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## BIFURCATION ANALYSIS OF A VACCINATION MATHEMATICAL MODEL WITH APPLICATION TO COVID-19 PANDEMIC

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**Abstract.** In this research, we propose a delayed vaccination model with the application for predicting the evolution of infectious cases related to COVID-19 disease. The main purpose of this paper is to show the existence of Hopf bifurcation that can explain the multiple waves that the world witnessed this recent times. Therefore, it can be used the length between the doses for the vaccine that considered for different vaccines and its effect on the evolution of the infectious cases. It has been shown that the investigated model can undergo Hopf bifurcation in presence of delay time lags to the vaccine against a COVID-19, and can lead to the persistence of the disease. The obtained mathematical findings are checked using graphical representations with proper interpretations on the manner of controlling the outbreak of COVID-19 disease.

**Keywords:** COVID-19 disease; Hopf bifurcation; delayed system; vaccination.

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## 1. INTRODUCTION

The American Johns Hopkins University reported that the total number of coronavirus infections in the world has risen to more than 254.3 million, and the total deaths to more than 5.1 million. According to the university's data, the total number of cases of coronavirus in the world reached 254,317,843, and the total number of deaths was 5,114,140. The United States topped the list of countries in terms of the number of deaths due to the virus with 765,762 deaths, and the total number of infections in it reached 47,308,698.

The U.S. Food and Drug Administration (FDA) has granted emergency use approval for some COVID-19 vaccines in the United States and worldwide. The FDA has agreed to use the Pfizer-Bioentech vaccine to prevent COVID-19 in people aged more above 16. Lately, the FDE has issued an emergency use authorization for the Pfizer-BioEntech vaccine for COVID-19 that aged between 5 and 15.

Vaccination can prevent infected individuals to develop sever symptoms developing that can lead to death. In addition, the immunity acquired from the COVID-19 vaccine may be better than the immunity acquired when infected with COVID-19.

Indeed, persons that received vaccination can return to their activities without any fear of the dangers of being infected from COVID-19, and without using protection materials (masks as an example). The recent use of different vaccines is the reason behind returning to our natural lifestyle without feat from the outcome of not wearing masks and the fear of being infected. Therefore, vaccination helped us in facing the pandemic. Experts suggest an additional dose of the COVID-19 vaccine for individuals fully vaccinated who may not have had a strong enough immune response.

Numerous mathematical models have been used to predict the outbreak of COVID 19 disease, with different approaches. For example, in [13, 16], the authors considered an age-structured model for modeling the spread of COVID-19 disease. In [12] the authors considered a system of ODEs that considers the asymptomatic and symptomatic individuals and its effects of the spread of COVID-19 in the north African countries. Different other approaches have been used in the past two years to predict the effectiveness of measured considered by governments, such as the papers [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 14, 15, 17, 18, 19]. Due to the large number of

vaccines used by different countries in the past year, the effect of a vaccination strategy on the evolution of infectious cases is mandatory to determine the effectiveness of the disease. In this regard, we investigate a vaccination mathematical model for COVID-19 disease that studies its evolution in our community. Our starting point is the model considered by Najj and Mohsen in [1], which is formulated as:

$$(1) \quad \begin{aligned} \frac{dS}{dt} &= \Lambda + (1-p)A - \frac{\beta SI}{N} - (\mu + \psi)S + \theta V, \\ \frac{dV}{dt} &= \psi S - \frac{\sigma \beta VI}{N} - (\mu + \theta)V, \\ \frac{dI}{dt} &= pA + \frac{\beta SI}{N} + \frac{\sigma \beta VI}{N} - (\mu + \alpha)I, \\ \frac{dR}{dt} &= \alpha I - \mu R. \end{aligned}$$

