_H^0 = \frac{r_H N_H}{\mu_H} \text{ and } S_M^0 = \frac{pc_s N_E}{\mu_M}.$$

Therefore,

$$E^0 = \left(S_H^0, 0, 0, S_M^0, 0\right) = \left(\frac{r_H N_H}{\mu_H}, 0, 0, \frac{pc_s N_E}{\mu_M}, 0\right).$$

In order to establish stability of the YFEP, we compute the basic reproduction number of the proposed model.

Theorem 2: The yellow fever free equilibrium point is locally asymptotically stable whenever the basic reproduction number $R_0 < 1$.

Proof: d Let $\Lambda =$ terms that contain secondary infection (disease class) and $\Psi =$ terms that do not contain secondary infection (non-disease class)

$$\Lambda = \begin{bmatrix} \frac{abI_M S_H}{N_H} \\ \frac{acI_H S_M}{N_H} \end{bmatrix},\ \Psi = \begin{bmatrix} -(\mu_H + \alpha_H + \delta_H) I_H \\ -\mu_M I_M \end{bmatrix}$$

Let $u = \frac{abI_M S_H}{N_H}$, $v = \frac{acI_H S_M}{N_H}$, $f = -(\mu_H + \alpha_H + \delta_H) I_H$ and $g = -\mu_M I_M$.

$$X = \begin{bmatrix} \frac{\partial u}{\partial I_H} & \frac{\partial u}{\partial I_M} \\ \frac{\partial v}{\partial I_H} & \frac{\partial v}{\partial I_M} \end{bmatrix} \text{and } Y = \begin{bmatrix} \frac{\partial f}{\partial I_H} & \frac{\partial f}{\partial I_M} \\ \frac{\partial g}{\partial I_H} & \frac{\partial g}{\partial I_M} \end{bmatrix}$$

$$X = \begin{bmatrix} 0 & \frac{ab}{N_H} S_H \\ \frac{ac}{N_H} S_M & 0 \end{bmatrix} \text{ and } Y = \begin{bmatrix} -(\mu_H + \alpha_H + \delta_H) & 0 \\ 0 & -\mu_M \end{bmatrix}$$

$$Y^{-1} = \begin{bmatrix} -\frac{1}{\mu_H + \alpha_H + \delta_H} & 0 \\ 0 & -\frac{1}{\mu_M} \end{bmatrix}$$

$$\left| XY^{-1} - \lambda I \right| = 0$$

$$\Rightarrow \begin{vmatrix} 0 - \lambda & -\frac{ab}{N_H \mu_M} S_H \\ -\frac{ac}{N_H (\mu_H + \alpha_H + \delta_H)} S_M & 0 - \lambda \end{vmatrix} = 0$$

$$\lambda^2 - \frac{a^2 bc}{N_H \mu_M (\mu_H + \alpha_H + \delta_H)} S_H S_M = 0$$

At yellow fever free equilibrium, we have,

$$R_0 = \lambda = \frac{a}{\mu_M} \sqrt{\frac{bcpc_s N_E r_H}{N_H \mu_H (\mu_H + \alpha_H + \delta_H)}} \qquad (*)$$

B. Yellow Fever − Endemic Equilibrium Point and stability

The yellow fever endemic equilibrium point is obtained when all compartments in the model are non zero positive. We get,

$$r_H N_H - \frac{ab}{N_H} I_M S_H - \mu_H S_H = 0 \quad (7) \qquad \frac{ab}{N_H} I_M S_H - \left(\mu_H + \alpha_H + \delta_H\right) I_H = 0 \quad (8)$$

$$\delta_H I_H - \mu_H R_H = 0 \quad (9) \qquad pc_s N_E - \frac{ac}{N_H} I_H S_M - \mu_M S_M = 0 \quad (10)$$

$$\frac{ac}{N_H} I_H S_M - \mu_M I_M = 0 \quad (11)$$

From equation (10),

$$S_M = \frac{pc_s N_E N_H}{acI_H - N_H \mu_M} \quad (12)$$

Substitute equation (12) into equation (11), we get,

$$I_M = \frac{ac}{\mu_M} I_H \left(\frac{pc_s N_E}{acI_H - N_H \mu_M} \right) \quad (13)$$

