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Stability and bifurcation analysis of a SIR model with saturated incidence rate and saturated treatment

Erika Rivero-Esquivel, Eric Avila-Vales, Gerardo García-Almeida*

Facultad de Matemáticas, Universidad Autónoma de Yucatán, Anillo Periférico Norte, Tablaje Cat. 13615, Col. Chuburná de Hidalgo Inn, Mérida, Yucatán, Mexico

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Abstract

We study the dynamics of a SIR epidemic model with nonlinear incidence rate, vertical transmission vaccination for the newborns and the capacity of treatment, that takes into account the limitedness of the medical resources and the efficiency of the supply of available medical resources. Under some conditions we prove the existence of backward bifurcation, the stability and the direction of Hopf bifurcation. We also explore how the mechanism of backward bifurcation affects the control of the infectious disease. Numerical simulations are presented to illustrate the theoretical findings.

Keywords: Local stability; Hopf bifurcation; Global stability; Backward bifurcation

1. Introduction

Mathematical models that describe the dynamics of infectious diseases in communities, regions and countries can contribute to have better approaches in the disease control in epidemiology. Researchers always look for thresholds, equilibria, periodic solutions, persistence and eradication of the disease. For classical disease transmission models, it is common to have one endemic equilibrium and that the basic reproduction number tells us that a disease is persistent if it is greater than 1, and dies out if it is less than 1. This kind of behavior associates to forward bifurcation. However, there are epidemic models with multiple endemic equilibria [7,4,11,2], within these models it can happen that a stable endemic equilibrium coexists with a disease free equilibrium, this phenomenon is called backward bifurcation [6].

In order to prevent and control the spread of infectious diseases like, measles, tuberculosis and influenza, treatment is an important and effective method. In classical epidemic models, the treatment rate of the infectious is assumed to be proportional to the number of the infective individuals [1]. Therefore we need to investigate how the application of treatment affects the dynamical behavior of these diseases. In that direction in [13], Wang and Ruan, considered the

* Corresponding author.
E-mail addresses: erika.rivero@correo.uady.mx (E. Rivero-Esquivel), avila@uady.mx (E. Avila-Vales), galmeida@uady.mx (G. García-Almeida).

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removal rate

$$T(I)=\begin{cases}k, & \text{if } I>0\\ 0, & \text{if } I=0.\end{cases}$$

In the following model

$$\begin{aligned}\frac{dS}{dt}&=A-dS-\lambda SI,\\ \frac{dI}{dt}&=\lambda SI-(d+\gamma)I-T(I),\\ \frac{dR}{dt}&=\gamma I+T(I)-dR,\end{aligned}$$

where S, I, and R denote the numbers of the susceptible, infective and recovered individuals at time t, respectively. The authors studied the stability of equilibria and prove the model exhibits Bogdanov–Takens bifurcation, Hopf bifurcation and Homoclinic bifurcation. In [14], the authors introduced a saturated treatment,

$$T(I)=\frac{\beta I}{1+\alpha I}.$$

Related works are [15,16,12].

Hu, Ma and Ruan [8] studied the model

$$\begin{aligned}\frac{dS}{dt}&=bm(S+R)-\frac{\beta SI}{1+\alpha I}-bS+p\delta I\\ \frac{dI}{dt}&=\frac{\beta SI}{1+\alpha I}+(q\delta-\delta-\gamma)I-T(I)\\ \frac{dR}{dt}&=\gamma I-bR+bm'(S+R)+T(I).\end{aligned}\tag{1}$$

The basic assumptions for the model (1) are, the total population size at time t is denoted by $N=S+I+R$. The newborns of S and R are susceptible individuals, and the newborns of I who are not vertically infected are also susceptible individuals, b denotes the death rate and birth rate of susceptible and recovered individuals, δ denotes the death rate and birth rate of infective individuals, γ is the natural recovery rate of infective individuals. q ($q\le 1$) is the vertical transmission rate, and we set $p=1-q$, then $0\le p\le 1$. Fraction m' of all newborns with mothers in the susceptible and recovered classes are vaccinated and appears in the recovered class, while the remaining fraction, $m=1-m'$, appears in the susceptible class, the incidence rate is described by a nonlinear function $\beta SI/(1+\alpha I)$, where β is a positive constant describing the infection rate and α is a nonnegative constant. The treatment rate of the disease is

$$T(I)=\begin{cases}kI, & \text{if } 0\le I\le I_0\\ u=kI_0, & \text{if } I>I_0,\end{cases}$$

where I_0 is the infective level at which the healthcare systems reach capacity.

In this work we will extend model (1) introducing the treatment rate $\frac{\beta_2 I}{1+\alpha_2 I}$, where $\alpha_2,\beta_2>0$, obtaining the following model

$$\begin{aligned}\frac{dS}{dt}&=bm(S+R)-\frac{\beta SI}{1+\alpha I}-bS+p\delta I\\ \frac{dI}{dt}&=\frac{\beta SI}{1+\alpha I}+(q\delta-\delta-\gamma)I-\frac{\beta_2 I}{1+\alpha_2 I}\\ \frac{dR}{dt}&=\gamma I-bR+bm'(S+R)+\frac{\beta_2 I}{1+\alpha_2 I}.\end{aligned}\tag{2}$$

Because $\frac{dN}{dt}=0$, the total number of population N is constant. For convenience, it is assumed that $N=S+I+R=1$. By using $S+R=1-I$, the first two equations of (2) do not contain the variable R. Therefore, system (2) is equivalent to the following 2-dimensional system:

$$\begin{aligned}\frac{dS}{dt} &= -\frac{\beta SI}{1+\alpha I} - bS + bm(1-I) + p\delta I\\ \frac{dI}{dt} &= \frac{\beta SI}{1+\alpha I} - p\delta I - \gamma I - \frac{\beta_2 I}{1+\alpha_2 I}.\end{aligned} \tag{3}$$

The parameters in the model are described below:

- S, I, R are the normalized susceptible, infected, and recovered population, respectively, therefore it follows that $S, I, R \le 1$.
- b is a positive number representing the birth and death rates of susceptible and recovered population.
- δ is a positive number representing the birth and death rates of infected population.
- γ is a positive number giving the natural recovery rate of infected population.
- q is positive ($q \le 1$) representing the vertical transmission rate (disease transmission from mother to son before or during birth). It is assumed that descendants of the susceptible and recovered classes belong to the susceptible class, in the same way the fraction of the newborns of the infected class not affected by vertical transmission.
- $p = 1 - q$ therefore $0 \le p \le 1$.
- m' is positive and it is the fraction of vaccinated newborns from susceptible and recovered mothers and therefore belong to the recovered class. $m = 1 - m' \ge 0$ is the rest of newborns, which belong to the susceptible class.
- β is positive, representing the infection rate, α is a positive saturation constant (in the model the incidence rate is given by the nonlinear function $\frac{\beta SI}{1+\alpha I}$).
- $\frac{\beta_2 I}{1+\alpha_2 I}$ is the treatment function, where $\alpha_2, \beta_2 > 0$.

We note that if $\alpha_2 = 0$ the treatment becomes bilinear, case considered in [8], whereas if $\beta_2 = 0$ treatment is null, not being of interest here. Therefore we will assume $\beta_2, \alpha_2 > 0$.

The paper is distributed as follows: in Section 2 we compute the equilibria points and determine the conditions of its existence (as real values) and positivity, in Section 3 we analyze the stability of the disease free equilibrium and endemic equilibria points in terms of value of $\mathcal{R}_0$ and the parameters of treatment function. Section 4 is dedicated to study Hopf bifurcation of the endemic equilibria points and Section 5 shows discussion of all our results and we give some control measures that could be effective to eradicate the disease in each case.

Following [8] we define

$$\mathcal{R}_0 := \frac{\beta m}{\beta_2 + p\delta + \gamma}. \tag{4}$$

When $\beta_2 = 0$, $\mathcal{R}_0$ reduces to

$$\mathcal{R}_0^* = \frac{\beta m}{p\delta + \gamma}, \tag{5}$$

which is the basic reproduction number of model (3) without treatment.

Lemma 1. *Given the initial conditions $S(0) = S_0 > 0, I(0) = I_0 > 0$, then the solution of (3) satisfies $S(t)$, $I(t) > 0\ \forall t > 0$ and $S(t) + I(t) \le 1$.*

Proof. Take the solution $S(t), I(t)$ satisfying the initial conditions $S(0) = S_0 > 0, I(0) = I_0 > 0$. Assume that the solution is not always positive, i.e., there exists a t_0 such that $S(t_0) \le 0$ or $I(t_0) \le 0$. By Bolzano's theorem there exists a $t_1 \in (0, t_0]$ such that $S(t_1) = 0$ or $I(t_1) = 0$, which can be written as $S(t_1)I(t_1) = 0$ for some $t_1 \in (0, t_0]$. Let

$$t_2 = \min\{t_i \mid S(t_i)I(t_i) = 0\}. \tag{6}$$

Assume first that $S(t_2) = 0$, then $\frac{dS(t_2)}{dt} > 0$ implies that S is increasing at $t = t_2$. Hence $S(t)$ is negative for values of $t < t_2$ near t_2, a contradiction. Therefore $S(t) > 0\ \forall t > 0$ and we must have $I(t_2) = 0$, so $\frac{dI(t_2)}{dt} = 0$. Note that if for some $t \ge 0$ $I(t) = 0$, then $\frac{dI(t)}{dt} = 0$. Then any solution with $I(0) = I_0 = 0$ will satisfy $I(t) = 0\ \forall t > 0$. By uniqueness of solutions we have that if $I(0) = I_0 > 0$, then $I(t)$ will remain positive for all $t > 0$. Therefore

$I(t_2) = 0$ leads to a contradiction. Hence both S and I are nonnegative for all $t > 0$. Finally, adding both derivatives of $S(t)$ and $I(t)$ we get:

$$\frac{d(S+I)}{dt} = -bS + bm - bmI - \gamma I - \frac{\beta_2 I}{1+\alpha_2 I}. \tag{7}$$

Since $S, I \geq 0$, if $S + I = 1$ then $0 \leq S \leq 1$, $0 \leq I \leq 1$. Analyzing the expression $-bS + bm - bmI$, we have that

$$-bS + bm - bmI = b(m - mI - S) = b(m - mI - 1 + I) = b(m - 1 + I(1-m)).$$

Note that by the definition of the model parameters, $1 - m = m' \geq 0$. Knowing that $I \leq 1$, then

$$I(1-m) \leq 1 - m \Rightarrow I(1-m) + m - 1 \leq 0. \tag{8}$$

Therefore $-bS + bm - bmI \leq 0$. Hence $\frac{d(S+I)}{dt} \leq 0$ and $S + I$ is non increasing along the line $S + I = 1$, implying that $S + I \leq 1$. Note also that $S + I$ cannot be greater than 1, otherwise from $R = 1 - (S + I)$, R would be negative, a nonsense. □

2. Existence and positivity of equilibria

Assume that system (3) has a constant solution (S_0, I_0), it is easy to see that $E = (m, 0)$ is the disease free equilibrium.