Here,  $S(t)$ ,  $V(t)$ ,  $I(t)$  and  $R(t)$  represent to the susceptible, vaccination, infected and recovery respectively. They studied and discussed the stability analysis of the model (1) without delay. In this work, we modify this model and study the delayed effect of taking the vaccination against a COVID-19 pandemic. Indeed, the vaccine will take some time until becomes effective. This conduct can be obtained by changing the term  $\psi S(t)$  by  $\psi S(t - \tau)$ . This assumption is put due to the vaccination policy for different vaccines, where most of them must take more than a dose to get full immunity to the disease. Based on this consideration and motivated by the work above, we incorporate the vaccine delay into the model (1) and study the following delayed system:

$$(2) \quad \begin{aligned} \frac{dS}{dt} &= \Lambda + (1-p)A - \frac{\beta SI}{N} - \mu S - \psi S(t - \tau) + \theta V, \\ \frac{dV}{dt} &= \psi S(t - \tau) - \frac{\sigma \beta VI}{N} - (\mu + \theta)V, \\ \frac{dI}{dt} &= pA + \frac{\beta SI}{N} + \frac{\sigma \beta VI}{N} - (\mu + \alpha)I, \\ \frac{dR}{dt} &= \alpha I - \mu R. \end{aligned}$$

With the initial conditions

$$S(0) > 0, \quad V(v) > 0, \text{ for } v \in [-\tau, 0], \quad I(0) \geq 0, \quad R(0) \geq 0.$$

And all the parameters meanings are similar in [1], and  $\tau$  is the vaccination delay against COVID-19 pandemic. In the next section, the conditions for local symbiotically stability is discuss by Routh-Hurwitz method under  $\tau > 0$ . Also, By taking the vaccine delay  $\tau$  as the bifurcation parameter, the conditions for the occurrence of Hopf bifurcation are investigated in Section 3. Further, some numerical results are confierd out for our analytic results in Section 4. Finally, the paper ends with conclusion of the work.

## 2. STABILITY AND HOPF BIFURCATION ANALYSIS OF STEADY STATE POINTS

Based on the results in [1], we know the model (2) has two equilibrium points are namely by disease free point  $E_0 = (S_0, V_0, 0)$  and endemic point  $E^* = (S^*, V^*, I^*)$ , as well as, the  $E_0$  is local stable without delay ( $\tau = 0$ ), under the  $\mathcal{R}_0 < 1$ . While, if  $\mathcal{R}_0 > 1$  we know the  $E^*$  became stable without delay, for more detail see [1].

Here we will study the Hopf bifurcation occurrence when take ( $\tau > 0$ ) as the bifurcation parameter. Then, we can rewrite the jacobian matrix and the characteristic equation of model (2), near  $E_0$  in below.

$$(3) \quad J(E_0) = \begin{pmatrix} Q_1 - Q_2 e^{-\lambda\tau} & b_{12} & b_{13} \\ Q_2 e^{-\lambda\tau} & b_{22} & b_{23} \\ 0 & 0 & \mathcal{R}_0 \end{pmatrix}.$$

Such that

$$Q_1 = -\mu, \quad Q_2 = \psi, \quad \mathcal{R}_0 = \frac{\beta(S_0 + \sigma V_0)}{N} - (\mu + \alpha), \quad b_{12} = \theta, \quad b_{13} = \frac{-\beta S_0}{N}, \quad b_{22} = -(\mu + \theta), \quad b_{23} = \frac{-\sigma \beta V_0}{N}.$$

Clearly, the characteristic equation of (3) about  $E_0$  is given by

$$(4) \quad \lambda^3 + M_1 \lambda^2 + M_2 \lambda + M_3 + (N_1 \lambda^2 + N_2 \lambda + N_3) e^{-\lambda\tau} = 0$$

here

$$\begin{aligned}
M_1 &= -(Q_1 + b_{22} + \mathcal{R}_0), \\
M_2 &= Q_1(b_{22} + \mathcal{R}_0) + b_{22} + \mathcal{R}_0, \\
M_3 &= -Q_1(\mathcal{R}_0 b_{22}), \\
N_1 &= Q_2, \\
N_2 &= -Q_2(b_{22} + b_{12} + \mathcal{R}_0), \\
N_3 &= Q_2 \mathcal{R}_0 (b_{22} + b_{12}).
\end{aligned}$$

