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A Delayed Mathematical Model to Break the Life Cycle of Anopheles Mosquito

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Abstract

In this paper, we propose a delayed mathematical model to break the life cycle of anopheles mosquito at the larva stage by incorporating a time delay τ at the larva stage that accounts for the period of growth or development to pupa. We prove local stability of the system's equilibrium and find the critical values for Hopf bifurcation to occur. Also, we find that the system's equilibrium undergoes stability switching from stable to periodic to unstable and vice versa when the time delay τ crosses the imaginary axis from the left half plane to the right half plane in the (Re, Im) plane. Finally, we perform some numerical simulations and the results agree well with the analytical analysis. This is the first time such a model is proposed.

Keywords: Delayed model; Anopheles mosquito; Malaria Control; Hopf bifurcation; Larva; Stability analysis

2010 AMS subject classifications: 97U99.

1 Introduction

Every year, one to three million deaths is attributed to malaria parasite in sub-Saharan Africa out of which one third are children. Much work has been done to genetically modify mosquitoes in the laboratory to hinder the parasite from transmission thus, making the mosquitoes refractory. This can be achieved by inserting of genes at appropriate site to create stable germline. The progress in this area is fairly recent.

Malaria is a killer disease, is one of the leading causes of death in many parts of the world. Its devastating effect has persisted for many decades. Despite the longevity of the disease, malaria, which has been brought under control in some developed countries, still constitutes a major health menace in many developing countries, where most areas of high endemic reside. Some African countries, especially countries within sub-Saharan Africa, still feature among the leading areas of high malaria endemic in the world [21]. According to World Health Organization report [34], an estimated of about 225 million malaria clinical cases occurred in 2009, with an estimated 781,000 malaria mortalities. Although these statistics reflect a reduction compared to an estimated 243 million malaria cases, with an estimated 863,000 malaria deaths, 89% of which occurred in Africa in 2008 [35], the reduction is not sufficient. Generally, susceptibility to malaria is universal, that is, any person living in a country where malaria is prevalent is at risk of contracting the disease. However, the impact of malaria is greatest amongst children below five [36], where one in every five childhood deaths is due to the effects of the disease, among pregnant women, and among people from non-malarious regions.

Temperature is known to affect the life stages of the mosquito parasite [3]. There is a general consensus that future changes in climate may alter the prevalence and incidence of malaria; however, there are conflicting views among authors [20], [39], [40], [11]. However, some authors argued that climate and ecology are the main factors the severity of malaria and the difficulty in controlling it [12]. Other factors that have led to difficulties in controlling malaria are socio-economic conditions, population growth, urbanization, drug resistance, deficiencies in health care systems, poor sanitation, lack of information and education, water storage, garbage disposal, unpaved roads, and drainage systems that generate good breeding stagess for malaria transmission close to human settlements [14], [23], [32]. Thus, research in malaria that integrates the disease dynamics with breeding sites/life cycle properties of the vector and the different developmental stages of the parasite may provide novel insights toward disease control and eradication.

Although malaria is deadly, it can be cured by administering anti-malaria drugs. However, in endemic regions, the malaria parasite develops resistance to such drugs and there is no effective vaccine for malaria. Consequently, prevention is the only other option. Prevention can be achieved through the use of prophylactic drugs and vector control strategies. To advance, plan, design, and implement effective or better vector control measures, a clear understanding of mosquito population dynamics, the disease dynamics, and mosquito interaction with the human population is necessary. We introduce a new approach to the development of models for malaria transmission, wherein the mosquito vector is placed at the centre of the transmission process. Our objective is to develop a mathematical model for the dynamics of malaria transmission that takes into consideration the population dynamics of the malaria vector and how these vectors interact with the human population. To do that, an understanding of the vector population demography and dynamics is needed.