Theorem 1. *System (3) has a positive disease-free equilibrium $E = (m, 0)$.*

In order to obtain positive solutions (S_0, I_0) of system (3), when $I_0 \neq 0$ then:

$$\frac{\beta S_0}{1+\alpha I_0} - p\delta - \gamma - \frac{\beta_2}{1+\alpha_2 I_0} = 0$$
$$S_0 = \frac{1+\alpha I_0}{\beta}\left(p\delta + \gamma + \frac{\beta_2}{1+\alpha_2 I_0}\right). \tag{9}$$

We obtain the following quadratic equation:

$$AI_0^2 + BI_0 + C = 0 \tag{10}$$

or

$$I_0^2 + (B/A)I_0 + C/A = 0, \tag{11}$$

where the coefficients are given by:

$$\begin{aligned} A &= \alpha_2(\beta(\gamma + bm) + \alpha b(p\delta + \gamma)) > 0,\\ B &= \beta(\gamma + \beta_2 + bm(1-\alpha_2)) + b\alpha(p\delta + \gamma + \beta_2) + b\alpha_2(p\delta + \gamma),\\ &= \beta(\gamma + \beta_2 + bm - bm\alpha_2) + b\alpha(1 - \mathcal{R}_0)(p\delta + \gamma + \beta_2) + \beta mb\alpha + b\alpha_2(p\delta + \gamma),\\ C &= b(p\delta + \gamma + \beta_2 - \beta m) = b(p\delta + \gamma + \beta_2)(1 - \mathcal{R}_0). \end{aligned} \tag{12}$$

Its roots are:

$$I_1 = \frac{-B - \sqrt{B^2 - 4AC}}{2A}$$
$$I_2 = \frac{-B + \sqrt{B^2 - 4AC}}{2A}. \tag{13}$$

Using these values in (9) we obtain,

$$S_1 = \frac{1+\alpha I_1}{\beta}\left(p\delta + \gamma + \frac{\beta_2}{1+\alpha_2 I_1}\right)$$
$$S_2 = \frac{1+\alpha I_2}{\beta}\left(p\delta + \gamma + \frac{\beta_2}{1+\alpha_2 I_2}\right). \tag{14}$$

Then our candidates for endemic equilibria are $E_1 = (S_1, I_1)$, $E_2 = (S_2, I_2)$.

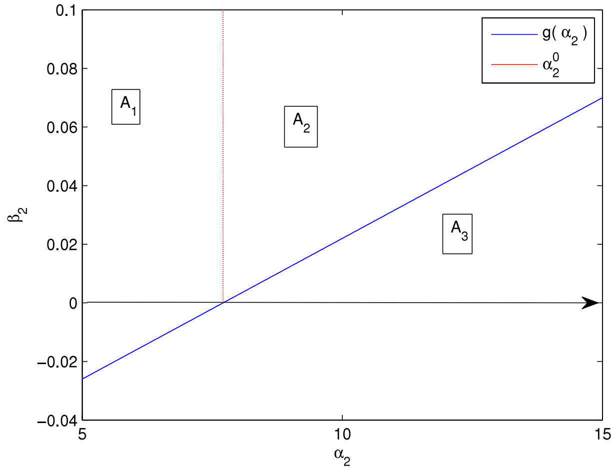

Fig. 1. Location of the sets A_1, A_2, A_3 in the plane $\alpha_2 - \beta_2$, for $\gamma = 0.01$, $\beta = 0.2$, $b = 0.2$, $m = 0.3$, $p = 0.02$, $\delta = 0.1$.

Note that $C = 0$ if and only if $\mathcal{R}_0 = 1$, $C > 0$ if and only if $\mathcal{R}_0 < 1$, and $C < 0$ if and only if $\mathcal{R}_0 > 1$. For $\mathcal{R}_0^* > 1$ we define the following sets:

$$\begin{aligned} A_1 &= \{(\beta_2, \alpha_2) : \beta_2 > 0, 0 < \alpha_2 \leq \alpha_2^0\}, \\ A_2 &= \{(\beta_2, \alpha_2) : \beta_2 \geq g(\alpha_2), \alpha_2 > \alpha_2^0 > 0\}, \\ A_3 &= \{(\beta_2, \alpha_2) : 0 < \beta_2 < g(\alpha_2), \alpha_2 > \alpha_2^0 > 0\} \end{aligned} \tag{15}$$

where

$$\alpha_2^0 = \frac{-\beta(mb\alpha + \gamma + bm)}{b(p\delta + \gamma - \beta m)}, \tag{16}$$

$$g(\alpha_2) = -\frac{1}{\beta}(b\alpha_2(p\delta + \gamma - \beta m) + \beta(\gamma + bm + mb\alpha)). \tag{17}$$

Define:

$$P_1 = 1 + \frac{1}{b\alpha(p\delta + \gamma + \beta_2)}[\beta(\gamma + \beta_2 + bm - bm\alpha_2) + \beta mb\alpha + b\alpha_2(p\delta + \gamma)]$$

$$\begin{aligned} R_0^+ &= 1 - \frac{1}{b\alpha^2(p\delta + \gamma + \beta_2)} \\ &\quad \times \left[\sqrt{-\beta\alpha(bm\alpha + \beta_2 + \gamma + bm - \alpha_2 bm) + \beta\alpha_2(\gamma + bm)} - \sqrt{\alpha_2(\beta\gamma + \beta bm + \alpha bp\delta + \alpha b\gamma)}\right]^2. \end{aligned} \tag{18}$$

Fig. 1 shows the location of these sets.

Theorem 2. *If $\mathcal{R}_0 > 1$ the system (3) has a unique (positive) endemic equilibrium E_2.*

Proof. If $\mathcal{R}_0 > 1$ then $C < 0$, then using Routh–Hurwitz criterion for $n = 2$, the quadratic equation has two real roots with different sign, I_1 and I_2, where $I_1 < I_2$. Hence there exists a unique positive endemic equilibrium $E_2 = (S_2, I_2)$. □

Theorem 3. *Let $0 < \mathcal{R}_0 \leq 1$. For system (3), if $\mathcal{R}_0^* \leq 1$ then there are no positive endemic equilibria. Otherwise, if $\mathcal{R}_0^* > 1$ the following propositions hold:*

1. *If $\mathcal{R}_0 = 1$ and $(\beta_2, \alpha_2) \in A_3$ the system (3) has a unique positive endemic equilibrium $E_2 = (S_2, I_2)$, where*

$$I_2 = -B/A, \qquad S_2 = \frac{1 + \alpha I_2}{\beta}\left(p\delta + \gamma + \frac{\beta_2}{1 + \alpha_2 I_2}\right).$$

2. *If* $\max\{P_1, R_0^+\} < \mathcal{R}_0 < 1$ *and* $(\beta_2, \alpha_2) \in A_3$*, the system* (3) *has a pair of positive endemic equilibria* E_1, E_2*.*
3. *If* $1 > \mathcal{R}_0 = R_0^+ > P_1$ *and* $(\beta_2, \alpha_2) \in A_3$*, the system* (3) *has a unique positive endemic equilibrium* $E_1 = E_2$*.*
4. *If* $1 > \mathcal{R}_0 = P_1$ *and* $(\beta_2, \alpha_2) \in A_3$*, the system* (3) *has no positive endemic equilibria.*
5. *If* $0 < \mathcal{R}_0 \le 1$ *and* $(\beta_2, \alpha_2) \in A_1 \cup A_2$*, the system* (3) *has no positive endemic equilibria.*
6. *If* $(\beta_2, \alpha_2) \in A_3$ *and* $0 < \mathcal{R}_0 < \max(R_0^+, P_1) < 1$*, then there are no positive endemic equilibria.*

Proof. If $0 < \mathcal{R}_0 \le 1$, then $C \ge 0$, so the roots of the equation $AI^2 + BI + C = 0$ are not real with different sign, but real with equal signs, complex conjugate or some of them are zero. If endemic equilibria exist and are positive, it is necessary that $B < 0$. After some calculations we can see that:

$$B < 0 \Leftrightarrow \mathcal{R}_0 > 1 + \frac{\beta(\gamma + \beta_2 + bm - bm\alpha_2) + \beta mb\alpha + b\alpha_2(p\delta + \gamma)}{b\alpha(p\delta + \gamma + \beta_2)} := P_1. \tag{19}$$

From the assumption that $\mathcal{R}_0 \le 1$ then $P_1 < 1$, hence the expression $\beta(\gamma+\beta_2+bm-bm\alpha_2)+\beta mb\alpha+b\alpha_2(p\delta+\gamma)$ must be negative, this happens if and only if

$$\beta_2 < -\frac{1}{\beta}(b\alpha_2(p\delta + \gamma - \beta m) + \beta(\gamma + bm + mb\alpha)) = g(\alpha_2). \tag{20}$$

If $\mathcal{R}_0^* \le 1$ then $-\frac{1}{\beta}(b\alpha_2(p\delta+\gamma-\beta m)+\beta(\gamma+bm+mb\alpha)) < 0$ and it is not possible to find a value of β_2 fulfilling the previous inequality, therefore there are no positive endemic equilibria.