Clearly, in case  $\tau > 0$  we have that the equation (4) has at least a pair of purely imaginary roots represented by  $\lambda = i\varpi$  in equation (4) and separating the real from imaginary parts, which gives in below results

$$\begin{aligned}
(5) \quad & cc(N_1\varpi^2 - N_3)\text{Sin}\varpi\tau + N_2\varpi\text{Cos}\varpi\tau = \varpi^3 - M_2\varpi, \\
& (N_3 - N_1\varpi^2)\text{Cos}\varpi\tau + N_2\varpi\text{Sin}\varpi\tau = M_1\varpi^2 - M_3.
\end{aligned}$$

Now, if squaring equations (5) and adding them, we get

$$(6) \quad \varpi^6 + h_1\varpi^4 + h_2\varpi^2 + h_3 = 0,$$

where

$$\begin{aligned}
h_1 &= Q_1^2 - Q_2^2 + b_{22}^2 + \mathcal{R}_0^2, \\
h_2 &= M_2^2 - N_2^2 - 2M_1M_3 + 2N_1N_3, \\
h_3 &= M_3^2 - N_3^2.
\end{aligned}$$

Putting  $K = \varpi^2$ , then equation (6) became

$$(7) \quad K^3 + h_1K^2 + h_2K + h_3 = 0.$$

According to Descartes rule of sign there is a unique positive root say  $\varpi_0$  satisfying equation (7). That is equation (6) has a positive root  $\varpi_0$ . Thus, equation (4) has at least a pair of purely imaginary roots  $i\varpi_0$  corresponding to the time delay  $\tau$ .

Obviously, when substituting  $\bar{\omega}_0$  in equation (5) and solving with simplified the result of system for  $\tau$ , we have

$$(8) \quad \tau_j = \frac{1}{\bar{\omega}_0} \text{Cos}^{-1} \frac{(N_2 - N_1 M_1) \bar{\omega}_0^4 + (M_1 N_3 + M_3 N_1 - N_2 M_2) \bar{\omega}_0^2 - M_3 N_3}{N_1^2 \bar{\omega}_0^4 + (N_2^2 - 2N_1 N_3) \bar{\omega}_0^2 + N_3^2} + \frac{2j\pi}{\bar{\omega}_0}, \quad j = 0, 1, 2, \dots$$

Next, we discuss the stability of the endemic equilibrium point of model (2). Then, we can evaluating the jacobian matrix and the characteristic equation near  $E^*$  in below.

$$(9) \quad J(E^*) = \begin{pmatrix} D_1 - D_2 e^{-\lambda\tau} & c_{12} & c_{13} \\ D_2 e^{-\lambda\tau} & c_{22} & c_{23} \\ c_{31} & c_{32} & c_{33} \end{pmatrix}.$$

Such that

$$D_1 = -\left(\frac{\beta I^*}{N} + \mu\right), \quad D_2 = \psi, \quad c_{12} = \theta, \quad c_{13} = \frac{-\beta S^*}{N}, \quad c_{22} = -\frac{\sigma \beta I^*}{N} - (\mu + \theta), \quad c_{23} = \frac{-\sigma \beta V^*}{N}, \\ c_{31} = \frac{\beta I^*}{N}, \quad c_{32} = \frac{\sigma \beta I^*}{N}, \quad c_{33} = \frac{\beta(S^* + \sigma V^*)}{N} - (\mu + \alpha).$$

Clearly, the characteristic equation of (9) about  $E^*$  is given by

$$(10) \quad \lambda^3 + \tilde{M}_1 \lambda^2 + \tilde{M}_2 \lambda + \tilde{M}_3 + (\tilde{N}_1 \lambda^2 + \tilde{N}_2 \lambda + \tilde{N}_3) e^{-\lambda\tau} = 0$$

here

$$\begin{aligned} \tilde{M}_1 &= -(D_1 + c_{22} + c_{33}), \\ \tilde{M}_2 &= D_1(c_{22} + c_{33}) - c_{13}c_{31} + c_{22}c_{33} - c_{23}c_{32}, \\ \tilde{M}_3 &= D_1(c_{23}c_{32} - c_{22}c_{33}) - c_{12}c_{23}c_{31} + c_{22}c_{13}c_{31}, \\ \tilde{N}_1 &= D_2, \\ \tilde{N}_2 &= -D_2(c_{22} + c_{33} + c_{12}), \\ \tilde{N}_3 &= D_2(c_{33}(c_{22} + c_{12}) - c_{32}(c_{13} + c_{23})). \end{aligned}$$