The malaria vector undergoes a complete metamorphosis, as it passes through four different life stages in its cycle: egg, larva, pupa and adult. The egg, larva and pupa stages are aquatic, while the adult stage is terrestrial. The entire cycle from egg laying to the emergence of the adult mosquito takes approximately 7-20 days, with 2-3 days spent in the egg stage, 4-10 days spent in the larva stage, and 2-4 days spent in the pupa stage [14]. While the average life span of the adult female mosquito ranges from 2-3 weeks, that of the males is approximately one week. As for the first three life stages, the life span of the adult mosquito depends on the species and ambient temperature. In addition to natural factors, survival of the adult female Anopheles mosquito also depends on its success in acquiring blood meals from humans. Therefore, in this research we propose a delayed model to break the life cycle at larva stage. To this end, we introduce a time delay τ at the larva compartment to account for the control measures (this can be bio-organism eg copecods or chemical substances). This is the firt such a delayed model is proposed.

2 Model derivation

In this section, we derive the delayed model from the life cycle of anopheles mosquito following the approached used in the paper by [22]. We make the following assumptions: The total population of anopheles mosquito is sub-divided into four compartments (Adults, Eggs, Larva, and Pupa). The birth rate b is constant and proportional to the total population b, there is a time delay τ in the growth or development to pupa at the larva stage cause by the introduction of control measures (can be natural enemy e.g bio-organisms or chemical substances) that can slow the growth process. Anopheles mosquito are assumed to transmit malaria only through direct contact.

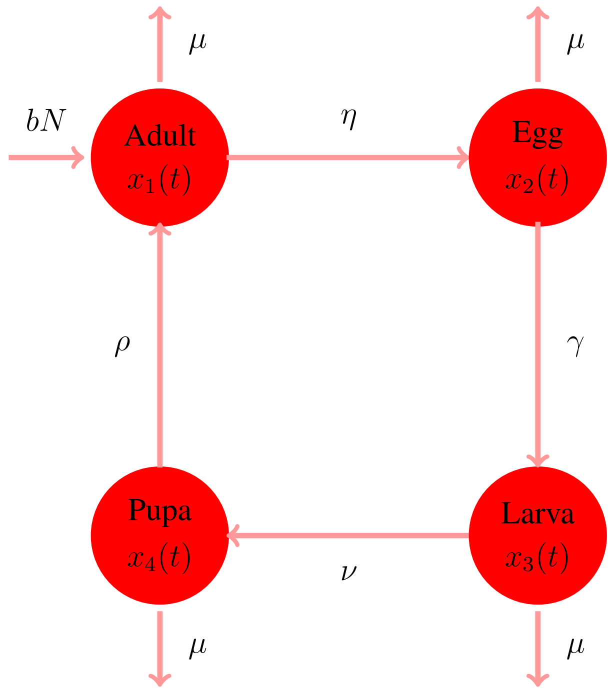


Figure 1: A flow chart of the life cycle of a mosquito

From the model assumptions and the flow chart in figure (1) above, we derive the following model. Let $x_1(t), x_2(t), x_3(t), x_4(t)$ be the number of Adult mosquitoes, Eggs, Larva, and Pupa at time t respectively. Then, the life cycle of anopheles mosquito is represented by the following model:

$$\begin{aligned} \dot{x}_1(t) &= bN - (\eta + \mu)x_1(t) + \rho x_4(t) \\ \dot{x}_2(t) &= \eta x_1(t) - (\gamma + \mu)x_2(t) \\ \dot{x}_3(t) &= \gamma x_2(t) - \nu x_3(t - \tau) - \mu x_3(t) \\ \dot{x}_4(t) &= \nu x_3(t - \tau) - (\rho + \mu)x_4(t) \end{aligned} \tag{1}$$

where b is the natural birth rate, η is the rate at which adult mosquitoes oviposit, μ is the natural death rate, γ is the rate at which the eggs hatch, ν is the rate at which larva develops to pupa, ρ is the rate at which pupa develops to adult mosquitoes. The initial data are $x_1(\theta) = \phi_1(\theta), x_2(\theta) = \phi_2(\theta), x_3(\theta) = \phi_3(\theta), x_4(\theta) = \phi_4(\theta))$ for $\tau \in [-\tau, 0]$, where $\phi = (\phi_1, \phi_2, \phi_3, \phi_4)^T \in C([-\tau, 0], \mathbb{R}^4)$ such that $\phi_i \geq 0, i = 1, 2, 3, 4$.