Now, if $\mathcal{R}_0^* > 1$ we have that:

1. If $\mathcal{R}_0 = 1$ then $C = 0$, Eq. (10) is transformed into

$$AI_0^2 + BI_0 = 0, \tag{21}$$

with $A > 0$. Its roots are $I_1 = 0$ and $I_2 = -B/A$, and there exists a unique endemic equilibrium that is positive if and only if $B < 0$, that is given by $E_2 = (S_2, I_2)$, where

$$\begin{aligned} I_2 &= -B/A \\ S_2 &= \frac{1+\alpha I_2}{\beta}\left(p\delta + \gamma + \frac{\beta_2}{1+\alpha_2 I_2}\right). \end{aligned} \tag{22}$$

Note that if $\alpha_2 > \alpha_2^0$ and $\mathcal{R}_0^* > 1$ then $g(\alpha_2) > 0$.

Hence A_3 is nonempty and its elements satisfy $B < 0$, therefore if $(\beta_2, \alpha_2) \in A_3$ there exists a unique positive endemic equilibrium E_2.

2. If $\mathcal{R}_0 < 1$ then $C > 0$ and the roots of the quadratic equation for I_0 must be real of equal sign or complex conjugate. By the previous part we know that if $(\beta_2, \alpha_2) \in A_3$ then $P_1 < 1$, moreover if $\mathcal{R}_0 > P_1$ then $B < 0$ and therefore both roots must have positive real part. Finally, to assure that equilibria are both real, we demand that $\Delta \ge 0$. Computing Δ:

$$\begin{aligned} \Delta &= B^2 - 4AC \\ &= A_2\mathcal{R}_0^2 + B_2\mathcal{R}_0 + C_2 = \Delta(\mathcal{R}_0), \end{aligned} \tag{23}$$

where:

$$A_2 = \alpha^2 b^2 (p\delta + \gamma + \beta_2)^2 \tag{24}$$

$$\begin{aligned} B_2 = &-2[\beta(\gamma + \beta_2 + bm(1-\alpha_2)) + \alpha b(p\delta + \gamma + \beta_2) + \beta mb\alpha \\ &+ b\alpha_2(p\delta + \gamma)]\alpha b(p\delta + \gamma + \beta_2) + 4\alpha_2(\beta(\gamma + bm)\alpha b(p\delta + \gamma)) \\ &\times b(p\delta + \gamma + \beta_2) \end{aligned} \tag{25}$$

$$\begin{aligned} C_2 = &(\beta(\gamma + \beta_2 + bm(1-\alpha_2)) + \alpha b(p\delta + \gamma + \beta_2) + \beta mb\alpha + b\alpha_2(p\delta + \gamma))^2 \\ &- 4\alpha_2(\beta(\gamma + bm) + \alpha b(p\delta + \gamma))b(p\delta + \gamma + \beta_2). \end{aligned} \tag{26}$$

The previous expression is a quadratic function of $\mathcal{R}_0$. To establish the region where $\Delta \geq 0$, it is necessary to know how the roots of $\Delta(\mathcal{R}_0)$ behave. The discriminant of the quadratic function $\Delta(\mathcal{R}_0)$ is

$$\Delta_2 = -16\,\alpha_2\, b^2\beta\ (p\delta + \gamma + \beta_2)^2\,(\beta\,\gamma + \beta\, bm + \alpha\, bp\delta + \alpha\, b\gamma) \times\ (\alpha(\alpha bm + \beta_2 + \gamma + bm) - \alpha_2(\gamma + bm + \alpha bm))\,. \tag{27}$$

If we assume that $\Delta_2 < 0$, then $\alpha_2 < \frac{\alpha(bm\alpha - \beta_2 + \gamma + bm)}{\gamma + bm + \alpha bm}$ and in this case we have that:

$$\gamma + \beta_2 + bm - bm\alpha_2 + bm\alpha > \frac{2\beta_2\alpha bm + (\gamma + bm)(\gamma + \beta_2 + bm + bm\alpha)}{\gamma + bm + \alpha bm} > 0. \tag{28}$$

So we get that $P_1 > 1 > \mathcal{R}_0$, which is a contradiction with the assumption in this part, therefore $\Delta_2 \geq 0$ and in consequence $\Delta(\mathcal{R}_0)$ has two real roots,

$$\begin{aligned}
R_0^- &= \frac{-B_2 - \sqrt{\Delta_2}}{2A_2} \\
&= 1 - \frac{1}{b\alpha^2(p\delta + \gamma + \beta_2)}[\sqrt{-\beta(\alpha(bm\alpha + \beta_2 + \gamma + bm - bm\alpha_2) - \alpha_2(\gamma + bm))} \\
&+ \sqrt{\alpha_2(\beta(\gamma + bm) + \alpha b(p\delta + \gamma))}]^2, \\
R_0^+ &= \frac{-B_2 + \sqrt{\Delta_2}}{2A_2} \\
&\times 1 - \frac{1}{b\alpha^2(p\delta + \gamma + \beta_2)}[\sqrt{-\beta(\alpha(bm\alpha + \beta_2 + \gamma + bm - bm\alpha_2) - \alpha_2(\gamma + bm))} \\
&- \sqrt{\alpha_2(\beta(\gamma + bm) + \alpha b(p\delta + \gamma))}]^2.
\end{aligned} \tag{29}$$

Note that due to the positivity of Δ_2 and (27), we have that

$$-\beta(\alpha(bm\alpha + \beta_2 + \gamma + bm - bm\alpha_2) - \alpha_2(\gamma + bm))$$

is positive, allowing its roots to be well defined. Analyzing the derivative of $\Delta(\mathcal{R}_0)$ we have that

$$\Delta'(R_0^+) = \sqrt{\Delta_2} > 0 \quad \text{and} \quad \Delta'(R_0^-) = -\sqrt{\Delta_2} < 0,$$

moreover $R_0^- < R_0^+$ making Δ positive for $\mathcal{R}_0 > R_0^+$ or $\mathcal{R}_0 < R_0^-$. Nevertheless

$$R_0^- = 1 + \frac{1}{b\alpha(p\delta + \gamma + \beta_2)}(\beta(\gamma + \beta_2 + bm - bm\alpha_2 + bm\alpha)) - \epsilon,$$

while

$$P_1 = 1 + \frac{1}{b\alpha(p\delta + \gamma + \beta_2)}(\beta(\gamma + \beta_2 + bm - bm\alpha_2 + bm\alpha)) + \epsilon_2,$$

with $\epsilon, \epsilon_2 > 0$, making $R_0^- < P_1 < R_0$. Therefore for $\mathcal{R}_0 > \max(P_1, R_0^+)$, we have that there exist two positive endemic equilibria E_1, E_2, proving this part.

3. If $(\beta_2, \alpha_2) \in A_3$ then $P_1 < 1$. If $1 > \mathcal{R}_0 > P_1$, then we have that $B < 0$ and $C > 0$, therefore we have a pair of roots of the quadratic for I with positive real part. In the previous part it was proven that for $P_1 < 1$ the discriminant $\Delta_2 \geq 0$ and both roots R_0^+, R_0^- are real and less than one. If $\mathcal{R}_0 = R_0^+$ then $\Delta = 0$ and both roots are fused in one $I_1 = -B/2A = I_2$. Therefore we have a unique positive endemic equilibrium $E_1 = E_2$.
4. If $(\beta_2, \alpha_2) \in A_3$ then $P_1 < 1$. If $\mathcal{R}_0 = P_1 < 1$ then $C > 0$, implying that the roots are complex conjugate or real of the same sign. Being $\mathcal{R}_0 = P_1$ then $B = 0$, implying that both roots have real part equal to zero, therefore there are no positive endemic equilibria.
5. If $0 < \mathcal{R}_0 \leq 1$ and $(\beta_2, \alpha_2) \in A_1 \cup A_2$ then $P_1 \geq 1$, therefore $\mathcal{R}_0 \leq P_1$, $B \geq 0$, and $C \geq 0$. Hence there are two roots with real part zero or negative, which are not positive equilibria.
6. If $(\beta_2, \alpha_2) \in A_3$ we have that $P_1 < 1$ and the roots of the discriminant R_0^+, R_0^- are real, in addition that $R_0^- < P_1$ and $R_0^+ < 1$ by definition of this case. If $0 < \mathcal{R}_0 < \max\{R_0^+, P_1\} < 1$, then $C > 0$ and the roots I_2, I_3 are complex conjugate or real with the same sign. If $\mathcal{R}_0 < P_1$ then $B > 0$, and the roots have negative real part, so there are

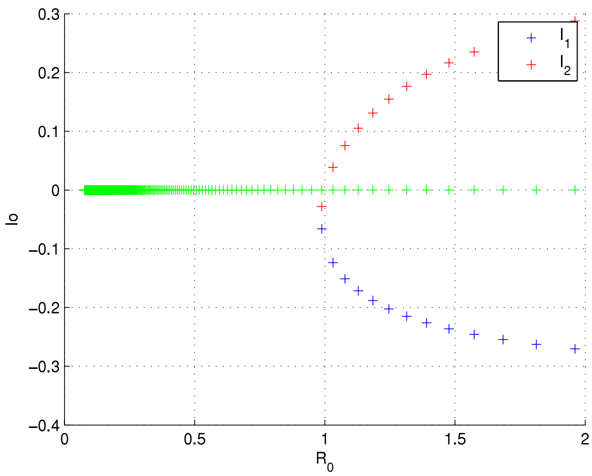

Fig. 2. Graph of $\mathcal{R}_0$ versus the values I of equilibria. Parameter values used are $\alpha = 0.4$, $\alpha_2 = 3.8$, $\beta = 0.2$, $b = 0.2$, $\gamma = 0.01$, $\delta = 0.01$, $p = 0.02$, $m = 0.1$. In this example β_2 varies from 0 to 0.025, therefore $\mathcal{R}_0$ varies between 0.5682 and 1.9682. $g(\alpha_2) = -0.0017$ and $\alpha_2^0 = 3.8776$, so $(\beta_2, \alpha_2) \in A_1 \cup A_2$. *Forward bifurcation* can be observed in $\mathcal{R}_0 = 1$.

not positive endemic equilibria. If $0 < \mathcal{R}_0 < R_0^+$ and $\mathcal{R}_0 > R_0^-$, then $\Delta < 0$ and the roots are complex conjugate, therefore there is not real endemic equilibria. If $0 < \mathcal{R}_0 < R_0^+$ and $\mathcal{R}_0 \leq R_0^- < P_1$, then it reduces to the first case in which there are not positive endemic equilibria.