Clearly, in case  $\tau > 0$  we have that the equation (10) has at least a pair of purely imaginary roots represented by  $\lambda = i\tilde{\omega}$  in equation (10) and separating the real from imaginary parts, which gives in below results

$$(11) \quad \begin{aligned} (\tilde{N}_1 \tilde{\omega}^2 - \tilde{N}_3) \text{Sin} \tilde{\omega} \tau + \tilde{N}_2 \tilde{\omega} \text{Cos} \tilde{\omega} \tau &= \tilde{\omega}^3 - \tilde{M}_2 \tilde{\omega}, \\ (\tilde{N}_3 - \tilde{N}_1 \tilde{\omega}^2) \text{Cos} \tilde{\omega} \tau + \tilde{N}_2 \tilde{\omega} \text{Sin} \tilde{\omega} \tau &= \tilde{M}_1 \tilde{\omega}^2 - \tilde{M}_3. \end{aligned}$$

By squaring equations (11) and adding them, we get

$$(12) \quad \tilde{\omega}^6 + \tilde{h}_1 \tilde{\omega}^4 + \tilde{h}_2 \tilde{\omega}^2 + \tilde{h}_3 = 0,$$

where

$$\begin{aligned} \tilde{h}_1 &= D_1^2 - D_2^2 + c_{22}^2 + c_{33}^2 + 2(c_{13}c_{31} + c_{23}c_{32}), \\ \tilde{h}_2 &= \tilde{M}_2^2 - \tilde{N}_2^2 - 2(\tilde{M}_1\tilde{M}_3 + \tilde{N}_1\tilde{N}_3), \\ \tilde{h}_3 &= \tilde{M}_3^2 - \tilde{N}_3^2. \end{aligned}$$

Putting  $\kappa = \tilde{\omega}^2$  in equation (12) we get

$$(13) \quad \kappa^3 + \tilde{h}_1 \kappa^2 + \tilde{h}_2 \kappa + \tilde{h}_3 = 0.$$

Clearly, by help the Descartes rule of sign there is a unique positive root say  $\tilde{\omega}_0$  satisfying equation (12). That is equation (11) has a positive root  $\tilde{\omega}_0$ . Thus, equation (9) has at least a pair of purely imaginary roots  $i\tilde{\omega}_0$  corresponding to the time delay  $\tau$ .

Obviously, when substituting  $\tilde{\omega}_0$  in equation (10) and solving with simplified the result of system for  $\tau$ , we have

$$(14) \quad \tau_j = \frac{1}{\tilde{\omega}_0} \text{Cos}^{-1} \frac{(\tilde{N}_2 - \tilde{N}_1 \tilde{M}_1) \tilde{\omega}_0^4 + (\tilde{M}_1 \tilde{N}_3 + \tilde{M}_3 \tilde{N}_1 - \tilde{N}_2 \tilde{M}_2) \tilde{\omega}_0^2 - \tilde{M}_3 \tilde{N}_3}{\tilde{N}_1^2 \tilde{\omega}_0^4 + (\tilde{N}_2^2 - 2\tilde{N}_1 \tilde{N}_3) \tilde{\omega}_0^2 + \tilde{N}_3^2} + \frac{2j\pi}{\tilde{\omega}_0}, \quad j = 0, 1, 2, \dots$$

Hence, define that the value of time delay when  $j = 0$ , we have  $\tau_0 = \min_{j \geq 0} \tau_j$ , then  $\lambda(\tau) = \gamma(\tau) + i\tilde{\omega}(\tau)$  be a root of equation (9), such that  $\gamma(\tau_0) = 0$  and  $\tilde{\omega}(\tau_0) = \tilde{\omega}_0$ . Then we have the following theorem.