3 Local stability analysis

It is obvious that model (1) has a trivial equilibrium $E^0 = (bN/\mu, 0, 0, 0)$ and a unique positive non-trivial equilibrium $E^* = (x_1^*, x_2^*, x_3^*, x_4^*)$, where

$$x_1^* = \frac{b[(\rho+\mu)(\nu+\mu)N + \rho\nu]}{(\eta+\mu)(\rho+\mu)(\nu+\mu) - \rho\nu\gamma\eta}, \quad x_2^* = \frac{\eta x_1^*}{\gamma+\mu},$$

$$x_3^* = \frac{\gamma\eta x_1^* + b}{\nu+\mu}, \quad x_4^* = \frac{\nu(\gamma\eta x_1^* + b)}{(\nu+\mu)(\rho+\mu)}.$$

The characteristic polynomial equation for the linearised system 1 is

$$\lambda^4 + p_0\lambda^3 + p_1\lambda^2 + p_2\lambda + p_3 + (q_0\lambda^3 + q_1\lambda^2 + q_2\lambda + q_3)e^{-\lambda\tau} = 0, \tag{2}$$

where

$$\begin{aligned}
p_0 &= 4\,\mu + \rho + \gamma + \eta,\\
p_1 &= \mu\,(\rho + \gamma + \eta + 3\,\mu) + 2\,\eta\,\mu + \eta\,\gamma + 3\,\mu^2 + \eta\,\rho + 2\,\mu\,\rho + \gamma\,\rho + 2\,\mu\,\gamma,\\
p_2 &= \mu\,(2\,\eta\,\mu + \eta\,\gamma + 3\,\mu^2 + \eta\,\rho + 2\,\mu\,\rho + \gamma\,\rho + 2\,\mu\,\gamma) + \eta\,\gamma\,\rho + \mu^3\\
&\quad + \mu\,\gamma\,\rho + \mu^2\rho + \eta\,\mu^2 + \mu^2\gamma + \eta\,\mu\,\rho + \eta\,\gamma\,\mu,\\
p_3 &= \mu\,(\eta\,\gamma\,\rho + \mu^3 + \mu\,\gamma\,\rho + \mu^2\rho + \eta\,\mu^2 + \mu^2\gamma + \eta\,\mu\,\rho + \eta\,\gamma\,\mu)\,,\\
q_0 &= \nu, \quad q_1 = \nu\,(\rho + \gamma + \eta + 3\,\mu)\,,\\
q_2 &= \nu\,(\mu\,(\rho + \gamma + \eta + 2\,\mu) + \gamma\,\rho + \mu\,\gamma + \eta\,\mu + \eta\,\rho + \mu^2 + \mu\,\rho + \eta\,\gamma)\,,\\
q_3 &= \nu\,\mu\,(\gamma\,\rho + \mu\,\gamma + \eta\,\mu + \eta\,\rho + \mu^2 + \mu\,\rho + \eta\,\gamma)\,.
\end{aligned} \tag{3}$$

If $\tau = 0$ the characteristic equation 2 becomes

$$\lambda^4 + (p_0+q_0)\lambda^3 + (p_1+q_1)\lambda^2 + (p_2+q_2)\lambda + (p_3+q_3) = 0. \tag{4}$$

By Routh-Hurwitz condition, we have the following necessary and sufficient conditions for 4 to have roots with negative real part

$$\begin{aligned}
H_1 &= p_0 + q_0 > 0\\
H_2 &= (p_0+q_0)(p_1+q_1) - (p_2+q_2) > 0\\
H_3 &= (p_0+q_0)[(p_1+q_1)(p_2+q_2) - (p_0+q_0)(p_3+q_3)] - (p_2+q_1)^2 > 0\\
H_4 &= p_3 + q_3 > 0.
\end{aligned} \tag{5}$$

$$H_i > 0, \quad i = 1, 2, 3, 4. \tag{A2}$$

Lemma 3.1.
If A2 is satisfied, then the characteristic equation 4 have roots with negative real part.

