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A DYNAMICAL ANALYSIS OF THE VIRUS REPLICATION EPIDEMIC MODEL

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Abstract. In this article, the stability and the computational algebraic properties of a virus replication epidemic model is investigated. The model is represented by a three dimensional dynamical system with six parameters. The conditions for the existence of Hopf bifurcation in the system are given. Then, the model with the Beddington-DeAngelis functional response instead of the original nonlinear response function has been studied in order to understand the effect of the Beddington-DeAngelis functional response on the qualitative properties of the system. The stability of the systems at the singular points is investigated and the conditions for the systems to have the analytic first integrals and Hopf bifurcation are given. Finally, the results are illustrated by giving numerical examples.

Keywords: epidemic model, stability, analytic first integral, algebraic invariant, Hopf bifurcation.

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1. Introduction

An interesting epidemic model for the spread of disease is the Susceptible-Infected-Recovered (SIR) model which models the interaction between the susceptible (S) population which are susceptible to the virus, the infected (I) population which are infected by the virus and are infectious and the recovered (R) population which are recovered and gained immunity. In 1927, Kermack and McKendrick proposed a model to predict the number of people infected by a contagious illness, i.e. plague in a closed population over time in London during 1665-1666 and in Bombay in 1906 and another contagious illness,i.e. cholera in London 1865. This model stands as one of the first implementations of the SIR model and is referred to as the Kermack-McKendrick model[1].

Evolutionary relations between the parameters of the SIR model were investigated by Anderson and May by developing the models and fitting data[2, 3]. The periodicity and the stability properties in epidomiological models were studied by Hethcote et.al.[4, 5]. Smith showed that a period two bifurcation occurs for the SIR model when the contact rate parameter exceeds a threshold value[6]. In 1994, Kuznetsov and Piccardi studied the

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bifurcations of the periodic solutions of the SIR model with parameter portrait[7]. The stability and bifurcation properties of the endemic equilibria of a generalized SIR model were studied by Huang et.al.[8]. of In 1998, pulse vaccination was studied as an application of the SIR model and shown that the infected population converges to zero at a stable equilibrium point[9]. Lyapunov and global stability properties of the SIR model and its generalizations were investigated in 2002[10].

The SIR model and its generalizations have been investigated with delay[11, 12, 13, 14, 15, 16] or without delay[17, 18, 19, 20]. Beretta and Takeuchi studied the stability properties of an SIR epidemic model with time delays when the present force of infection depends on the number of the past infectives[21]. In this work they have shown that a disease free equilibrium state exists if there is no endemic equilibrium and if it exists, it is stable. In a more recent work, Ma et.al. gave the length of the time delay provided that the endemic equilibrium is global asymptotically stable by using the method by Freedman et.al.[22] to obtain the eventual lower bound[23]. Xu et.al. proposed a SIR epidemic model with nonlinear incidence and time delay and partially obtained the global stability of the endemic equilibrium for some given case[24]. Later, McCluskey enhanced this analysis to fully determine the global asymptotically stability of the endemic equilibrium whenever it exists[25]. Sun et. al. investigated the Hopf bifurcation for a virus infection model with an immune delay and two intracellular delays[26].

The SIR model is given by the following system[1]

$$\begin{aligned}\frac{dS}{dt} &= -\frac{\beta IS}{N},\\ \frac{dI}{dt} &= \frac{\beta IS}{N} - \gamma I,\\ \frac{dR}{dt} &= \gamma I\end{aligned} \tag{1}$$

where S, I and R denote the numbers of the susceptible, the infected and the recovered population at time t, respectively. The parameter β denotes the infection rate and γ denotes the recovery rate. The parameters are assumed to be nonnegative. In the original SIR model no birth or death, i.e. no addition or removal of nodes from the population are assumed. However in real life, when the virus is fatal the node can not gain immunity and dies. Therefore, the node does not become susceptible again and has to be removed from the population. For this reason, the generalizations of the SIR model representing more realistic applications have to be taken into consideration.

In 1996, Nowak and Bangham presented a general framework to find the relationship between the immune responses, the abundance of the virus and the virus diversity for a generalized epidemic model of persistent viruses[27]. In this work they have proposed a generalized epidemic model to show the interaction between a replicating virus and the host cells. The model contains three differential equations representing susceptible cells, infected cells and free virus particles. Here, free virus particles are replicated by the susceptible cells. The model is often known to represent the dynamics of host-parasite interactions of the persistent viruses such as HIV, HBV, etc. They have presented the stability of the equilibria of the model. However, they have not performed a Hopf bifurcation analysis which often arise in population models and describe many important characteristics of the biological systems. In this work, Hopf bifurcation analysis for the model with the help of a new approach involving algebraic invariants are performed. Also, the model with the Beddington-DeAngelis functional response is investigated. This functional response was introduced by Beddington[28] and DeAngelis[29] independently to model parasite-host interactions in predator-prey systems. The Beddington-DeAngelis functional response presents a more realistic consumption of predator over prey. Hence, it is interesting to study the Hopf bifurcation properties of the virus replication epidemic model with the Beddington-DeAngelis functional response.