**Theorem** The roots of the characteristic equation (9), satisfy the following transversality condition hold

$$(15) \quad \left[ \frac{d(\text{Re}\lambda(\tau))}{d\tau} \right]_{\tau=\tau_0} \neq 0,$$

under

$$(16) \quad \tilde{M}_2^2 - \tilde{N}_2^2 - 2(\tilde{M}_1\tilde{M}_3 + \tilde{N}_1\tilde{N}_3) > 0.$$

**Proof:** By using  $\lambda(\tau)$  in equation (9) and differentiating the result equation with respect to  $\tau$ , we get that

$$(17) \quad \left\{ 3\lambda^2 + 2\tilde{M}_1\lambda + \tilde{M}_2 + (2\tilde{N}_1\lambda + \tilde{N}_2)e^{-\lambda\tau} - \tau(\tilde{N}_1\lambda^2 + \tilde{N}_2\lambda + \tilde{N}_3)e^{-\lambda\tau} \right\} \frac{d\lambda}{d\tau} = \lambda(\tilde{N}_1\lambda^2 + \tilde{N}_2\lambda + \tilde{N}_3)e^{-\lambda\tau}.$$

Thus

$$(18) \quad \left( \frac{d\lambda}{d\tau} \right)^{-1} = \frac{3\lambda^2 + 2\tilde{M}_1\lambda + \tilde{M}_2}{-\lambda(\lambda^3 + \tilde{M}_1\lambda^2 + \tilde{M}_2\lambda + \tilde{M}_3)} + \frac{2\tilde{N}_1\lambda + \tilde{N}_2}{\lambda(\tilde{N}_1\lambda^2 + \tilde{N}_2\lambda + \tilde{N}_3)} - \frac{\tau}{\lambda}.$$

Since,  $\lambda = i\tilde{\omega}_0$  at  $\tau = \tau_0$ , then equation (18) can be rewrite in below

$$(19) \quad \left( \frac{d\lambda}{d\tau} \right)^{-1} = \frac{-3\tilde{\omega}_0^2 + 2\tilde{M}_1i\tilde{\omega}_0 + \tilde{M}_2}{i\tilde{\omega}_0(i\tilde{\omega}_0^3 + \tilde{M}_1\tilde{\omega}_0^2 - \tilde{M}_2i\tilde{\omega}_0 - \tilde{M}_3)} + \frac{2\tilde{N}_1i\tilde{\omega}_0 + \tilde{N}_2}{i\tilde{\omega}_0(\tilde{N}_2i\tilde{\omega}_0 + \tilde{N}_3 - \tilde{N}_1\tilde{\omega}_0^2)} - \frac{\tau_0}{i\tilde{\omega}_0}.$$

As well as, if

$$(20) \quad \operatorname{sgn} \left[ \frac{d(\operatorname{Re}\lambda)}{d\tau} \right]_{\tau=\tau_0} = \operatorname{sgn} \left[ \operatorname{Re} \left( \frac{d\lambda}{d\tau} \right)^{-1} \right]_{\lambda=i\tilde{\omega}_0}.$$

Accordingly, from the fact

$$\begin{aligned} \operatorname{Re} \left[ \frac{3\lambda^2 + 2\tilde{M}_1\lambda + \tilde{M}_2}{-\lambda(\lambda^3 + \tilde{M}_1\lambda^2 + \tilde{M}_2\lambda + \tilde{M}_3)} \right] &= \frac{2\tilde{M}_1(\tilde{M}_1\tilde{\omega}_0^2 - \tilde{M}_3) - (\tilde{M}_2 - 3\tilde{\omega}_0^2)(\tilde{\omega}_0^2 - \tilde{M}_2)}{\tilde{\omega}_0^2(\tilde{\omega}_0^2 - \tilde{M}_2)^2 + (\tilde{M}_1\tilde{\omega}_0^2 - \tilde{M}_3)^2}, \\ \operatorname{Re} \left[ \frac{2\tilde{N}_1\lambda + \tilde{N}_2}{\lambda(\tilde{N}_1\lambda^2 + \tilde{N}_2\lambda + \tilde{N}_3)} \right] &= \frac{2\tilde{N}_1(\tilde{N}_3 - \tilde{N}_1\tilde{\omega}_0^2) - \tilde{N}_2^2}{\tilde{N}_2^2\tilde{\omega}_0^2 + (\tilde{N}_3 - \tilde{N}_1\tilde{\omega}_0^2)^2}, \\ \operatorname{Re} \left[ \frac{\tau}{\lambda} \right] &= \operatorname{Zero}. \end{aligned}$$