The above result is true only when $\tau = 0$.

Now if $\tau > 0$, we let $\lambda = i\xi\ (\xi > 0)$ be a root of the characteristic equation 2, then

$$\xi^4 - ip_0\xi^3 - p_1\xi^2 + ip_2\xi + p_3 + (-iq_0\xi^3 - 2q_1\xi^2 + iq_2\xi + q_3)(\cos(\xi\tau) - i\sin(\xi\tau)) = 0. \tag{6}$$

Separating equation 6 into real and imaginary parts we have

$$\begin{array}{ll} \xi^4 - p_1\xi^2 + p_3 & = (q_1\xi^2 - q_3)\cos(\xi\ (\tau)) + (q_0\xi^3 - q_2\xi)\sin(\xi\ (\tau)), \\ -p_0\xi^3 + p_2\xi + & = (q_0\xi^3 - q_2\xi)\cos(\xi\ (\tau)) - (q_1\xi^2 - q_3)\sin(\xi\ (\tau)). \end{array} \tag{7}$$

Squaring both sides of 7 and adding we have the following

$$\xi^8 + s_0\xi^6 + s_1\xi^4 + s_2^2 + s_3 = 0, \tag{8}$$

where $s_0 = {p_0}^2 - {q_0}^2 - 2\,p_1,\ s_1 = 2\,p_3 + {p_1}^2 + 2\,q_0q_2 - {q_1}^2 - 2\,p_0p_2,$
$s_2 = -2\,p_1p_3 + 2\,q_1q_3 + {p_2}^2 - {q_2}^2,\ s_3 = {p_3}^2 - {q_3}^2$. Let $z = \xi^2$, then

$$z^4 + s_0z^3 + s_1z^2 + s_2z + s_3 = h(z). \tag{9}$$

From 9

$$\frac{dh(z)}{dz} = 4z^3 + 3s_0z^2 + 2s_1z + s_2 = g(z). \tag{10}$$

Let $y = z + \frac{s_0}{4}$ then $g(z) = 0$,

$$\Rightarrow y^3 + ay + b = 0, \tag{11}$$

where $a = \frac{8s_0 - 3s_0^2}{16},\ b = \frac{s_0^3 - 4s_0s_1 + 8s_2}{32}$.

By Cardano's theorem, we have

$$\begin{array}{ll} Q & = \frac{24s_1 - 9s_0^2}{144} \\ R & = \frac{216s_0s_1 - 432s_2 - 54s_0^3}{3456} \\ D & = Q^3 + R^2 \\ K_1 & = \sqrt[3]{R + \sqrt{D}} \\ K_2 & = \sqrt[3]{R - \sqrt{D}} \end{array} \tag{12}$$

and then

$$\begin{array}{ll} z_1 & = K_1 + K_2 - \frac{s_0}{4} \\ z_2 & = -\frac{K_1 + K_2}{2} - \frac{3s_0}{12} + \frac{i\sqrt{3}}{2}(K_1 - K_2) \\ z_3 & = -\frac{K_1 + K_2}{2} - \frac{3s_0}{12} - \frac{i\sqrt{3}}{2}(K_1 - K_2) \end{array} \tag{13}$$

Assume that $D > 0$, then the equation $g(z) = 0$ has one real root namely; $z_1^* = z_1$ and two complex conjugates, if $D = 0$, then all roots of $g(z) = 0$ are real and at least two are equal, namely; $z_1, z_2 = z_3$, where $z_2^* = \max\{z_1, z_2\}$, if $D < 0$, then all roots of $g(z) = 0$ are real and distinct, namely; z_1, z_2, z_3, where $z_3^* = \max\{z_1, z_2, z_3\}$.