In section 1, results on the stability of the equilibria and Hopf bifurcation analysis for the epidemic model with virus replication are presented and results are illustrated by giving a numerical example. In section 2, the same analyses is performed by replacing the simple nonlinear functional response with the Beddington-DeAngelis type nonlinear functional response in the model. We present our findings in comparison with the classic virus replication model.

2. The virus replication epidemic model

The epidemic model containing replication of the virus is given as[30, 31, 27]

$$\begin{aligned}\frac{dx}{dt} &= N - ax - bxz\\ \frac{dy}{dt} &= bxz - cy\\ \frac{dz}{dt} &= dy - ez.\end{aligned} \tag{2}$$

Here, N is the constant population and a is the death rate of the uninfected population, b is the infection rate, c is the death rate of the infected population, d is the production rate and e is the decline rate of the recovered population which contains the free virus. All parameters are assumed to be positive to represent physical values.

Theorem 2.1. *System (2) has at least one stable equilibrium.*

Proof. The equilibria of system (2) are $E_1(\frac{N}{a}, 0, 0)$ and $E_2(\frac{ce}{bd}, \frac{bdN-ace}{bcd}, \frac{bdN-ace}{bce})$ and the Jacobian matrix is

$$\begin{pmatrix} -a-bz & 0 & -bx \\ bz & -c & bx \\ 0 & d & -e \end{pmatrix}.$$

The eigenvalues of the Jacobian matrix at E_1 are $-a$ and $-\frac{c+e}{2} \pm \frac{\sqrt{a(4bdN+a(c-e)^2)}}{2a}$. Hence, E_1 is a stable equilibrium point.

Since we are not able to calculate the eigenvalues of the Jacobian at the equilibrium E_2 by linear stability analysis, the Routh-Hurwitz criterion[32] is applied. The characteristic polynomial of the Jacobian matrix at E_2 is

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0$$

where

$$\begin{aligned} A &= \frac{bdN}{ce} + c + e,\\ B &= \frac{bdN(c+e)}{ce},\\ C &= bdN - ace. \end{aligned}$$

We conclude that if $N > \frac{ace}{bd}$, then E_2 is also a stable equilibrium point. □

Now we look for the algebraic invariants and possible existence of Hopf bifurcation on the invariant planes of system (2)[33]. We reduce the flow on the invariant plane since the computations are to heavy and we need to impose some conditions on parameters to perform further qualitative analysis of the system. Instead of performing numerical analysis, i.e. choosing some parameters randomly, we look for conditions when the system has simpler geometric structure-admits an invariant surface or first integral and then study the obtained subsystem in more detail. Many systems with complex behavior such as a chemical reaction system[34], a two prey-one predator system[35], the May-Leonard model[36] and a gene model[37] have been investigated with the help of the method of algebraic invariants.

Remark 2.1. *In system* (2) *Hopf bifurcation occurs at* E_1 *if* $c = -e$ *and* $4bdN + a(c-e)^2 < 0$. *However, at* E_2 *we can not find eigenvalues. Hence, it is possible to study Hopf bifurcation for the reduced system on the invariant plane, to find Hopf bifurcation for the three dimensional system.*

We use the following approach to obtain the conditions in Theorem 2.3. In similar, we also obtain the conditions for the existence of the first integral of system (2) which are listed in Theorem 2.4. Let

$$f_1(x_1, ..., x_n) = 0, ..., f_k(x_1, ..., .x_n) = 0 \qquad (A)$$

be a polynomial system and let $I = \langle f_1, ..., f_k \rangle \subset k[x_1, ..., x_n]$ be the corresponding with the implicit ordering of the variables $x_1 > ... > x_n$.

Definition 2.1. *Let* I *be an ideal in* $k[x_1, ..., x_n]$ *and fix* $m \in \{0, ..., n-1\}$. *The m-th elimination ideal of* I *is the ideal* $I_m = I \cap k[x_{m+1}, ..., x_n]$.

To eliminate $x_1, ..., x_m (0 \leq m < n)$ from system (A) one can use the following theorem (see [33] for the proof).

Theorem 2.2. *(Elimination Theorem). Fix the lexicographic term order on the ring* $k[x_1, ..., x_n]$ *with* $x_1 > x_2 > ... > x_n$ *and let* G *be a Groebner basis for an ideal* I *of* $k[x_1, ..., x_n]$ *with respect to this order. Then for every* m, $0 \leq m \leq n-1$, *the set* $G_m := G \cap k[x_{m+1}, ..., x_n]$ *is a Groebner basis for the m-th elimination ideal* I_m.

Using the Elimination Theorem we can determine the invariant algebraic surfaces of the form

$$L = a_0 + a_1 x + a_2 y + a_3 z + a_4 xy + a_5 xz + a_6 yz \tag{3}$$

of system (2).