So, we can write it in the following

$$(21) \quad \left[ \operatorname{Re} \left( \frac{d\lambda}{d\tau} \right) \right]_{\tau=\tau_0}^{-1} = \frac{2\tilde{M}_1(\tilde{M}_1\tilde{\omega}_0^2 - \tilde{M}_3) - (\tilde{M}_2 - 3\tilde{\omega}_0^2)(\tilde{\omega}_0^2 - \tilde{M}_2)}{\tilde{\omega}_0^2(\tilde{\omega}_0^2 - \tilde{M}_2)^2 + (\tilde{M}_1\tilde{\omega}_0^2 - \tilde{M}_3)^2} + \frac{2\tilde{N}_1(\tilde{N}_3 - \tilde{N}_1\tilde{\omega}_0^2) - \tilde{N}_2^2}{\tilde{N}_2^2\tilde{\omega}_0^2 + (\tilde{N}_3 - \tilde{N}_1\tilde{\omega}_0^2)^2}.$$

It easy to see that, equation (21) dose not equal zero if and only if the condition (15) is hold. Hence, the obtained result shows that the eigenvalue equation (9) crosses the imaginary axis from left to right as  $\tau$  passes through  $\tau_0$ . Then model (2) losses it is stability near  $E^*$  and undergoes the Hopf bifurcation when  $\tau = \tau_0$ .



### 3. NUMERICAL SIMULATION

In this section we check our computation, we perform some numerical simulations. We choose a set of hypothetical parameters as follows

$$(22) \quad \Lambda = 500, A = 25, \psi = 0.22, \beta = 0.1, \mu = 0.1, p = 0.1, \alpha = 0.2, \theta = 0.05, \sigma = 0.1.$$

For the parameter, the trajectory of model (2) converges to the stable to  $E^*$  at  $\tau = 11 < \tau_0 = 14.3$ ; converges to the periodic at  $\tau = 14.3 = \tau_0$  see Figures (1) and (2) respectively. Again the trajectory of model (2) converges to increasing the periodic at  $\tau = 15 > \tau_0$ , see Figure (3). Now, if we take the values of  $\beta = 0.01, p = 0$  and  $\tau = 11$ , with keep the other parameters in equation (22) we get the trajectory of model (2) converges to the stability to  $E_0$ ; a periodic at  $\tau = 14.3 = \tau_0$  see Figures (4) and (5) respectively.