According to Lemma 2.2 in Li and Hu [38], we have the following

Lemma 3.2.

1. *If $s_3 < 0$, then equation 9 has at least one positive root.*

2. *If $s_3 \geq 0$, then equation 9 has no positive root if and only if one of these conditions holds:*

$$(a)\ D > 0 \text{ and } z_1^* \leq 0;\ (b)\ D = 0 \text{ and } z_2^* \leq 0;\ (c)\ D < 0 \text{ and } z_3^* \leq 0.$$

3. *If $s_3 \geq 0$, then equation 9 has at least a positive root if and only if one of these conditions holds:*

$$(a)\ D > 0,\ z_1^* > 0, \text{ and } h(z_1^*) < 0;\ (b)\ D = 0,\ z_2^* > 0 \text{ and } h(z_2^*) < 0;$$
$$(c)\ D < 0\ z_3^* \leq 0 \text{ and } h(z_3^*) < 0.$$

Now, suppose that equation 9 have four postive real roots, given by $z_1,\ z_2,\ z_3,\ z_4$, then equation 8 also have positive real roots, namely; $\xi_1 = \sqrt{z_1},\ \xi_2 = \sqrt{z_2},\ \xi_3 = \sqrt{z_3},\ \xi_4 = \sqrt{z_4}$.

From 2, we find the critical time delay τ_0 as follows

$$\tau_n^j = \frac{1}{\xi}\left[\arctan\left\{-\frac{\omega\ (q_0\omega^6+(-q_0p_1-q_2+p_0q_1)\,\omega^4+(-p_0q_3+q_2p_1-p_2q_1+q_0p_3)\,\omega^2+p_2q_3-q_2p_3)}{(q_1-q_0p_0)\,\omega^6+(-q_3+q_2p_0+q_0p_2-q_1p_1)\,\omega^4+(q_3p_1+q_1p_3-q_2p_2)\,\omega^2-q_3p_3}\right\}+j\pi\right], \tag{14}$$

where $n = 1, 2, 3, 4,\ j = 0, 1, 2, ...$ Then (τ_n^j) are solutions of 6 and $\lambda = \pm i\xi_n$ are a pair of purely imaginary roots of 2 with $\tau = \tau_n^j$. We define

$$\tau_0 = \tau_{n_0}^0 = \min_{1\leq n\leq 4}\{\tau_n^0\},\ \xi_0 = \xi_{n_0},$$

where $n_0 \in \{1, 2, 3, 4\}$. Then τ_0 is the first value of τ such that 2 have purely imaginary roots.

Let $\lambda(\tau) = \alpha(\tau) \pm i\xi(\tau)$ be the root of 2, around $\tau = \tau_n^j$ satisfying $\alpha(\tau_n^j) = 0,\ \xi(\tau_n^j) = \xi_0(n = 1, 2, 3, 4,\ j = 0, 1, 2...)$.

Lemma 3.3.
Suppose $h^{'}(z_n) \neq 0$ $(n = 1, 2, 3, 4)$, where $h(z)$ is defined by 9, then the following transversality condition holds:

$$\frac{dRe\{\lambda(\tau)\}}{d\tau}\bigg|_{\tau=\tau_n^j} \neq 0. \tag{15}$$

Moreover, the sign of $\frac{dRe\{\lambda(\tau)\}}{d\tau}\bigg|_{\tau=\tau_n^j}$ is consistent with that of $h^{'}(z_n)$.

Theorem 3.1.
Suppose that A2 holds, we have the following:

1. *The quasi-polynomial 2 have roots with negative real parts and the steady state solution of system 1 is stable if $s_3 \geq 0$ and one of these conditions holds:*

   (a) $D > 0$ *and* $z_1^* \leq 0$; (b) $D = 0$ *and* $z_2^* \leq 0$; (c) $D < 0$ *and* $z_3^* \leq 0$.