Substitute equation (13) into equation (8), we get,

$$S_H = \frac{N_H \mu_M \left(acI_H - N_H \mu_M\right)\left(\mu_H + \alpha_H + \delta_H\right)}{a^2 bpcc_s N_E} \quad (14)$$

Substitute equation (13) into equation (7), we get,

$$S_H = \left(\frac{r_H N_H k_2 \left(acI_H - k_2\right)}{k_1 I_H + k_2 \mu_H \left(acI_H - k_2\right)} \right) \quad (15)$$

Where,

$k_1 = a^2 bcc_s pN_E$

$k_2 = \mu_M N_E$

$k_3 = \mu_H + \alpha_H + \delta_H$

Comparing equation (14) and (15), we get,

$$I_H^* = \frac{k_1 r_H N_H - k_2^2 k_3 \mu_H}{k_1 k_3 + k_2 k_3 \mu_H ac} \quad (16)$$

Substitute equation (16) into equation (14), we get,

$$S_H^* = \frac{k_2}{k_1} \left(\frac{ac\left(k_1 r_H N_H - k_2^2 k_3 \mu_H\right) + k_1 k_2 k_3 + k_2^2 k_3 \mu_H ac}{k_1 + k_2 \mu_H ac} \right) \quad (17)$$

Substitute equations (16) and (17) into equation (8), we get,

$$I_M^* = \frac{k_3 I_H^* N_H}{abS_H^*} \quad (18)$$

Substitute equation (16) into equation (9), we get,

$$R_H^* = \frac{\delta_H I_H^*}{\mu_H} \qquad (19)$$

We study the stability of the equilibria through the linearization of the system. We shall do this by defining $Y = \left(\hat{S}_H, \hat{I}_H, \hat{R}_H, \hat{S}_M, \hat{I}_M\right)$ as the equilibrium of our delayed system (1) to (5). Then by setting

$S_H(t) = y_1(t) + \hat{S}_H$, $I_H(t) = y_2(t) + \hat{I}_H$,
$R_H(t) = y_3(t) + \hat{R}_H$, $S_M(t) = y_4(t) + \hat{S}_M$
and $I_M(t) = y_5(t) + \hat{I}_M$, then the linearized system is obtained by computing the Jacobian matrix given as;

$$|J - \lambda I| = \begin{vmatrix} -\frac{ab}{N_H}\hat{I}_M e^{-\lambda\tau} - \mu_H - \lambda & 0 & 0 & 0 & -\frac{ab}{N_H}\hat{S}_H e^{-\lambda\tau} \\ \frac{ab}{N_H}\hat{I}_M e^{-\lambda\tau} & -(\mu_H + \alpha_H + \delta_H) - \lambda & 0 & 0 & \frac{ab}{N_H}\hat{S}_H e^{-\lambda\tau} \\ 0 & \delta_H & -\mu_H - \lambda & 0 & 0 \\ 0 & -\frac{ac}{N_H}\hat{S}_M e^{-\lambda\tau} & 0 & -\frac{ac}{N_H}\hat{I}_H e^{-\lambda\tau} - \mu_M - \lambda & 0 \\ 0 & \frac{ac}{N_H}\hat{S}_M e^{-\lambda\tau} & 0 & \frac{ac}{N_H}\hat{I}_H e^{-\lambda\tau} & -\mu_M - \lambda \end{vmatrix} = 0$$

On simplifying, we get,

$$\left.\begin{aligned} &\lambda^5 + k_1\lambda^4 + k_2\lambda^3 + k_3\lambda^2 + k_4\lambda + k_5 + \left(p_1\lambda^4 + p_2\lambda^3 + p_3\lambda^2 + p_4\lambda + p_5\right)e^{-\lambda\tau} \\ &+\left(q_1\lambda^3 + q_2\lambda^2 + q_3\lambda + q_4\right)e^{-2\lambda\tau} + \left(r_1\lambda^2 + r_2\lambda + r_3\right)e^{-3\lambda\tau} \end{aligned}\right] = 0$$

(20)