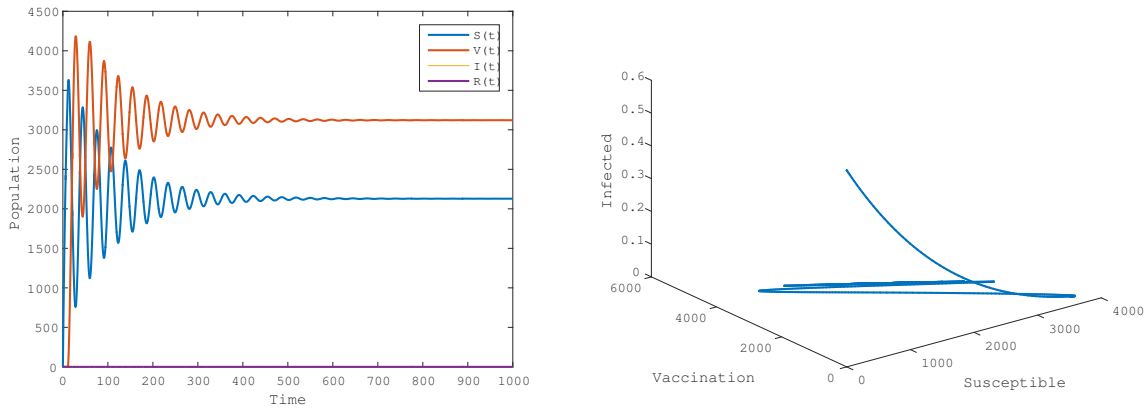


FIGURE 1. The solution and the phase trajectories of the model (2) to  $E_0$  before Hopf bifurcation occurs  $\tau = 11$ .

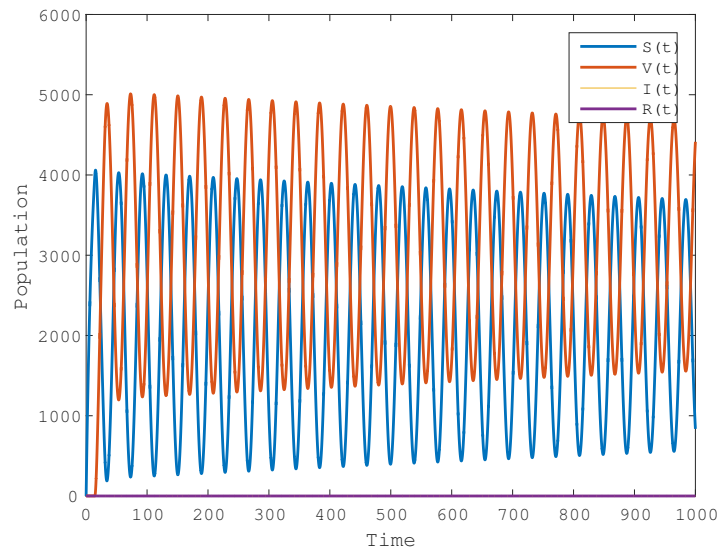


FIGURE 2. The solution and the phase trajectories of the model (2) to  $E_0$  after Hopf bifurcation occurs  $\tau = 14.3$ .

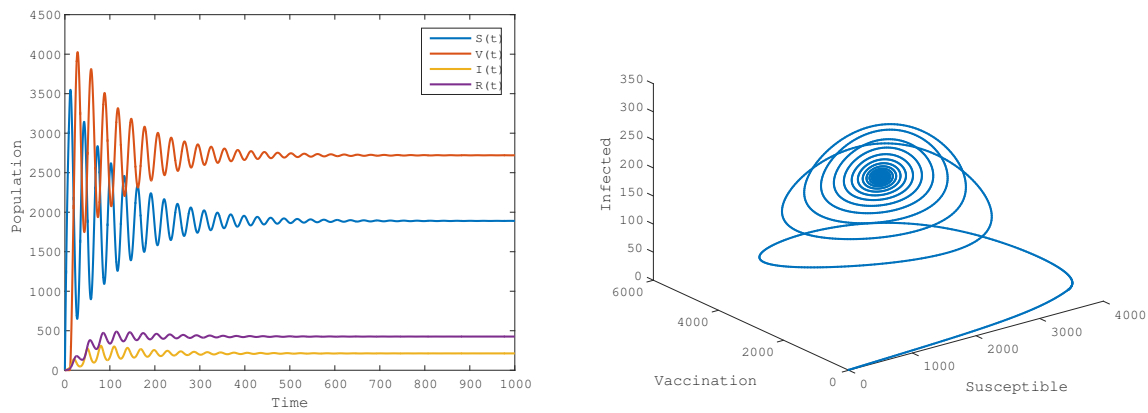


FIGURE 3. The solution and the phase trajectories of the model (2) to  $E^*$  before Hopf bifurcation occurs  $\tau = 11$ .