Theorem 3 gives us a complete scenario of the existence of endemic equilibria. When $\mathcal{R}_0^* \leq 1$ we have that $\mathcal{R}_0 < 1$, it follows from the fact that $\mathcal{R}_0 < \mathcal{R}_0^*$ whenever $\beta_2 > 0$; then system (3) has only a disease free equilibrium and no endemic equilibria.

Otherwise, when $\mathcal{R}_0^* > 1$, if $(\beta_2, \alpha_2) \in A_1 \cup A_2$ then we have no endemic equilibria for $0 < \mathcal{R}_0 < 1$ and a unique endemic equilibrium E_2 when $\mathcal{R}_0 > 1$, so there exists a forward bifurcation in $\mathcal{R}_0 = 1$ from the disease free equilibrium to E_2 (see Fig. 2). If $(\beta_2, \alpha_2) \in A_3$ there exist two positive endemic equilibria whenever $\max\{P_1, R_0^+\} < \mathcal{R}_0 < 1$ (P_1 and $\mathcal{R}_0^+$ depend on β_2), we can observe the backward bifurcation of the equilibrium E to two endemic equilibria (see Fig. 3).

As an immediate consequence of the previous theorem we have that if $\mathcal{R}_0 > 1$ there exists a unique positive endemic equilibrium, while if $\mathcal{R}_0 < 1$ and the conditions of the second part are fulfilled, there exist two positive endemic equilibria. Hence we have the following corollary: $\square$

Corollary 1. *If $\mathcal{R}_0 = 1$, $\mathcal{R}_0^* > 1$ and $(\beta_2, \alpha_2) \in A_3$, system (3) has a backward bifurcation of the disease-free equilibrium E.*

Proof. First we note that if $(\beta_2, \alpha_2) \in A_3$ then R_0^+ is real less than one and $P_1 < 1$, therefore we can find a neighborhood of points in the interval $(\max\{R_0^+, P_1\}, 1)$. By case 2 of theorem, if $\mathcal{R}_0$ lies in this neighborhood there exist two positive endemic equilibria E_1, E_2; for $\mathcal{R}_0 = 1$ there exists a unique positive endemic equilibrium E_2, while the other endemic equilibrium becomes zero. Finally for $\mathcal{R}_0 > 1$ there exists a unique positive endemic equilibrium as the zero "endemic" equilibrium becomes negative. $\square$

3. Characteristic equation and stability

The characteristic equation of the linearization of system (3) in the equilibrium (S_0, I_0) is given by:

$$\det(DF - \lambda I), \tag{30}$$

where

$$DF = \begin{pmatrix} \dfrac{\partial f_1}{\partial S} & \dfrac{\partial f_1}{\partial I} \\ \dfrac{\partial f_2}{\partial S} & \dfrac{\partial f_2}{\partial I} \end{pmatrix}. \tag{31}$$

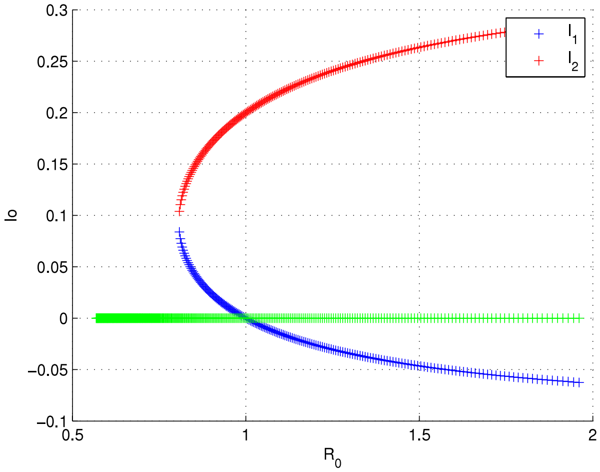

Fig. 3. Graph of $\mathcal{R}_0$ versus the values I of equilibria. In this example β_2 varies from 0 to 0.025 therefore $\mathcal{R}_0$ varies between 0.5682 and 1.9682. Parameter values used are $\alpha = 0.4, \alpha_2 = 16, \beta = 0.2, b = 0.2, \gamma = 0.01, \delta = 0.01, p = 0.02, m = 0.1$. $g(\alpha_2) = 0.1188$ and $\alpha_2^0 = 3.8776$, so $(\beta_2, \alpha_2) \in A_3$. *Backward bifurcation* can be observed in $\mathcal{R}_0 = 1$ and the existence of two positive endemic equilibria whenever $\max\{P_1, R_0^+\} < \mathcal{R}_0 < 1$.

Matrix is evaluated in the equilibrium (S_0, I_0). Functions f_1, f_2 are the following:

$$f_1 = -\frac{\beta S I}{1+\alpha I} - bS + bm(1-I) + p\delta I \tag{32}$$

$$f_2 = \frac{\beta S I}{1+\alpha I} - p\delta I - \gamma I - \frac{\beta_2 I}{1+\alpha_2 I}. \tag{33}$$

Computing the matrix DF we obtain:

$$DF(S, I) = \begin{pmatrix} \dfrac{-\beta I}{1+\alpha I} - b & \dfrac{-\beta S}{(1+\alpha I)^2} - bm + p\delta \\ \dfrac{\beta I}{1+\alpha I} & \dfrac{\beta S}{(1+\alpha I)^2} - p\delta - \gamma - \dfrac{\beta_2}{(1+\alpha_2 I)^2} \end{pmatrix}. \tag{34}$$

3.1. Stability of disease free equilibrium

For the disease free equilibrium $E = (m, 0)$ the Jacobian matrix is:

$$DF(m, 0) = \begin{pmatrix} -b & -\beta m - bm + p\delta \\ 0 & \beta m - p\delta - \gamma - \beta_2 \end{pmatrix}.$$

Theorem 4. *If $\mathcal{R}_0 < 1$ then the equilibrium $E = (m, 0)$ of model (3) is locally asymptotically stable, while if $\mathcal{R}_0 > 1$ then it is unstable.*

Proof. The characteristic equation for the equilibrium E is given by

$$\begin{aligned} P(\lambda) &= \det(DF(m,0) - \lambda I_{2x2}) \\ &= \det \begin{pmatrix} -b-\lambda & -\beta m - bm + p\delta \\ 0 & \beta m - p\delta - \gamma - \beta_2 - \lambda \end{pmatrix} \\ &= (-b-\lambda)(\beta m - p\delta - \gamma - \beta_2 - \lambda). \end{aligned} \tag{35}$$

Eq. (35) has two real roots $\lambda_1 = -b$ and $\lambda_2 = \beta m - p\delta - \gamma - \beta_2$. By Hartman–Grobman's theorem, if the roots of (35) have non-zero real part then the solutions of system (3) and its linearization are qualitatively equivalent. If

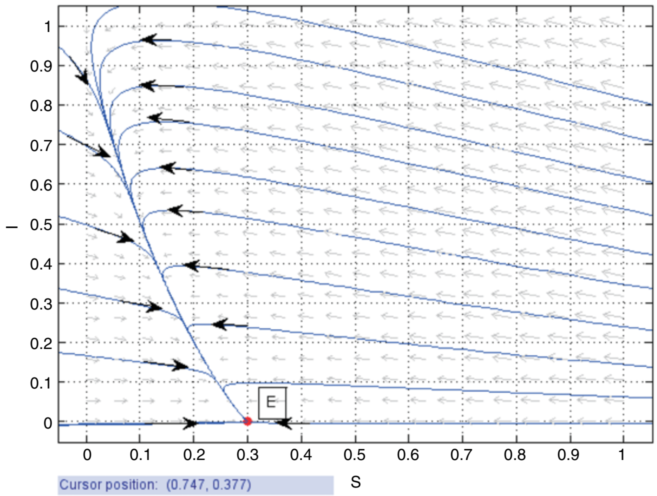

Fig. 4. Global stability of equilibrium E.

both roots have negative real part then the equilibrium E is locally asymptotically stable, whilst if any of the roots has positive real part the equilibrium is unstable. Clearly $\lambda_1 < 0$, but $\lambda_2 < 0$ if and only if

$$\beta m - p\delta - \gamma < \beta_2,$$

if and only if $\mathcal{R}_0 < 1$. □

According to the previous theorem and Theorem 3 we obtain the following result for the global stability of equilibrium E.

Theorem 5. *If* $0 < \mathcal{R}_0 < 1$ *and one of the following conditions holds:*

- $\mathcal{R}_0^* \leq 1$.
- $\mathcal{R}_0 = P_1$ *and* $(\beta_2, \alpha_2) \in A_3$.
- $(\beta_2, \alpha_2) \in A_1 \cup A_2$.
- $(\beta_2, \alpha_2) \in A_3$ *and* $0 < \mathcal{R}_0 < \max\{R_0^+, P_1\}$.