Consider the system

$$\dot{x} = P(x, y, z), \qquad \dot{y} = Q(x, y, z), \qquad \dot{z} = R(x, y, z). \tag{4}$$

Let

$$\mathfrak{D} := \frac{\partial}{\partial x} P(x, y, z) + \frac{\partial}{\partial y} Q(x, y, z) + \frac{\partial}{\partial z} R(x, y, z)$$

be the vector field associated to (4) and let L be a polynomial in the variables x, y, z. The polynomial L defines an invariant algebraic surface $L = 0$ of system (4) if

$$\mathfrak{D} L = LK$$

for some polynomial $K(x, y, z)$. The polynomial K is called the cofactor of L and has degree at most $n-1$, if the maximal degree of the polynomials P, Q and R is n. Since the polynomials on the right hand side of system (2) are of degree at most 2 we look for the cofactors of the form $K = b_0 + b_1 x + b_2 y + b_3 z$ and the invariant algebraic surfaces of the form (3).

We perform all the computations in the computer algebra systems MATHEMATICA and SINGULAR[38].

In the next theorem we list the cases when system (2) has at least one invariant algebraic surface of degree one or two.

Theorem 2.3. *System (2) has an invariant surface of degree one or two if one of the following conditions is satisfied.*

i. $b = 0$
ii. $a - c = 0$
iii. $a - e = 0$
iv. $d = a \pm \frac{e}{2} = c \pm \frac{e}{2} = 0$
v. $d = a \pm 2e = c \pm 2e = 0$
vi. $d = a \pm e = c \pm e = 0$
vii. $d = e = 0$

Proof. If $b = 0$, system (2) has the invariant plane $l_1 = 1 - \frac{a}{N}x$ with the cofactor $-a$.

If $a = c$, system (2) has the invariant plane $l_2 = 1 - \frac{c}{N}x - \frac{c}{N}y$ with the cofactor $-c$.

If $a = e$, system (2) has the invariant plane $l_3 = 1 - \frac{e}{N}x - \frac{e}{N}y + \frac{e(e-c)}{dN}z$ with the cofactor $-e$.

If $d = a \pm \frac{e}{2} = c \pm \frac{e}{2} = 0$, the invariant plane of system (2) is $l_4 = 1 \pm \frac{e}{2N}x \pm \frac{e}{2N}y$ with the cofactor $-\frac{e}{2}$.

If $d = c \pm 2e = a \pm 2e = 0$, the invariant plane of system(2) is $l_5 = 1 \pm \frac{2e}{\beta}x \pm \frac{2e}{\beta}y$ with the cofactor $2e$.

If $d = 0$ and $a = c = \mp e$, system (2) has the invariant plane $l_6 = 1 \pm \frac{e}{N}x \pm \frac{e}{N}y$ with the cofactor e. Additionally system (2) has the invariant surface $l_7 = 1 - \frac{b}{N}xz$ with the cofactor $-bz$ if $d = 0$ and $a = c = -e$.

If $d = e = 0$, system (2) has the invariant surface $l_8 = 1 - \frac{a}{N}x - \frac{b}{N}xz$ with the cofactor $-c - e$. □

Remark 2.2. *Squares of the invariant planes are invariant surfaces with the cofactors which are two times of the cofactors of those invariant planes. That is, if* $l_1 = 1 - \frac{a}{N}x$ *is an invariant plane of system (2) for* $b = 0$ *with the cofactor* $-a$*, then* $l_1' = (1 - \frac{a}{N}x)^2$ *is a trivial invariant surface of system (2) with the cofactor* $-2a$*.*

Moreover, multiples of the invariant planes are invariant surfaces. For example, another trivial invariant surface of system (2) is $l_{23}' = 1 - \frac{2bd}{ce}x - \frac{bd(c+e)^2}{2c^2e^2}y - \frac{b(c^2-e^2)}{2c^2e}z + \frac{b^2d^2}{c^2e^2}x^2 + \frac{b^2d^2}{c^2e^2}y^2 + \frac{2b^2d^2}{c^2e^2}xy + \frac{b^2d(c-e)}{c^2e^2}xz + \frac{b^2d(c-e)}{c^2e^2}yz$ *with the cofactor* $-c - e$ *when* $Nbd - \frac{c}{2}(c+e) = a - \frac{c+e}{2} = 0$ *is satisfied, which is a combination of the invariant planes* l_2 *and* l_3*.*

Theorem 2.4. *System (2) has a first integral if one of the following conditions is satisfied.*

i. $b = c = 0$
ii. $b = e = 0$
iii. $d = e = 0$
iv. $b = a + c = 0$
v. $b = a + e = 0$
vi. $b = c + e = 0$
vii. $d = a + e = c + e = 0$

Proof. System has the first integrals $\Psi_1 = 1 + y$ and $\Psi_2 = 1 + y + y^2$, if $b = c = 0$.

If $b = e = 0$, system (2) has the first integrals $\Psi_1 = 1 + y + \frac{c}{d}z$ and $\Psi_2 = 1 + y + \frac{c}{d}z + yz + \frac{d}{2c}y^2 + \frac{c}{2d}z^2$.

If $d = e = 0$, system (2) has the first integrals $\Psi_1 = 1 + z$ and $\Psi_2 = 1 + z + z^2$. If additionally $c = N = 0$ is satisfied, system (2) has the additional integral $\Psi_3 = 1 + \frac{a}{b}y + xz + yz$.