2. *The quasi-polynomial 2 have roots with negative real parts and the steady state solution of system 1 is asymptotically stable if $\tau \in [0, \tau_0)0$ for $s_3 < 0$ or $s_3 \geq 0$ and one of these conditions holds:*

   (a) $D > 0,$ $z_1^* > 0,$ *and* $h(z_1^*) < 0$; (b) $D = 0,$ $z_2^* > 0$ *and* $h(z_2^*) < 0$;
   (c) $D < 0$ $z_3^* \leq 0$ *and* $h(z_3^*) < 0$.

3. *If the conditions in $(2.)$ hold and also $h^{'}(z_n) \neq 0$, then the system 1 have periodic solutions arising from the Hopf bifurcation at $\tau = \tau_n^j(n = 1, 2, 3, 4, j = 0, 1, 2...)$.*

In the figures below, we illustrate the above stability results and also numerically compute real part of the leading eigenvalue of the characteristic equation using traceDDE suite in MATLAB and plot the results in gnuplot. By varying the natural clearance rate μ, we investigate how stability changes in the τ, ν plane, and also the effects on the dynamical behaviour of the system.

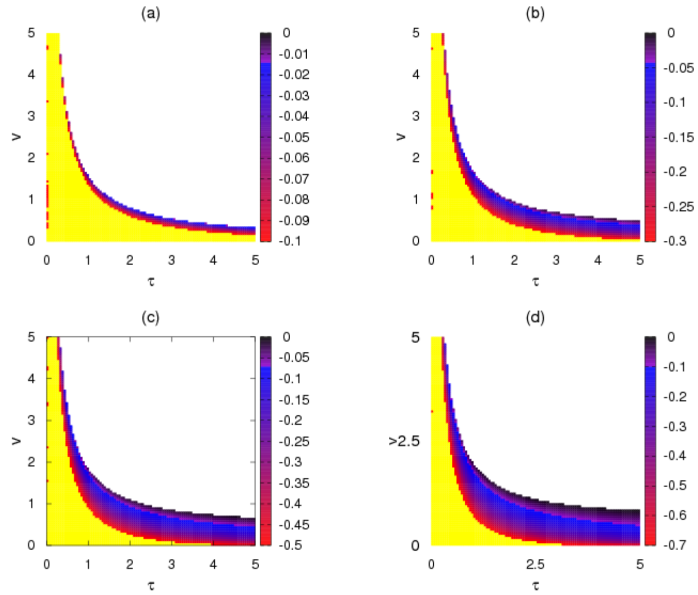
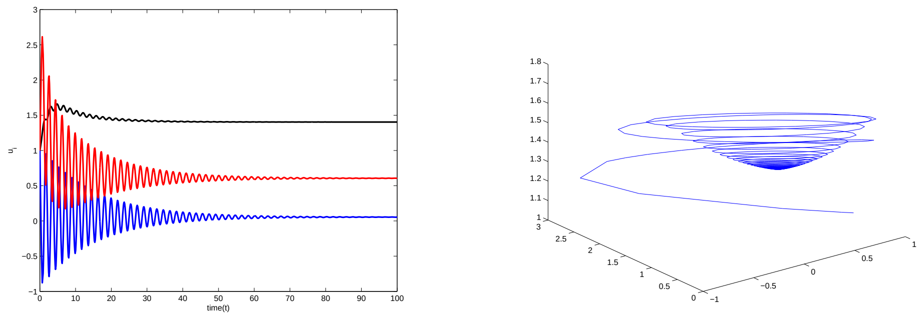


Figure 2: Stability charts: (a) $\mu = 0.1$, (b) $\mu = 0.3$, (c) $\mu = 0.5$, (d) $\mu = 0.7$. The color in the figures corresponds to the real part of the leading eigenvalue of the characteristic quasi-polynomial

From the figures above, we can see that μ played an important role in the dynamical behaviour of the system (1). The colors in the figures stand for: yellow "most stable region", red "more stable region", dark-violet "stable region", black "critical line or Hopf region" and the remaining area (white) corresponds to "unstable region". As μ increased, the dynamics of the system also increased in the (τ, ν) plane. Again, we observed that change in γ has similar system dynamics as above. Therefore, in general in the (τ, ν) plane, the overall dynamical behaviour of the system is determined by the parameters μ and γ.