Where,

$k_1 = \alpha_H + 2\mu_M + \delta_H + 3\mu_H$
$k_2 = \mu_M^2 + 3\mu_H^2 + 2\alpha_H\mu_M$
$+ 2\mu_M\delta_H + 6\mu_M\mu_H + 2\delta_H\mu_H$

$$k_3 = \mu_M^2\alpha_H + \mu_M^2\delta_H + 3\mu_M^2\mu_H + \mu_H^2\alpha_H + \mu_H^3$$
$$+\mu_H^2\delta_H + 6\mu_H^2\mu_M + 4\mu_M\alpha_H\mu_H + 4\mu_M\delta_H\mu_H$$
$$k_4 = 2\mu_H^3\mu_M + 3\mu_M^2\mu_H^2 + 2\alpha_H\mu_H^2\mu_M$$
$$+2\mu_M\delta_H\mu_H^2 + 2\alpha_H\mu_H\mu_M^2 + 2\mu_M^2\mu_H\delta_H$$
$$k_5 = \mu_M^2\mu_H^3 + \alpha_H\mu_M^2\mu_H^2 + \mu_M^2\delta_H\mu_H^2$$
$$p_1 = \frac{a}{N_H}\left(b\hat{I}_M + c\hat{I}_H\right)$$
$$p_2 = \frac{ac\hat{I}_H}{N_H}\left(\delta_H + 3\mu_H + \alpha_H + \mu_M\right)$$
$$+\frac{ab\hat{I}_M}{N_H}\left(\delta_H + 2\mu_H + \alpha_H + 2\mu_M\right)$$

$$p_3 = \frac{ac\mu_H\hat{I}_H}{N_H}\left(\begin{array}{l}\frac{\mu_M\delta_H}{\mu_H} + 2\delta_H + 3\mu_H \\ +\frac{2\alpha_H}{\mu_H} + \frac{\alpha_H\mu_M}{\mu_H} + 3\mu_M\end{array}\right)$$
$$+\frac{ab\hat{I}_M}{N_H}\left(\begin{array}{l}\mu_H^2 + 2\mu_M\delta_H + \delta_H\mu_H \\ +4\mu_M\mu_H + \alpha_H\mu_M + \mu_M^2 + 2\alpha_H\mu_M\end{array}\right)$$
$$p_4 = \frac{ac\mu_H\hat{I}_H}{N_H}\left(\begin{array}{l}\mu_H^2 + \delta_H\mu_H + \alpha_H\mu_H + 3\mu_M\mu_H \\ +\alpha_H\mu_M + 2\mu_M\delta_H + 2\alpha_H\mu_M\end{array}\right)$$
$$+\frac{ab\mu_M\hat{I}_M}{N_H}\left(\begin{array}{l}2\mu_H^2 + \mu_M\delta_H + 2\delta_H\mu_H \\ +2\mu_M\mu_H + 2\alpha_H\mu_H + \alpha_H\mu_M\end{array}\right)$$
$$p_5 = \left(\alpha_H + \delta_H + \mu_H\right)\left(\frac{ac\mu_M\mu_H^2\hat{I}_H}{N_H} + \frac{ab\mu_M^2\mu_H\hat{I}_M}{N_H}\right)$$
$$q_1 = \frac{a^2bc}{N_H^2}\left(\hat{I}_H\hat{I}_M + \hat{S}_M\hat{S}_H\right)$$
$$q_2 = \frac{a^2bc}{N_H^2}\left(\begin{array}{l}2\mu_H\hat{I}_H\hat{I}_M + 2\mu_H\hat{S}_M\hat{S}_H + \delta_H\hat{I}_H\hat{I}_M \\ +\alpha_H\hat{I}_H\hat{I}_M + \mu_M\hat{I}_H\hat{I}_M + \mu_M\hat{S}_M\hat{S}_H\end{array}\right)$$

$$q_3 = \frac{a^2bc}{N_H^2}\begin{pmatrix} \mu_H^2\hat{S}_M\hat{S}_H + 2\mu_H\mu_M\hat{S}_M\hat{S}_H \\ +\mu_H^2\hat{I}_H\hat{I}_M + \mu_M\delta_H\hat{I}_H\hat{I}_M \\ +\mu_H\delta_H\hat{I}_H\hat{I}_M + \mu_H\alpha_H\hat{I}_H\hat{I}_M \\ +2\mu_H\mu_M\hat{I}_H\hat{I}_M + \mu_M\alpha_H\hat{I}_H\hat{I}_M \end{pmatrix}$$