If $b = 0$ and $a = -c$, the first integral of system (2) is $\Psi_1 = 1 + y + \frac{c}{N}xy$.

If $b = 0$ and $a = -e$, the first integral of system (2) is $\Psi_1 = 1 + \frac{N}{e}y + \frac{N(c-e)}{de}z + xy + \frac{c-e}{d}xz$.

If $b = 0$ and $c = -e$, system (2) has the first integral $\Psi_1 = 1 + yz + -\frac{d}{2e}y^2$.
If $d = 0$ and $a = c = -e$, system (2) has the first integral $\Psi_1 = 1 + \frac{N}{e}z + xz + yz$. $\square$

Theorem 2.5. *System* (2) *has stable Hopf bifurcation, if* $b > 0$, $c > 0$, $d < 0$ *and* $e < -c$.

Proof. We will look for Hopf bifurcation on the invariant plane of system (2). For this, we choose the invariant plane $l_3 = 1 - \frac{e}{N}x - \frac{e}{N}y + \frac{e(e-c)}{dN}z$ which exists when $a = e$. By using the transformation

$$x = \frac{N}{e} + X - Y - \frac{c}{d}Z + \frac{e}{d}Z, y = Y, z = Z$$

we rewrite system (2) as

$$\begin{aligned} \frac{dX}{dt} &= -eX, \\ \frac{dY}{dt} &= \frac{be(e-c)Z^2 + bdeXZ - bdeYZ - cdeY + bdNZ}{de}, \\ \frac{dZ}{dt} &= dY - eZ. \end{aligned} \tag{5}$$

According to the equilibria of system (5), there exists a possibility for a stable Hopf bifurcation to occur at the nontrivial equilibrium point $(0, \frac{bdN-ce^2}{bcd}, \frac{bdN-ce^2}{bce})$. First, we move system (5) to this equilibrium point to have system

$$\begin{aligned} \frac{dX}{dt} &= -eX, \\ \frac{dY}{dt} &= \frac{1}{cde}(bce(e-c)Z^2 + bcdeXZ - bcdeYZ + (bd^2N - cde^2)X \\ &\quad + (cde^2 - c^2de - bd^2N)Y + (2c^2e^2 - ce^3 - bcdN + bdeN)Z), \\ \frac{dZ}{dt} &= dY - eZ, \end{aligned} \tag{6}$$

so that system (6) can have Hopf bifurcation at the origin if $N = -\frac{c^2e}{bd}$. The reduced system on $X = 0$ is then

$$\begin{aligned} \frac{dY}{dt} &= \frac{1}{cde}(bce(e-c)Z^2 - bcdeYZ + (cde^2 - c^2de - bd^2N)Y \\ &\quad + (2c^2e^2 - ce^3 - bcdN + bdeN)Z), \\ \frac{dZ}{dt} &= dY - eZ \end{aligned} \tag{7}$$

By calculating the first Lyapunov coefficient to check the stability of the Hopf bifurcation, we obtain $\alpha = \frac{\beta cde}{2(ce(c-e)+bdN)}$, $\gamma = \frac{\beta(c(c+e)-e^2)}{2de}$ and

$$g_1 = -\frac{\beta b^2cd^3}{e(3c^3(c+2ce) + 3(d^2+e^2)^2 - 2ce(d^2+3e^2) - c^2(2d^2+3e^2))}.$$

For a stable Hopf bifurcation to occur, $g_1 < 0$ must be satisfied. We also look for a nonnegative equilibrium point in order to have physical meaning. Hence, we obtain the condition for a stable Hopf bifurcation as $b > 0$, $c > 0$, $d < 0$ and $e < -c$. $\square$

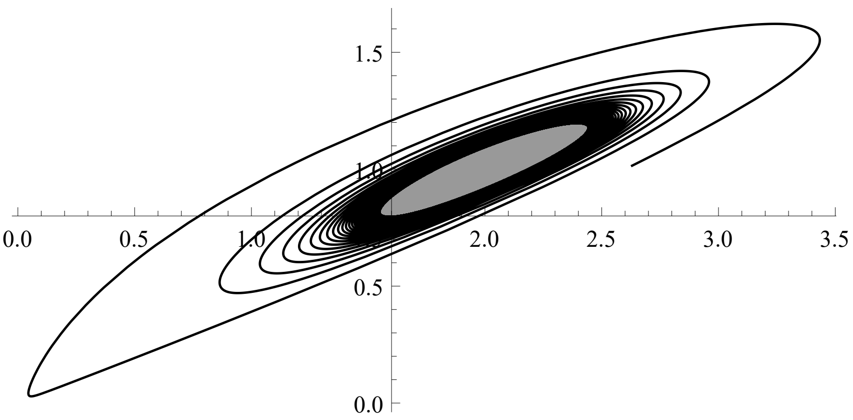

FIGURE 1. Stable Hopf bifurcation for system (8)