Then equilibrium E of system (3) *is globally asymptotically stable.*

Proof. If $0 < \mathcal{R}_0 < 1$ then by Theorem 4 the equilibrium E is locally asymptotically stable. If any of the given conditions holds then by Theorem 3 there are no endemic equilibria in the region $D = \{S(t), I(t) \geq 0\ \forall t > 0,\ S(t) + I(t) \leq 1\}$, which it was proven to be positively invariant in Lemma 1. By [10, page 245] any solution of (3) starting in D must approach either an equilibrium or a closed orbit in D. By [9, theorem 3.41] if the solution path approaches a closed orbit, then this closed orbit must enclose an equilibrium. Nevertheless, the only equilibrium existing in D is E and it is located in the boundary of D, therefore there is no closed orbit enclosing it, totally contained in D. Hence any solution of system (3) with initial conditions in D must approach the point E as t tends to infinity. □

Example 1. Take the following values for the parameters: $\alpha = 0.4, \alpha_2 = 10, \beta = 0.2, b = 0.2, \gamma = 0.01, \delta = 0.01, p = 0.02, m = 0.3, \beta_2 = 0.1$. Equilibrium $E = (0.3, 0)$, $\mathcal{R}_0 = 0.5445 < 1$. By Theorem 4, E is locally asymptotically stable, $\alpha_2^0 = 7.42 < \alpha_2$ and $g(\alpha_2) = -0.1864 < \beta_2$, therefore $(\beta_2, \alpha_2) \in A_2$. By Theorem 3 there are no positive endemic equilibria. Finally by Theorem 5 we have that E is globally stable. See Fig. 4.

Theorem 6. *If* $\mathcal{R}_0 = 1$ *and* $\beta_2 \neq g(\alpha_2)$ *then equilibrium E is unstable. It is a transcritical bifurcation point. Moreover, if* $(\beta_2, \alpha_2) \in A_1 \cup A_2$ *the region* $D = \{S(t), I(t) \geq 0\ \forall t > 0,\ S(t) + I(t) \leq 1\}$, *previously defined in the proof of Theorem 5, is contained in the stable manifold of E.*

Proof. If $\mathcal{R}_0 = 1$ one of the eigenvalues of the Jacobian matrix of the system is zero, hence we cannot apply Hartman–Grobman's theorem. In order to establish the stability of equilibrium E we apply central manifold theory. Making the change of variables, $\hat{S} = S - m$, $\hat{I} = I$, we obtain the equivalent system

$$\begin{aligned}\frac{d\hat{S}}{dt} &= -\frac{\beta(\hat{S}+m)\hat{I}}{1+\alpha\hat{I}} - b\hat{S} - bm\hat{I} + p\delta\hat{I}\\ \frac{d\hat{I}}{dt} &= \frac{\beta(\hat{S}+m)\hat{I}}{1+\alpha\hat{I}} - p\delta\hat{I} - \gamma\hat{I} - \frac{\beta_2\hat{I}}{1+\alpha_2\hat{I}}.\end{aligned} \tag{36}$$

Because $\hat{I} = I$ we ignore the hat and use only I. This new system has an equilibrium in $\hat{E} = (0, 0)$ and its Jacobian matrix in that point is

$$DF(m, 0) = \begin{pmatrix} -b & -\beta m - bm + p\delta \\ 0 & 0 \end{pmatrix}. \tag{37}$$

Using change of variables $S = u - \frac{(\gamma + beta2 + bm)v}{b}$, $I = v$ and $\beta m = p\delta + \gamma + \beta_2$ we obtain the equivalent system (see Appendix A):

$$\begin{aligned}\frac{dv}{dt} &= 0u + f(v, u)\\ \frac{du}{dt} &= -bu + g(v, u),\end{aligned} \tag{38}$$

where f and g are defined in Appendix A.

By [3], system (3) has a center manifold of the form $u = h(v)$ and the flow in the center manifold (and therefore in the system) is given by the equation

$$v' = f(v, h(v)) \sim f(v, \phi(v)),$$

where $h(v) = a_0v^2 + a_1v^3 + O(v^4)$, and a_i's are given in Appendix A. Expanding the Taylor series of f we obtain the flow equation

$$\begin{aligned}v' &= -\frac{b^3\beta m + b^2\beta^2 m + b^3\gamma\alpha_2 - b^2\beta p\delta + b^3\alpha\beta m + b^3 p\delta\alpha_2 - b^3\beta m\alpha_2}{b^3}v^2 + O(v^3)\\ &= Hv^2 + O(v^3).\end{aligned} \tag{39}$$

Therefore the dynamics of solutions near the equilibrium $\hat{E} = (0, 0)$ is given by the quadratic term, whenever this term is not zero. We note that $H = 0$ if and only if

$$\alpha_2 = \frac{-\beta(bm + \beta m - p\delta + b\alpha m)}{b(p\delta + \gamma - \beta m)}. \tag{40}$$

Substituting again $\mathcal{R}_0 = 1$, expressed as $\beta m = p\delta + \gamma + \beta_2$, we obtain $H = 0$ if and only if $\beta_2 = g(\alpha_2)$.

If $(\beta_2, \alpha_2) \in A_3$ then $H > 0$. $v' > 0$ for $v \neq 0$. If $(\beta_2, \alpha_2) \in A_1 \cup A_2$ then $H < 0$, $v' < 0$ for $v \neq 0$. In both cases $\hat{E}$ is unstable. Moreover, if $(\beta_2, \alpha_2) \in A_1 \cup A_2$ then $H < 0$ and $v' < 0$ for $v > 0$. Recalling $v(t) = I(t)$ we have under this assumption that $I'(t) < 0$ for $I > 0$ therefore $I(t) \to 0^+$, while as $v_1 = (1, 0)$ is the stable direction of the point E then $S(t) \to 0$, therefore the solutions in the region D approach the equilibrium E as $t \to \infty$.

Remark. When $\mathcal{R}_0 = 1$ we have the attractor direction in the x axis, but in direction of y axis the equilibrium is neither attractor or repulsor, so E is unstable but it is not a saddle point. In this case it is a transcritical bifurcation point. □

Example 2. Take the following values for the parameters: $\beta = 0.2$, $\alpha = 0.4$, $\delta = 0.01$, $\gamma = 0.01$, $\alpha_2 = 10$, $m = 0.3$, $p = 0.02$, $b = 0.2$, $\beta_2 = 0.0498$. In this case $\mathcal{R}_0 = 1$, $\alpha_2^0 = 1.8876$ and $g(\alpha_2) = 0.4040$, hence $(\beta_2, \alpha_2) \in A_3$. By the first case of Theorem 3 the system has a unique endemic equilibrium in $S_2 = 0.11210$, $I_2 = 0.4781$. By Theorem 6 the equilibrium E is a transcritical bifurcation point, see Fig. 5.

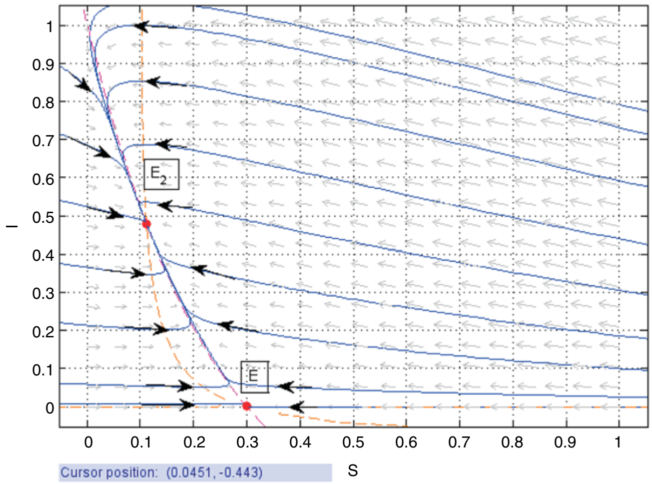

Fig. 5. Phase plane of the system for $\mathcal{R}_0 = 1$ with $(\beta_2, \alpha_2) \in A_3$.

Example 3. If we take the same values as in the previous example except $\alpha_2 = 2$, then $g(\alpha_2) = 0.0056 < \beta_2$, hence $(\beta_2, \alpha_2) \in A_2$. By Theorem 3 the system has no endemic equilibria, and by Theorem 6 the point E is a transcritical bifurcation point. Moreover, the region D is totally contained in the stable manifold, see Fig. 6.