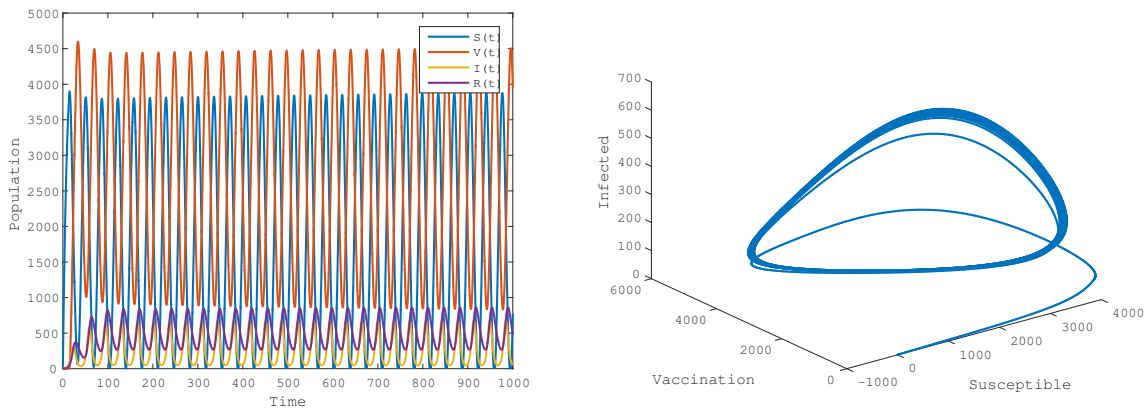


FIGURE 4. The solution and the phase trajectories of the model (2) to  $E^*$  after Hopf bifurcation occurs  $\tau = 14.3$ .

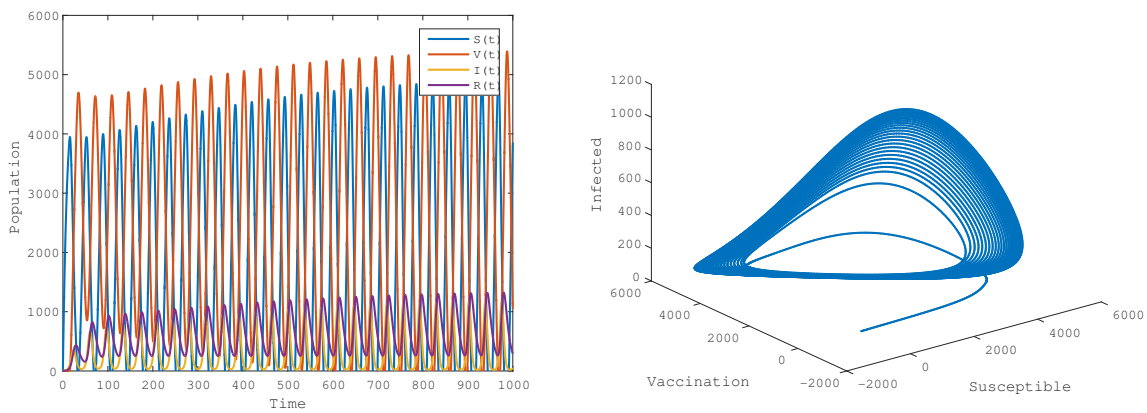


FIGURE 5. The solution and the phase trajectories of the model (2) to  $E^*$  before Hopf bifurcation occurs  $\tau = 15$ .

#### **4. CONCLUSION AND RESULTS**

In this manuscript we discussed the impact of delay in vaccination on COVID-19 and proved that large delay will leads the extinction of disease while for small delay the persistence observed. For this The we provided the Hopf bifurcation analysis of the suggested model and highlighted the importance of the vaccine against a COVID-19 virus spread. It has been shown that the investigated model can undergo Hopf bifurcation in presence of delay time lags to vaccine against a COVID-19, about for all the possible equilibrium points. The obtained theoretical results are checked using numerical simulations with a brief discussion on the biological relevance.

#### **AUTHORS' CONTRIBUTIONS**

The authors declare that the study was realized in collaboration with equal responsibility. All authors read and approved the final manuscript.

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#### **CONFLICT OF INTERESTS**

The authors declare that there is no conflict of interests.

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