Example 2.1. *Choosing the parameter values as* $\{b, c, d, e\} = \{1, 1, -1, -2\}$*, we have the two dimensional projection*

$$\begin{aligned} \frac{dv}{dt} =& 3w^2 - vw - v + \frac{99}{100}w, \\ \frac{dw}{dt} =& -v + 2w \end{aligned} \tag{8}$$

of system (2)*. System* (8) *goes under Hopf bifurcation at the equilibrium point* $(\frac{101}{50}, \frac{101}{50})$ *with the eigenvalues* $\frac{1}{200}(-1 \pm i\sqrt{40399})$*. The stable Hopf bifurcation bifurcating from this equilibrium point is shown in figure 1.*

3. SIR model with the Beddington-DeAngelis functional response

Beddington[28] and DeAngelis[29] introduced the Beddington-DeAngelis functional response in 1975. The SIR model with Beddington-DeAngelis infection rate is given by

$$\begin{aligned} \frac{dx}{dt} =& N - ax - \frac{bxz}{1 + \alpha x + \beta z}, \\ \frac{dy}{dt} =& \frac{bxz}{1 + \alpha x + \beta z} - cy, \\ \frac{dz}{dt} =& dy - ez \end{aligned} \tag{9}$$

where all parameters are given as in section 1 except for the parameters α and β are the inhibitory effect parameters with respect to the Beddington-DeAngelis response function. We assume that all parameters are nonnegative to reflect physical values.

Theorem 3.1. *System* (9) *has at least one stable equilibrium.*

Proof. The Jacobian matrix of system (9) is

$$\begin{pmatrix} -a - \frac{bz(1+\beta z)}{(1+\alpha x+\beta z)^2} & 0 & -\frac{bx(1+\alpha x)}{(1+\alpha x+\beta z)^2} \\ \frac{bz(1+\beta z)}{(1+\alpha x+\beta z)^2} & -c & \frac{bx(1+\alpha x)}{(1+\alpha x+\beta z)^2} \\ 0 & d & -e \end{pmatrix}$$

and the equilibrium points are $E_1(\frac{N}{a}, 0, 0)$ and

$$E_2(x_2, y_2, z_2) = E_2(\frac{ce + d\beta N}{d(b + a\beta) - ce\alpha}, \frac{bdN - ce(a + \alpha N)}{c(d(b + a\beta) - ce\alpha)}, \frac{d(bdN - ce(a + \alpha N))}{ce(d(b + a\beta) - ce\alpha)}).$$

The eigenvalues of the Jacobian matrix of system (9) at equilibrium E_1 are $-a$ and $-\frac{c+e}{2} \pm \frac{\sqrt{(a+\alpha N)(4bdN+(a+\alpha N)(c-e)^2)}}{2(a+\alpha N)}$. Hence E_1 is a stable equilibrium considering $a > 0$ and $N \neq -\frac{a}{\alpha}$ and therefore one stable equilibrium of system (9) is guaranteed.

Now we give criteria for E_2 to be a stable equilibrium of system (9). We obtain the characteristic equation of system (9) at E_2 as

$$\lambda^3 + A\lambda^2 + B\lambda + C = 0$$

where

$$\begin{aligned}
A &= \frac{ce(bd(c+e) + ace\alpha) + ((bd - ce\alpha)^2 + bd^2(a + c + e)\beta)N}{bd(ce + d\beta N)}, \\
B &= (ac^2e^2((c+e)\alpha - d\beta) + abd^2(c+e)\beta N \\
&\quad + (bd - ce\alpha)((c+e)(bd - ce\alpha) + cde\beta)N)/(bd(ce + d\beta N)), \\
C &= \frac{ce(d(b + a\beta) - ce\alpha)(bdN - ce(a + \alpha N))}{bd(ce + d\beta N)}.
\end{aligned}$$

According to the Routh-Hurwitz criterion we conclude that if

$$\begin{aligned}
&(ac^2e^2((c+e)\alpha - d\beta) + abd^2(c+e)\beta N + (bd - ce\alpha) \\
&((c+e)(bd - ce\alpha) + cde\beta)N)(ce(bd(c+e) + ace\alpha) \\
&+((bd - ce\alpha)^2 + bd^2(a + c + e)\beta)N) \\
&-bcde(ce\alpha - d(b + a\beta))(ce + d\beta N)(-bdN + ce(a + \alpha N)) > 0
\end{aligned}$$

and $A, B, C \geq 0$, $x_2 \geq 0, y_2 \geq 0, z_2 \geq 0$ and $bd(ce + d\beta N) \neq 0$ are satisfied then E_2 is also a stable equilibrium of system (9). □

Theorem 3.2. *The invariant planes $l_{1,\ldots,7}$ given in corresponding cases of Theorem 2.3 are also invariant planes of system* (9). *Additionally system* (9) *has an invariant surface if one of the following cases are satisfied.*

i. $\beta = a - \frac{c+e}{2} = N(bd - ce\alpha) - \frac{ce}{2}(c + e) = 0$
ii. $d = \alpha = a - c - e = 0$
iii. $d = a - \frac{c+e}{2} = N\alpha + \frac{c+e}{2} = 0$
iv. $d = a - \frac{c}{2} = b + \beta(e - \frac{c}{2}) = 0$
v. $d = \beta(a - e) - b = a + N\alpha = 0$
vi. $a - 2c = c\alpha + d\beta = b + e\beta = 0$
vii. $a - 2e = e\alpha + d\beta = b + c\beta = 0$
viii. $d = \alpha = \beta = a + e = 0$
ix. $d = \alpha = a - 2e = c - e = 0$