3.2. Stability of endemic equilibria

The general form of the Jacobian matrix is

$$DF = \begin{pmatrix} -\dfrac{\beta I}{1+\alpha I} - b & -\dfrac{\beta S}{(1+\alpha I)^2} - bm + p\delta \\ \dfrac{\beta I}{1+\alpha I} & \dfrac{\beta S}{(1+\alpha I)^2} - p\delta - \gamma - \dfrac{\beta_2}{(1+\alpha_2 I)^2} \end{pmatrix}. \tag{41}$$

Therefore the characteristic equation for an endemic equilibrium is

$$P(\lambda) = \left(-\frac{\beta I}{1+\alpha I} - b - \lambda\right)\left(\frac{\beta S}{(1+\alpha I)^2} - p\delta - \gamma - \frac{\beta_2}{(1+\alpha_2 I)^2} - \lambda\right) - \left(\frac{\beta I}{1+\alpha I}\right)\left(-\frac{\beta S}{(1+\alpha I)^2} - bm + p\delta\right). \tag{42}$$

Denote:

$$C_I := \frac{\beta I}{1+\alpha I} \tag{43}$$

$$C_S := \frac{\beta S}{(1+\alpha I)^2} \tag{44}$$

$$D_I := \frac{\beta_2}{(1+\alpha_2 I)^2}. \tag{45}$$

Then the characteristic polynomial is rewritten as

$$P(\lambda) = \lambda^2 + W\lambda + U \tag{46}$$

where:

$$W = C_I + b - C_S + p\delta + \gamma + D_I \tag{47}$$

$$U = C_I\gamma + C_I D_I - bC_S + bp\delta + b\gamma + bD_I + C_I bm. \tag{48}$$

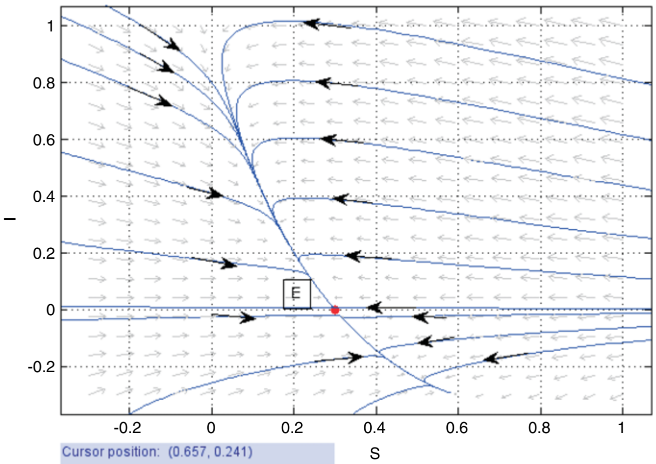

Fig. 6. Phase plane for $\mathcal{R}_0 = 1$ with $(\beta_2, \alpha_2) \in A_2$.

By Routh–Hurwitz criteria for $n = 2$ if the coefficient W and the independent term U are positive then the roots of the characteristic equation have negative real part and therefore the endemic equilibrium is locally asymptotically stable. Note that whenever the equilibria are positive, C_I, C_S, D_I will be positive as well. Let us analyze the stability according to the value of $\mathcal{R}_0$.

Theorem 7. *Whenever the equilibrium E_1 exists it is a saddle and therefore unstable.*

Proof. Consider $E_1 = (S_1, I_1)$ and its characteristic polynomial (46). By Routh–Hurwitz criterion for quadratic polynomials, its roots have negative real part if and only if $U > 0$ and $W > 0$, where U, W depend on E_1. Moreover, when $U < 0$ its roots are both real with different sign and when $U > 0$ and $W < 0$ the roots have positive real part. Computing the value of U and expressing S_1 in terms of I_1 we obtain

$$U = \frac{I_1(a_1 I_1^2 + b_1 I_1 + c_1)}{(1+\alpha I_1)(1+\alpha_2 I_1)^2} = \frac{I_1 F(I_1)}{(1+\alpha I_1)(1+\alpha_2 I_1)^2} \tag{49}$$

where:

$$\begin{aligned} a_1 &= \alpha_2^2(\beta\gamma + bp\alpha\delta + b\alpha\gamma + bm\beta) = \alpha_2 A > 0, \\ b_1 &= 2\alpha_2(\beta\gamma + bp\alpha\delta + b\alpha\gamma + bm\beta) = 2A > 0, \\ c_1 &= \beta\beta_2 + bm\beta + bp\alpha\delta + b\alpha\beta_2 + \beta\gamma - b\alpha_2\beta_2 + b\alpha\gamma = B - \alpha_2 C. \end{aligned} \tag{50}$$

We are assuming that equilibrium E_1 exists and it is positive, and this happens (by previous section) when $B < 0$ and $C > 0$, so $c_1 < 0$. The sign of U is equal to $\operatorname{sgn}(F(I_1))$. $F(I_1)$, has two roots of the form:

$$I* = \frac{-b_1 + \sqrt{b_1^2 - 4a_1c_1}}{2a_1} \tag{51}$$

$$I** = \frac{-b_1 - \sqrt{b_1^2 - 4a_1c_1}}{2a_1} \tag{52}$$

where $b_1^2 - 4a_1c_1 > 0$ and therefore $I*$ and $I**$ are both real values with $I** < 0$. $F(I_1) > 0$ for $I_1 > I*$ and $I_1 < I**$, but second condition never holds because $I_1 > 0$, so $F(I_1) < 0$ for $0 < I_1 < I*$.

Computing $I*$ in terms of A, B, C:

$$I* = -\frac{1}{\alpha_2} + \frac{1}{\alpha_2 A}\sqrt{(A^2 - \alpha_2 AB + \alpha_2^2 AC)}. \tag{53}$$

Substituting $\Delta = B^2 - 4AC > 0$

$$
\begin{aligned}
I* &= -\frac{1}{\alpha_2} + \frac{1}{\alpha_2 A}\sqrt{\left(A^2 - \alpha_2 AB + \frac{\alpha_2^2}{4}(B^2 - \Delta)\right)} \\
&= -\frac{1}{\alpha_2} + \frac{1}{2\alpha_2 A}\sqrt{(2A - \alpha_2 B)^2 - \alpha_2^2 \Delta} \\
&> -\frac{1}{\alpha_2} + \frac{1}{2\alpha_2 A}\left(\sqrt{(2A - \alpha_2 B)^2} - \sqrt{\alpha_2^2 \Delta}\right) \\
&= \frac{-B - \sqrt{\Delta}}{2A} = I_1.
\end{aligned} \tag{54}
$$

Therefore $U < 0$ and the equilibrium E_1 is a saddle. □

Theorem 8. *Assume the conditions of Theorem 3 for existence and positivity of the endemic equilibrium E_2. Let a_1, b_1, c_1 defined by Eqs. (50).*

- *If $b_1^2 - 4a_1c_1 < 0$, then E_2 is unstable for $s < 0$ and locally asymptotically stable for $s > 0$.*
- *If $b_1^2 - 4a_1c_1 \geq 0$, E_2 is locally asymptotically stable for $I_2 > I*$ and $s > 0$, whereas that it is unstable for $I_2 < I*$ or $I_2 > I*$ and $s < 0$.*

With $s = m_1(-B + \sqrt{B^2 - 4AC}) + 2Am_2$,

$$
\begin{aligned}
m_1 &= (r + \beta_2\alpha - \beta_2\alpha_2 + 2b\alpha_2)A^2 - \alpha_2^2 rAC - AB\alpha_2(b\alpha_2 + 2r) + B^2\alpha_2^2 r, \\
m_2 &= bA^2 - AC\alpha_2(b\alpha_2 + 2r) + \alpha_2^2 rBC, \\
r &= \alpha(p\delta + b + \gamma) + \beta.
\end{aligned} \tag{55}
$$

Proof. Consider $E_2 = (S_2, I_2)$ be real and positive, and its characteristic polynomial (46). We will have that the equilibrium is unstable when $U < 0$ or $U > 0, W < 0$, and locally asymptotically stable when $U > 0, W > 0$. Following the previous proof

$$
U = \frac{I_2(a_1 I_2^2 + b_1 I_2 + c_1)}{(1 + \alpha I_2)(1 + \alpha_2 I_2)^2} = \frac{I_2 F(I_2)}{(1 + \alpha I_2)(1 + \alpha_2 I_2)^2} \tag{56}
$$

where a_1, b_1, c_1 are the same as in previous theorem. Therefore $\mathrm{sgn}(U) = \mathrm{sgn}(F(I_2))$. We have seen that $F(I_2)$ has two roots $I*$ and $I**$.

- If $b_1^2 - 4a_1c_1 < 0$ the roots are not real, so $F(I_2)$ has a single sign for all values of I_2 and $\mathrm{sgn}(F(I_2)) = \mathrm{sgn}(c_1) = \mathrm{sgn}(B - \alpha_2 C)$. Using the fact that

$$
b_1^2 - 4a_1c_1 = 4A(A - B\alpha_2 + \alpha_2^2 C) < 0, \tag{57}
$$

we can obtain that $c_1 > 0$, so $U > 0$. Now,

$$
\begin{aligned}
W &= \frac{1}{(1 + \alpha I_2)(1 + \alpha_2 I_2)^2}[{\alpha_2}^2\,(\alpha\,\gamma + b\alpha + \beta + \alpha\,p\delta)\,{I_2}^3 \\
&+ \alpha_2\,(b\alpha_2 + 2\,\alpha\,p\delta + 2\,b\alpha + 2\,\alpha\,\gamma + 2\,\beta)\,{I_2}^2 \\
&+ (\alpha\,p\delta + b\alpha + \beta + \alpha\,\beta_2 - \beta_2\,\alpha_2 + \alpha\,\gamma + 2\,b\alpha_2)\,I_2 + b] \\
&= \frac{G(I_2)}{(1 + \alpha I_2)(1 + \alpha_2 I_2)^2}.
\end{aligned} \tag{58}
$$

By using the division algorithm,

$$
\begin{aligned}
G(I_2) &= (AI_2^2 + BI_2 + C)P(I_2) \\
&\quad + \frac{1}{A^2}[((r + \beta_2\alpha - \beta_2\alpha_2 + 2b\alpha_2)A^2 - \alpha_2^2 rAC - AB\alpha_2(b\alpha_2 + 2r) + B^2\alpha_2^2 r)I_2
\end{aligned}
$$

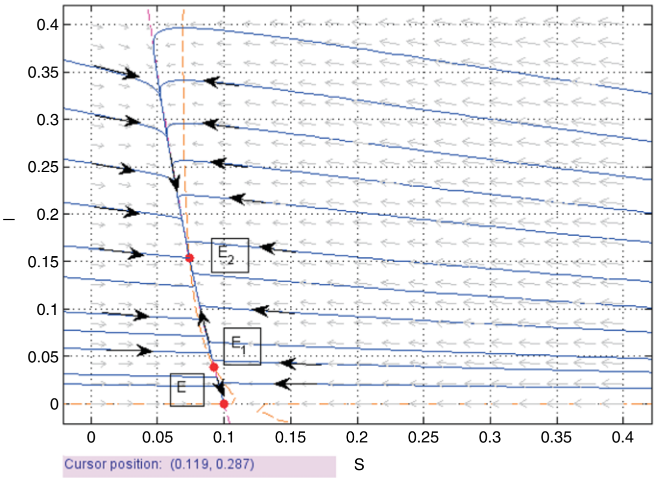

Fig. 7. Phase plane with three equilibria.