$$q_4 = \frac{a^2bc\mu_H\mu_M}{N_H^2}\begin{pmatrix} \delta_H\hat{I}_H\hat{I}_M + \mu_H\hat{S}_M\hat{S}_H \\ +\mu_H\hat{I}_H\hat{I}_M + \alpha_H\hat{I}_H\hat{I}_M \end{pmatrix}$$

$$r_1 = \frac{2a^3b^2c}{N_H^3}\hat{S}_M\hat{S}_H\hat{I}_M$$

$$r_2 = \frac{2a^3b^2c\hat{S}_M\hat{S}_H\hat{I}_M}{N_H^3}\left(\mu_H + \mu_M\right)$$

$$r_3 = \frac{2a^3b^2c\mu_H\mu_M}{N_H^3}\hat{S}_M\hat{S}_H\hat{I}_M$$

By substituting the yellow fever endemic equilibrium point $E^1 = \left(S_H^*, I_H^*, R_H^*, S_M^*, I_M^*\right)$ into the equation 21, we get,

$$\begin{bmatrix} \lambda^5 + k_1\lambda^4 + k_2\lambda^3 + k_3\lambda^2 + k_4\lambda + k_5 \\ +\left(p_1\lambda^4 + p_2\lambda^3 + p_3\lambda^2 + p_4\lambda + p_5\right)e^{-\lambda\tau} \\ +\left(q_1\lambda^3 + q_2\lambda^2 + q_3\lambda + q_4\right)e^{-2\lambda\tau} \\ +\left(r_1\lambda^2 + r_2\lambda + r_3\right)e^{-3\lambda\tau} \end{bmatrix} = 0 \quad (21)$$

If $\tau = 0$, then

$$\phi(\lambda) = \lambda^5 + \left(k_1 + p_1\right)\lambda^4 + \left(k_2 + p_2 + q_1\right)\lambda^3$$
$$+\left(k_3 + p_3 + q_2 + r_1\right)\lambda^2 + \left(k_4 + p_4 + q_3 + r_2\right)\lambda$$
$$+k_5 + p_5 + q_4 + r_3$$

Since the model parameters are all positives, then the roots $\phi(\lambda)$ have negative real parts which implies that it is asymptotically stable. For $\tau > 0$ corollary 2.4 from [18] ensures that, if the yellow fever endemic equilibrium E^1 is unstable for a particular value of the delay parameter, then roots of the characteristic equation (21) must intersect the imaginary axis. Thus, to prove the stability of the YFEP, we use the contradictory assumption; i.e., we assume that λ =iω, ω > 0 is the root of Equation (21). Putting $\lambda = i\omega$ into Equation (20) yields

$$(i\omega)^5 + k_1(i\omega)^4 + k_2(i\omega)^3 + k_3(i\omega)^2 + k_4(i\omega) + k_5 + \left(p_1(i\omega)^4 + p_2(i\omega)^3 + p_3(i\omega)^2 + p_4(i\omega) + p_5\right)e^{-(i\omega)\tau} + \left(q_1(i\omega)^3 + q_2(i\omega)^2 + q_3(i\omega) + q_4\right)e^{-2(i\omega)\tau} + \left(r_1(i\omega)^2 + r_2(i\omega) + r_3\right)e^{-3(i\omega)\tau} = 0$$

Separating the real and imaginary part, we get,

$$\begin{aligned} & k_1\omega^4 - k_3\omega^2 + k_5 = -p_1\omega^4\cos(\omega\tau) \\ & + p_3\omega^2\cos(\omega\tau) - p_5\cos(\omega\tau) \\ & + p_2\omega^3\sin(\omega\tau) - p_4\omega\sin(\omega\tau) \\ & + q_2\omega^2\sin(2\omega\tau) - q_4\cos(2\omega\tau) \\ & + q_1\omega^3\sin(2\omega\tau) - q_3\omega\sin(2\omega\tau) \\ & + r_1\omega^2\cos(3\omega\tau) - r_3\cos(3\omega\tau) \\ & + r_2\omega\sin(3\omega\tau) \end{aligned} \quad (22)$$

$$\begin{aligned} & \omega^5 - k_2\omega^3 + k_4\omega = p_2\omega^3\cos(\omega\tau) \\ & - p_4\omega\cos(\omega\tau) + p_1\omega^4\sin(\omega\tau) \\ & - p_3\omega^2\sin(\omega\tau) + p_5\sin(\omega\tau) \\ & + q_1\omega^3\cos(2\omega\tau) - q_3\omega\cos(2\omega\tau) \\ & - q_2\omega^2\sin(2\omega\tau) + q_4\sin(2\omega\tau) \\ & - r_2\omega\cos(3\omega\tau) - r_1\omega^2\sin(3\omega\tau) \\ & + r_3\sin(3\omega\tau) \end{aligned} \quad (23)$$