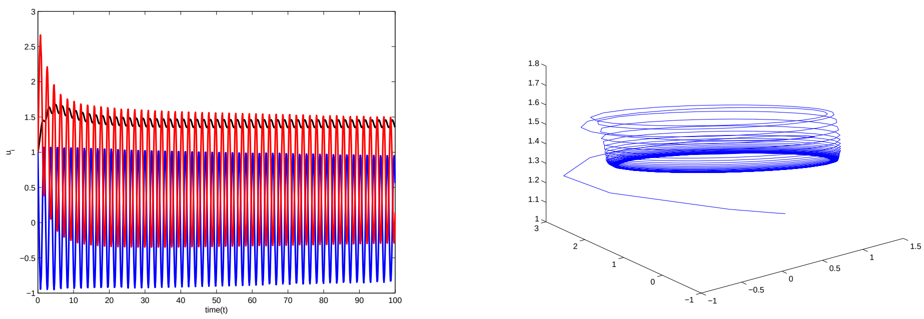
4 Numerical simulation

In this section, we present some numerical simulations using *dde23* suit in Matlab. We will show stable, periodic and unstable solutions as τ is varied. We have stability switches from stable to periodic to unstable and to stable as τ takes on the critical values τ_0 or as τ crosses the imaginary axis. In the first simulation, we take $\tau < \tau_0$, and we have stable solutions ($\tau = 0.45, \tau_0 = 0.85$).



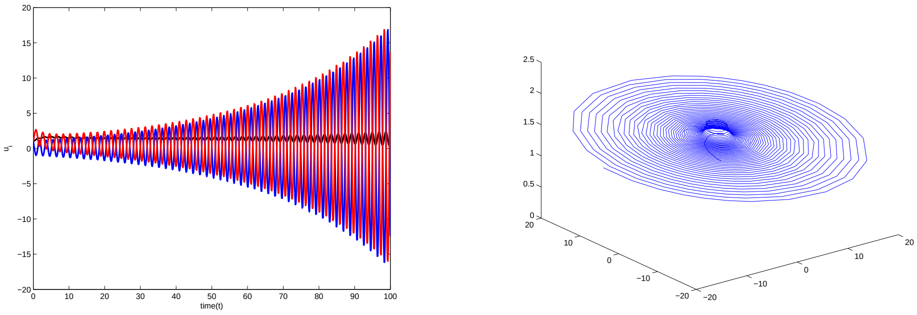
(a) (b)

Figure 3: stable solutions and phase portrait of system 1 for $\tau = 0.45$



(a) (b)

Figure 4: periodic solutions and phase portrait of system 1 for $\tau = 0.85$



(a) (b)

Figure 5: Unstable solutions and phase portrait of system 1 for $\tau = 0.95$

5 Conclusion

In this paper, we derived a mathematical model to break the life cycle of a mosquito that incorporate a time delay at the larva stage that accounts for the period of growth and development to pupa. We prove the local stability of the system's equilibrium and the critical values for Hopf bifurcation to occur. We find that the model undergoes stability switching from stable to periodic and to unstable when the time delay τ crosses the imaginary axis from the left half plane to the right half plane in the (Re, Im) plane. That is, the system's equilibrium E^* is stable if $\tau < \tau_0$ (see figure 3), if $\tau = \tau_0$, E^* loses its stability and a Hopf bifurcation occurs which means, a family of periodic solutions bifurcate from E^* (see figure 4). And if $\tau > \tau_0$, then E^* is unstable as seen in figure 5.

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