$$+ bA^2 - AC\alpha_2(b\alpha_2 + 2r) + \alpha_2^2 rBC],$$

$$= (AI_2^2 + BI_2 + C)P(I_2) + \frac{m_1 I_2 + m_2}{A^2} \tag{59}$$

where $P(I_2)$ is a polynomial in I_2 of degree one. Being I_2 a coordinate of an equilibrium then $AI_2^2 + BI_2 + C = 0$ and

$$G(I_2) = \frac{m_1 I_2 + m_2}{A^2}.$$

Hence $\text{sgn}(W) = \text{sgn}(G(I_2)) = \text{sgn}(\frac{m_1 I_2 + m_2}{A^2}) = \text{sgn}(m_1 I_2 + m_2)$. Substituting the value of I_2,

$$m_1 I_2 + m_2 = \frac{m_1}{2A}(-B + \sqrt{B^2 - 4AC}) + m_2.$$

It follows that $\text{sgn}(m_1 I_2 + m_2) = \text{sgn}(m_1(-B + \sqrt{B^2 - 4AC}) + 2Am_2) = \text{sgn}(s)$. Therefore E_2 is unstable if $s < 0$ and locally asymptotically stable if $s > 0$.

- When $b_1^2 - 4a_1c_1 \geq 0$, we have two real roots $I*$, $I**$ of $F(I_2)$. As we saw in the proof of previous theorem, $F(I_2) > 0$ for $I_2 > I*$ and $I_2 < I**$ (which does not hold because $I** < 0$), and $F(I_2) < 0$ for $0 < I_2 < I*$. So, if $0 < I_2 < I*$ the equilibrium E_2 is unstable.

  When $I_2 > I*$ then $U > 0$ and the sign of W depends on the sign of s, therefore the equilibrium is locally asymptotically stable for $s > 0$ and unstable for $s < 0$. □

Example 4. In Fig. 7 we show an example with three equilibria points: E, E_1 and E_2. The parameters used are fixed as in Fig. 3, and $\beta_2 = 0.013$. We can see that, in fact, E_1 is a saddle, while E and E_2 are stable.

4. Hopf bifurcation

By previous section we know that the system (3) has two positive endemic equilibria under the conditions of Theorem 3. Equilibrium E_1 is always a saddle, so its stability does not change and there is no possibility of a Hopf bifurcation in it. So let us analyze the existence of a Hopf bifurcation of equilibrium $E_2 = (S_2, I_2)$. Analyzing the characteristic equation for E_2, it has a pair of pure imaginary roots if and only if $U > 0$ and $W = 0$.

Theorem 9. *Suppose the existence and positivity of the endemic equilibrium E_2, and one of the following conditions:*

- $b_1^2 - 4a_1c_1 < 0$,
- $b_1^2 - 4a_1c_1 \geq 0$, $I_2 > I*$.

Let s be defined as in Theorem 8. System (3) undergoes a Hopf bifurcation of the equilibrium E_2 at $s = 0$. Moreover, if $\bar{a}_2 < 0$, there is a family of stable periodic orbits of (3) as s decreases from 0; if $\bar{a}_2 > 0$, there is a family of unstable periodic orbits of (3) as s increases from 0.

Proof. The characteristical polynomial for E_2 has a pair of pure imaginary roots iff $U > 0$ and $W = 0$. From the proof of Theorem 8 we have that $U > 0$ if and only if $b_1^2 - 4a_1c_1 < 0$ or $b_1^2 - 4a_1c_1 \geq 0$ and $I_2 > I*$.

Although, $\mathrm{sgn}(W) = \mathrm{sgn}(s)$, so $W = 0$ if and only if $s = 0$. By first part of theorem 3.4.2 of [5] the roots λ and $\bar{\lambda}$ of (46) for E_2 vary smoothly, so we can affirm that near $s = 0$ these roots are still complex conjugate and

$$\begin{aligned}\left.\frac{dRe(\lambda(s))}{ds}\right|_{s=0} &= \frac{d}{ds}\left(\frac{1}{2}W(s)\right)\\ &= \frac{1}{2}\frac{d}{ds}\left(\frac{s}{2A^3(1+\alpha I_2)(1+\alpha_2 I_2)^2}\right)\\ &= \frac{1}{4A^3(1+\alpha I_2)(1+\alpha_2 I_2)^2} \neq 0.\end{aligned} \tag{60}$$

Therefore $s = 0$ is the Hopf bifurcation point for (3).

To analyze the behavior of the solutions of (3) when $s = 0$ we make a change of coordinates to obtain a new equivalent system to (3) with an equilibrium in $(0, 0)$ in the x–y plane (see Appendix B). Under this change the system becomes:

$$\begin{aligned}\frac{dx}{dt} &= \frac{a_{11}x + a_{12}y + c_1xy + c_2y^2}{1+\alpha y+\alpha I_2},\\ \frac{dy}{dt} &= \frac{a_{21}x + a_{22}y + c_3xy + c_4xy^2 + c_5y^2 + c_6y^3}{(1+\alpha y+\alpha I_2)\,(1+\alpha_2 y+\alpha_2 I_2)}\end{aligned} \tag{61}$$

where the a_{ij}'s and c_i's are defined in Appendix B.

System (61) and (3) are equivalent (Appendix B), so we can work with (61). This system has a pair of pure imaginary eigenvalues if and only if (3), has them too. Computing Jacobian matrix $DF(0, 0)$ of (61)

$$DF(0,0) = \begin{bmatrix} \dfrac{a_{11}}{1+\alpha I_2} & \dfrac{a_{12}}{(1+\alpha I_2)} \\ \dfrac{a_{21}}{(1+\alpha_2 I_2)\,(1+\alpha I_2)} & \dfrac{a_{22}}{(1+\alpha_2 I_2)\,(1+\alpha I_2)} \end{bmatrix}. \tag{62}$$

$$Tr(DF(0,0)) = Tr(Df(S_2, I_2)), \qquad \det(DF(0,0)) = \det(Df(S_2, I_2)).$$

So condition $W = 0$ is equivalent to $a_{11}(1 + \alpha_2 I_2) + a_{22} = 0$ and $U > 0$ equivalent to $a_{22}a_{11} - a_{12}a_{21} > 0$.

System (61) can be rewritten as

$$\frac{dx}{dt} = \frac{a_{11}x}{1+\alpha I_2} + \frac{a_{12}y}{1+\alpha I_2} + G_1(x, y) \tag{63}$$

$$\frac{dy}{dt} = \frac{a_{21}x}{(1+\alpha I_2)\,(1+\alpha_2 I_2)} + \frac{a_{22}y}{(1+\alpha I_2)\,(1+\alpha_2 I_2)} + G_2(x, y) \tag{64}$$

where G_1, G_2 are defined in Appendix B.

Let $\Lambda = \sqrt{\det(DF(0,0))}$. We use the change of variable $u = x$, $v = \frac{a_{11}}{\Lambda(1+\alpha I_2)} + \frac{a_{12}y}{\Lambda(1+\alpha I_2)}$, to obtain the following equivalent system:

$$\begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} 0 & \Lambda \\ -\Lambda & 0 \end{pmatrix}\begin{pmatrix} u \\ v \end{pmatrix} + \begin{pmatrix} H_1(u,v) \\ H_2(u,v) \end{pmatrix} \tag{65}$$

where

$$H_1(u,v) = -\frac{((-a_{12}c_1 + a_{11}c_2)\,u + (-\Lambda c_2\alpha I_2 + \Lambda a_{12}\alpha - \Lambda c_2)\,v)\,((\Lambda + \Lambda\alpha I_2)\,v - a_{11}u)}{a_{12}\left((\alpha\Lambda + \Lambda\alpha^2 I_2)\,v + a_{12} - \alpha a_{11}u + a_{12}\alpha I_2\right)} \tag{66}$$

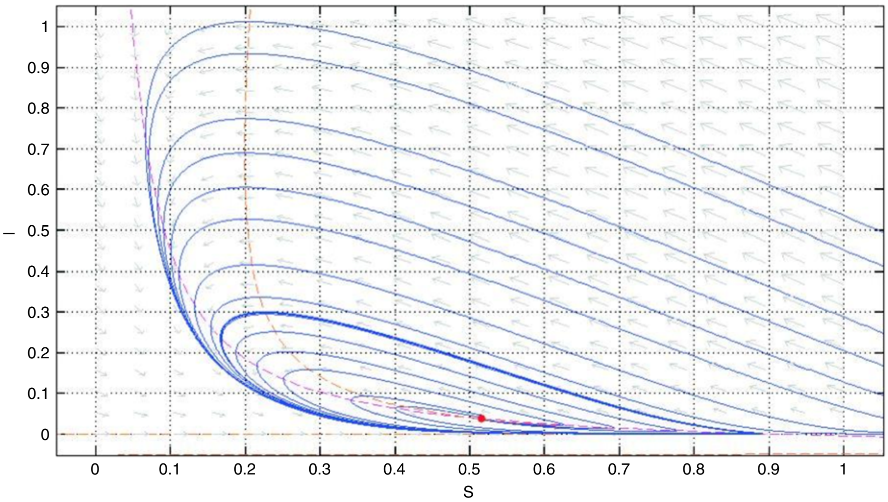

Fig. 8. Existence of a limit cycle in the phase plane. The parameters used are $\beta = 0.2, \alpha = 0.8, \gamma = 0.01, \delta = 0.03, b = 0.01, p = 0.2, m = 0.9, \alpha_2 = 21, \beta_2 = 0.15$. In this case we have that $\mathcal{R}_0 = 1.0843373493975903614 > 1$, so we have a single endemic equilibrium $E_2 = (0.51579943753899313111, 0.037237521747155859148)$. $b_1^2 - 4a_1c_1 = 0.002078697600 > 0$, $I* = -0.034459056594790116219 < I_2$, so we have a Hopf bifurcation at $s = 0$, moreover and $s = -0.000061701527663761846660$ and we can observe the limit cycle around E_2.