Proof. If $\beta = a - \frac{c+e}{2} = N(bd - ce\alpha) - \frac{ce}{2}(c+e) = 0$, system (2) has the invariant surface

$$l_8 = 1 + \frac{2(\alpha ce - bd)}{ce}x + (\frac{\alpha ce - bd}{ce})^2 x^2 - \frac{2bd(c+e)^2(bd - \alpha ce)}{c^2e^2(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}y + \frac{8bd(bd - \alpha ce)^2}{c^2e^2(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}xy + \frac{4bd(bd - \alpha ce)^2}{c^2e^2(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}y^2 - \frac{2b(bd - \alpha ce)(c^2 - e^2)}{c^2e(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}z + \frac{4b(c-e)(bd - \alpha ce)^2}{c^2e^2(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}xz + \frac{4b(c-e)(bd - \alpha ce)^2}{c^2e^2(\alpha c^2 + 4bd - 2\alpha ce + \alpha e^2)}yz$$

with the cofactor $-c - e$.

If $d = \alpha = a - c - e = 0$, system (2) has the invariant surface $l_9 = 1 - \frac{c+e}{N}x - \frac{b(c+e)}{ce}z + \frac{b(c+e)}{eN}xz + \frac{(c+e)(b+\beta e)}{eN}yz$ with the cofactor $-c - e$.

If $d = a - \frac{c+e}{2} = N\alpha + \frac{c+e}{2} = 0$, system (2) has the invariant surface $l_{10} = 1 + 2\alpha x + \alpha^2 x^2 + \frac{2(bc+be)}{c(c-e)}z + \frac{4\alpha b}{c-e}xz - \frac{2(-2\alpha b + \alpha\beta c - \alpha\beta e)}{c-e}yz$ with the cofactor $-c - e$.

If $d = a - \frac{c}{2} = b + \beta(e - \frac{c}{2}) = 0$, system (2) has the invariant surface $l_{11} = 1 - \frac{c}{N}x + \frac{c^2}{4N^2}x^2 + \frac{(-c^2 - 2\alpha cN)}{2\alpha N^2}y - \frac{bc^2}{\alpha(c^2 - 3ce + 2e^2)N}z + \frac{bc^2}{\alpha(c-2e)N^2}xz$ with the cofactor $-c$.

If $d = \beta(a - e) - b = a + N\alpha = 0$, system (2) has the invariant surface $l_{12} = 1 + 2\alpha x + \alpha^2 x^2 + \frac{2\alpha\beta N}{e + 2\alpha N}z + 2\alpha\beta xz$ with the cofactor $2\alpha N$.

If $a - 2c = c\alpha + d\beta = b + e\beta = 0$, system (2) has the invariant surface

$$l_{13} = 1 + \frac{2\beta d}{\alpha N}x + \frac{2\alpha\beta d(d\beta + e\alpha)}{\alpha^3 eN + \alpha^2\beta dN - \alpha\beta de - 2\beta^2 d^2}y + \frac{2\beta^2 d^2(2\beta d + \alpha e)}{N(\alpha^3 eN + \alpha^2\beta dN - \alpha\beta de - 2\beta^2 d^2)}xy + \frac{\beta^2 d^2(2\beta d + \alpha e)}{N(\alpha^3 eN + \alpha^2\beta dN - \alpha\beta de - 2\beta^2 d^2)}y^2 + \frac{2\beta^3 d^2}{\alpha^3 eN + \alpha^2\beta dN - \alpha\beta de - 2\beta^2 d^2}z - \frac{2\beta^3 d^2(2\beta d + \alpha e)}{\alpha N(\alpha^3 eN + \alpha^2\beta dN - \alpha\beta de - 2\beta^2 d^2)}xz$$

with the cofactor $\frac{2\beta d}{\alpha}$.

If $a - 2e = e\alpha + d\beta = b + c\beta = 0$ system (2) has the invariant surface

$$l_{14} = 1 + \frac{2\beta d}{\alpha N}x + \frac{2\alpha\beta d(\alpha c + \beta d)}{\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2}y + \frac{2\beta^2 d^2(\alpha c + 2\beta d)}{N(\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2)}xy + \frac{\beta^2 d^2(\alpha c + 2\beta d)}{N(\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2)}y^2 + \frac{2\alpha\beta c(\alpha c + 2\beta d)}{\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2}z + \frac{2\beta^2 cd(\alpha c + 2\beta d)}{N(\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2)}xz + \frac{2\beta^2 d(\alpha^2 c^2 + 3\alpha\beta cd + 2\beta^2 d^2)}{\alpha N(\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2)}yz + \frac{\beta^2(\alpha c + \beta d)^2(\alpha c + 2\beta d)}{\alpha^2 N(\alpha^3 cN + \alpha^2\beta dN - \alpha\beta cd - 2\beta^2 d^2)}z^2$$

with the cofactor $\frac{2\beta d}{\alpha}$.