Squaring and adding equation (22) and (23), we get,

$$\left(k_1\omega^4 - k_3\omega^2 + k_5\right)^2 + \left(\omega^5 - k_2\omega^3 + k_4\omega\right)^2 = H(\omega)$$

The expansion of the right hand side of equation (22) and (23) is cumbersome, therefore we represent it with $H(\omega)$, however, the computation is done on MATLAB and expressed in the appendix.

$$\omega^{10} + \left(k_1^2 - 2k_2\right)\omega^8 + \left(2k_4 + k_2^2 - 2k_1k_3\right)\omega^6 + \left(2k_1k_5 - 2k_2k_4 + k_3^2\right)\omega^4 + \left(k_4^2 - 2k_3k_5\right)\omega^2 + k_5^2 - H(\omega) = 0 \quad (24)$$

If $\varepsilon = \omega^2$, then (24) becomes

$$\varepsilon^5 + m_1\varepsilon^4 + m_2\varepsilon^3 + m_3\varepsilon^2 + m_4\varepsilon + m_5 - H(\omega) = 0 \quad (25)$$

Where,

$$\left.\begin{aligned} m_1 &= k_1^2 - 2k_2 \\ m_2 &= 2k_4 + k_2^2 - 2k_1k_3 \\ m_3 &= 2k_1k_5 - 2k_2k_4 + k_3^2 \\ m_4 &= k_4^2 - 2k_3k_4 \\ m_5 &= k_5^2 \end{aligned}\right\} \qquad (26)$$

Clearly, if $m_1 > 0, m_2 > 0, m_3 > 0, m_4 > 0$ and $m_5 > 0$ and $m_5 > H(\omega)$ are satisfied simultaneously, then by the Routh–Hurwitz criterion, equation (25) will always have roots with negative real part. This contradicts our assumption for instability that $\lambda = i\omega$ is a root of equation (21). Hence, the yellow fever endemic equilibrium of the system is locally asymptotically stable for $\tau>0$. This completes the proof.

population in figure 4.1, the infected human population in figure 4.2, the susceptible mosquito population in figure 4.3 and the infected mosquito population in figure 4.4, for different time delays. We also compared some parameters in the model in figures 4.5 to 4.7. We took the history to be integer values for all compartments. In essence, we choose $S_H = 10,\ I_H = 0,\ R_H = 0,\ S_M = 20,\ N_E = 100,\ N_H = 50$ and $I_M = 0.$

Parameters	Values
A	0.5 (assumed)
B	0.6
μ_H	0.035(assumed)
α_H	0.000035(assumed)
r_H	0.0095(assumed)
δ_H	0.143
p	0.15
μ_M	0.09
c	0.8
c_s	0.07

Computation of basic reproduction number

The basic reproduction number (R_0) is a term that describes the expected number of infections generated by one case in a susceptible population. R_0 is a threshold for stability of the yellow fever free equilibrium point. In order to compute the R_0, we substitute the parameter values in table with initial values for the variables $N_E = 100$ and $N_H = 50$ into equation 3.27, we get

$$R_0 = \frac{0.5}{0.09}\sqrt{\frac{0.6(0.8)(0.15)(100)(0.0095)(0.07)}{50(0.035)(0.035+0.000035+0.143)}}$$

$$R_0 = 0.68876$$

Successful computation gives 0.68876. This shows that the yellow fever free equilibrium point is locally asymptotically stable. Therefore, a few infected species introduced into a completely susceptible population will, on average fail to reproduce themselves, and the disease will not spread.

Recommendations and Future work

The difference between our proposed model and a non-time delayed model is in the precision of stability. A non-delay model does not pay attention or ignores the time difference between a susceptible human and an infected human.

We can also use a distributed delay by introducing the delay after exposure τ_1, the delay due to the minimum duration of the disease τ_2 and the delay due to the minimum time with immunity τ_3

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