If $d = \alpha = \beta = a + e = 0$, system (2) has the invariant surface $l_{15} = 1 - \frac{b}{N}xz$ with the cofactor $-bz$.

If $d = \alpha = a - 2e = c - e = 0$, system (2) has the invariant surface $l_{16} = 1 - \frac{2e}{N}x - \frac{2b}{e}z + \frac{2b}{N}xz + \frac{2(b+\beta e)}{N}yz$ with the cofactor $-2e$. □

Theorem 3.3. *System* (9) *has the same first integrals given for the cases in Theorem 2.3.*

Theorem 3.4. *In system* (9) *Hopf bifurcation can occur on the invariant plane* l_2 *of system* (9).

Proof. System (9) after the corresponding transformation with respect to the invariant plane $l_1 = 1 - \frac{e}{N}x - \frac{e}{N}y + \frac{e(e-c)}{dN}z$ which exists if $a = e$ is

$$\begin{aligned}
\frac{dX}{dt} =& - eX,\\
\frac{dY}{dt} =&(cde\alpha Y^2 + (be(e-c))Z^2 - cde\alpha XY + bdeXZ - (bde + ce(d\beta - c\alpha\\
&+ \alpha e))YZ - (cd(e+\alpha N))Y + bdNZ)/(de\alpha X - de\alpha Y - (e\alpha(c-e)\\
&- de\beta)Z + d(e+\alpha N)),\\
\frac{dZ}{dt} =&dY - eZ
\end{aligned} \tag{10}$$

The Jacobian matrix of system (10) is

$$\begin{pmatrix} -e & 0 & 0 \\ J_{21} & J_{22} & J_{23} \\ 0 & d & -e \end{pmatrix}$$

where

$$\begin{aligned}
J_{21} =& \frac{bd^2e^2Z(1+\beta Z)}{(de\alpha X - de\alpha Y + (de\beta + e\alpha(e-c))Z + d(e+\alpha N))^2},\\
J_{22} =& (-\alpha^2cd^2e^2X^2 - \alpha^2cd^2e^2Y^2 - e^2(\beta(b+\beta c)d^2 + \alpha^2c(c-e)^2\\
&+ 2\alpha\beta cd(e-c))Z^2 + 2\alpha^2cd^2e^2XY + (2\alpha cde^2(-\beta d + \alpha(c-e)))XZ\\
&+ 2\alpha cde^2(\beta d + \alpha(e-c))YZ - 2\alpha cd^2e(e+\alpha N)X + 2\alpha cd^2e(e+\alpha N)Y\\
&- de(e((b+2\beta c)d + 2\alpha c(e-c)) + 2\alpha cN(\beta d + \alpha(e-c)))Z - cd^2(e+\alpha N)^2)\\
&/(de\alpha X - de\alpha Y + (de\beta + e\alpha(e-c))Z + d(e+\alpha N))^2,\\
J_{23} =& (bd^2e^2\alpha X^2 + bd^2e^2\alpha Y^2 + be(e\alpha(c(c-2e) + e^2) - de\beta(c+e))Z^2\\
&- 2bd^2e^2\alpha XY + 2bde\alpha(e(e-c))XZ + 2bde\alpha(e(c-e))YZ + bd^2e(e+2\alpha N)X\\
&- bd^2e(e+2\alpha N)Y + 2bde(e-c)(e+\alpha N)Z + bd^2N(e+\alpha N)\\
&/(de\alpha X - de\alpha Y + (de\beta + e\alpha(e-c))Z + d(e+\alpha N))^2.
\end{aligned}$$

The equilibrium points of system (10) are $F_0(0,0,0)$ and

$$F_1\left(0, \frac{ce(e+\alpha N) - bdN}{c(ce\alpha - d(b+e\beta))}, \frac{d(ce(e+\alpha N)) - bdN)}{ce(ce\alpha - d(b+e\beta)))}\right).$$

The eigenvalues of the Jacobian matrix at F_0 are $-e$ and

$$\frac{1}{2(e+\alpha N)}(-(c+e)(e+\alpha N) \pm \sqrt{(e+\alpha N)(e(c-e)^2 + (4bd + \alpha(c-e)^2)N)}).$$

We see that Hopf bifurcation can not occur at F_0 for physical values of the parameters. However if we assume $c = -e < 0$ system (10) can go through Hopf bifurcation at F_0 under one of the following set of conditions.

i. $b < 0$, $d > -\frac{\alpha(c-e)^2}{4b}$ and $N > -\frac{e(c-e)^2}{4bd+\alpha(c-e)^2}$,
ii. $b > 0$, $\alpha = 0$, $d > 0$, $N < -\frac{e(c-e)^2}{4bd}$ and hence $N < 0$,
iii. $b > 0$, $\alpha > 0$, $d > 0$, $-\frac{e}{\alpha} < N < -\frac{e(c-e)^2}{4bd+\alpha(c-e)^2}$ and hence $N < 0$,

iv. $b > 0$, $\alpha < 0$, $0 < d < -\frac{\alpha(c-e)^2}{4b}$, $-\frac{e}{\alpha} < N < -\frac{e(c-e)^2}{4bd+\alpha(c-e)^2}$ and hence $N < 0$,

v. $b > 0$, $\alpha < 0$, $d \geq -\frac{\alpha(c-e)^2}{4b}$, $N > -\frac{e}{\alpha}$ and hence $N < 0$,

vi. $b > 0$, $e > 0$, $d < -\frac{\alpha(c-e)^2}{4b}$, $N > -\frac{e(c-e)^2}{4bd+\alpha(c-e)^2}$ and hence $d < 0$.

The eigenvalues of the Jacobian matrix at F_1 are $-e$ and

$$\frac{-1}{2bd^2(ce+d\beta N)}(d(bd^2N(b+\beta(c+e))+bcde(c-2\alpha\beta)+\alpha c^2e^2(e+\alpha\beta))\pm\sqrt{\Delta})$$

where

$$\begin{aligned}\Delta = {} & (d^2(b^4d^4\beta^2+c^4e^4\alpha^2(e+\alpha\beta)^2-2b^3d^3\beta(c^2e-de\beta+c\beta(d\beta+2e\alpha)) \\ & +b^2d^2(c^3e^2(c+4e)+2c^2e\beta(d\beta(c+e)+e\alpha(2c+e))+(d^2\beta^2(c-e)^2 \\ & +4cde\alpha\beta(c-e)+6c^2e^2\alpha^2)\beta^2)-2bc^2de^2(e+\alpha\beta)(c^2e\alpha+d\alpha\beta^2(c-e) \\ & +2ce\alpha^2\beta-2d\beta(ce+d\beta^2)).\end{aligned}$$

Hopf bifurcation can occur at F_1 if

$$\frac{\alpha ce}{b+\beta e} < d < \frac{\alpha ce}{b}$$

and

$$\beta = \frac{-bc^2de-\alpha c^2e^3}{b^2d^2+b\beta cd^2-2b\alpha cde+b\beta d^2e+\alpha^2c^2e^2} < 0$$

is satisfied.

We move system (10) to F_1 to have system

$$\begin{aligned}\frac{dx}{dt} = & -ex, \\ \frac{dy}{dt} = & (\alpha c^2de(bd-\alpha ce+\beta de)y^2-bc(c-e)e(bd-\alpha ce+\beta de)z^2+\alpha c^2de(\alpha ce \\ & -d(b+\beta e))xy+bcde(bd-\alpha ce+\beta de)xz-ce(bd-\alpha ce+\beta de) \\ & ((b+\beta c)d+\alpha c(e-c))yz+d(bd-\alpha ce)(bdN-ce(e+\alpha N))x \\ & -d(b^2d^2N+\alpha c^2e^2(e+\alpha N)+bcd(ce+\beta dN-e(e+2\alpha N)))y \\ & +(b^2d^2(e-c)N+c^2e^2(\beta d+\alpha(e-c))(e+\alpha N)+bcde(2c(e+\alpha N) \\ & -e(e+2\alpha N)))z)/(\alpha cde(bd-\alpha ce+\beta de)x+\alpha cde(\alpha ce-d(b+\beta e))y \\ & +ce(bd-\alpha ce+\beta de)(\beta d+\alpha(e-c))z+bd^2(ce+\beta dN)), \\ \frac{dz}{dt} = & dy-ez\end{aligned} \tag{11}$$

Then by introducing $x = 0$ into system (11) we have the following reduced system.

$$\begin{aligned}\frac{dy}{dt} = & (\alpha c^2de(bd-\alpha ce+\beta de)y^2-bc(c-e)e(bd-\alpha ce+\beta de)z^2+\alpha c^2de(\alpha ce \\ & -ce(bd-\alpha ce+\beta de)-d(b^2d^2N+\alpha c^2e^2(e+\alpha N) \\ & +bcd(ce+\beta dN-e(e+2\alpha N)))y \\ & +(b^2d^2(e-c)N+c^2e^2(\beta d+\alpha(e-c))(e+\alpha N)+bcde(2c(e+\alpha N) \\ & -e(e+2\alpha N)))z)/(\alpha cde(\alpha ce-d(b+\beta e))y \\ & +ce(bd-\alpha ce+\beta de)(\beta d+\alpha(e-c))z+bd^2(ce+\beta dN)), \\ \frac{dz}{dt} = & dy-ez\end{aligned} \tag{12}$$

We see that system (2) can be reduced to two dimensions by using the transformation defined by the algebraic invariant plane as in system (1). So, Hopf bifurcation exists for system (2). However, it is not possible to calculate the first Lyapunov coefficient to find the stability of the Hopf bifurcation for system (2). □

4. Conclusion

In this paper, we have investigated the stability and Hopf bifurcation properties of an original version and a generalized version with the Beddington-DeAngelis functional response epidemic model with virus replication. We have used the methods of computational algebra, i.e. invariant planes where usual methods fail. Both models show Hopf bifurcation. We have found the parameter conditions for a stable Hopf bifurcation to occur for the original virus replication model. However, it is not possible to find parametre conditions for the stability of the Hopf bifurcation of the virus replication model with the Beddington-DeAngelis functional response although the both models have the same invariant planes.

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