$$H_2(u, v) = -\frac{1}{h(u, v)}\left[(\Lambda(1 + \alpha I_2)v - a_{11}u)\left(A_1v^2 + A_2uv + A_3v + A_4u^2 + A_5u\right)\right], \tag{67}$$

and $A_1, \ldots, A_5, h(u, v)$ are defined in Appendix B. Let

$$\begin{aligned}\bar{a}_2 = {} & \frac{1}{16}[(H_1)_{uuu} + (H_1)_{uvv} + (H_2)_{uuv} + (H_2)_{vvv}] + \frac{1}{16(-\Lambda)}[(H_1)_{uv}((H_1)_{uu} + (H_1)_{vv}) \\ & - (H_2)_{uv}((H_2)_{uu} + (H_2)_{vv}) - (H_1)_{uu}(H_2)_{uu} + (H_1)_{vv}(H_2)_{vv}]\end{aligned} \tag{68}$$

where

$$(H_1)_{uuu} = \frac{\partial}{\partial u}\left(\frac{\partial}{\partial u}\left(\frac{\partial H_1}{\partial u}\right)\right)(0, 0),$$

and so on ($\bar{a}_2$ is explicitly expressed in Appendix B).

Then by theorem 3.4.2 of [5] if $\bar{a}_2 \neq 0$ then there exists a surface of periodic solutions, if $\bar{a}_2 < 0$ then these cycles are stable, but if $\bar{a}_2 > 0$ then cycles are repelling (See Fig. 8). □

5. Discussion

As we said in the introduction, traditional epidemic models have always stability results in terms of $\mathcal{R}_0$, such that we need only reduce $\mathcal{R}_0 < 1$ to eradicate the disease. However, including the treatment function brings new epidemic equilibria that make the dynamics of the model more complicated. Now, let us discuss some control strategies for the infectious disease, analyzing the parameters of the treatment function (α_2, β_2) and looking for conditions that allow us to eliminate the disease. We make this study by cases.

A first approach is focused on the definition of $\mathcal{R}_0$, we can see that $\mathcal{R}_0$ decreases when β_2 increases, so the first measure suggesting control is a big value for β_2. But this is not always a good way to proceed. Let us divide our analysis in the following cases:

Case 1: *There is no positive endemic equilibrium for* $\mathcal{R}_0 \leq 1$. This happens when $\mathcal{R}_0^* \leq 1$ (by Theorem 3) or when $\mathcal{R}_0^* > 1$ and $(\alpha_2, \beta_2) \in A_1 \cup A_2$ (Theorem 3, number 5). In this case if $\mathcal{R}_0 > 1$ there is a unique positive endemic equilibrium, therefore there exists a bifurcation at $\mathcal{R}_0 = 1$: from the disease free equilibrium, which is globally asymptotically stable for $0 < \mathcal{R}_0 < 1$ (by Theorem 4) and unstable for $\mathcal{R}_0 = 1$ and $\beta_2 \neq g(\alpha_2)$ (Theorem 6), to the positive endemic equilibrium E_2 as $\mathcal{R}_0$ increases. E_2 will be locally asymptotic stable or unstable depending on

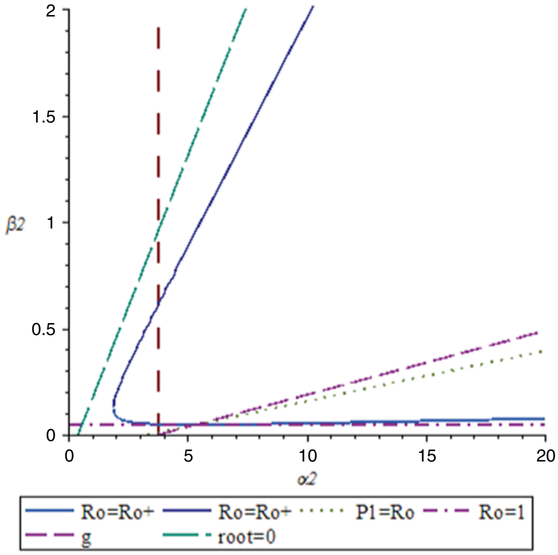

Fig. 9. Bifurcation diagram in terms of β_2 and α_2. The values of the parameters taken are $\alpha = 0.4$, $\beta = 0.3$, $b = 0.2$, $\gamma = 0.03$, $\delta = 0.05$, $p = 0.3$, $m = 0.3$. Here $\mathcal{R}_0 < \mathcal{R}_0^+$ inside the solid curve ($\mathcal{R}_0 = \mathcal{R}_0^+$) and $\mathcal{R}_0 > \mathcal{R}_0^+$ outside it, whenever (β_2, α_2) is in its domain (under the long dashed line "root=0"). $\mathcal{R}_0 < 1$ above the dot-lined line and $\mathcal{R}_0 > 1$ under it; $\mathcal{R}_0 < P_1$ above the dotted line and $\mathcal{R}_0 > P_1$ under that one. The areas A_1, A_2, A_3 are delimited by the dashed line $g = 0$ and $\alpha_2 = 3.8$. In this case the endemic equilibria E_1 and E_2 exist both in the area delimited by the line $\mathcal{R}_0 = 1$ and the dotted line $\mathcal{R}_0 = P_1$, while E_2 exists by itself under the line $\mathcal{R}_0 = 1$.

Theorem 8 or surrounded by a limit cycle (Theorem 9). If conditions for Hopf bifurcation hold then the stability of the limit cycle is determined by $\bar{a}_2$; when $\bar{a}_2 < 0$ the periodic orbit is stable and therefore E_2 is unstable, while if $\bar{a}_2 > 0$ then the periodic orbit is unstable and E_2 is stable. In this case the best way to eradicate the disease is finding parameters that allow $\mathcal{R}_0 < 1$, because then all the infectious states tend to $I = 0$.

Case 2: *There exist endemic equilibria for* $\mathcal{R}_0 \leq 1$. This happens when $(\alpha_2, \beta_2) \in A_3$. The existence of endemic equilibria is determined by the relationship between $\mathcal{R}_0$ and $\max\{P_1, \mathcal{R}_0^+\}$. Let $F(\alpha_2, \beta_2) = \mathcal{R}_0 - \mathcal{R}_0^+$, $G(\alpha_2, \beta_2) = \mathcal{R}_0 - P_1$, and focus on the implicit curves defined by $F = 0$ and $G = 0$. These curves divide the domain A_3 in another ones (see Fig. 9):

$$\begin{aligned}
A_3^1 &= \{(\alpha_2, \beta_2) \in A_3, 0 < \mathcal{R}_0 < \mathcal{R}_0^+\}\\
A_3^2 &= \{(\alpha_2, \beta_2) \in A_3, \mathcal{R}_0 > \mathcal{R}_0^+\}\\
A_3^3 &= \{(\alpha_2, \beta_2) \in A_3, 0 < \mathcal{R}_0 < P_1\}\\
A_3^4 &= \{(\alpha_2, \beta_2) \in A_3, \mathcal{R}_0 > P_1\}.
\end{aligned} \tag{69}$$

If $(\alpha_2, \beta_2) \in A_3^2 \cap A_3^4$ then there exist two endemic equilibria E_1 (a saddle) and E_2 (stable or unstable depending on conditions of Theorem 8 and possibly with a periodic orbit around (Theorem 9)), but when $\mathcal{R}_0 = 1$ one of them becomes negative, leaving us with E_2. In this case $\mathcal{R}_0 < 1$ is not a sufficient condition to control the disease, because even with $\mathcal{R}_0 < 1$ we have endemic positive equilibria that could be stable and then the disease will tend to a non zero value; also we have the possibility of a periodic solution, or biologically, an outbreak that will apparently "disappear" but will re-emerge after some time.

The best way in this case is ensuring $(\alpha_2, \beta_2) \in (A_3^2 \cap A_3^4)^c$ because then we do not have endemic equilibria for $\mathcal{R}_0 < 1$ and the disease free will be globally asymptotically stable.

Acknowledgments

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Appendix A. Computing center manifold

The Jacobian matrix of system (36) is

$$DF(m,0)=\begin{pmatrix}-b & -\beta m-bm+p\delta\\ 0 & 0\end{pmatrix}. \tag{A.1}$$

With eigenvalues $\lambda_1=-b$ and $\lambda_2=0$ and respective eigenvectors $v_1=(1,0)$ and $v_2=(-\frac{\gamma+\beta_2+bm}{b},1)$. Using the eigenvectors to establish a new coordinate system we define:

$$\begin{pmatrix}\hat{S}\\ I\end{pmatrix}=\begin{pmatrix}1 & -\dfrac{\gamma+\beta_2+bm}{b}\\ 0 & 1\end{pmatrix}\begin{pmatrix}u\\ v\end{pmatrix},\quad \text{or}\quad \begin{pmatrix}u\\ v\end{pmatrix}=\begin{pmatrix}1 & \dfrac{\gamma+\beta_2+bm}{b}\\ 0 & 1\end{pmatrix}\begin{pmatrix}S\\ I\end{pmatrix}. \tag{A.2}$$

Under this transformation the system becomes

$$\begin{aligned}
\frac{du}{dt}&=\frac{d}{dt}\hat{S}(t)+\frac{(\gamma+\beta_2+bm)\frac{d}{dt}I(t)}{b}\\
&=-\frac{\beta\left(\hat{S}+m\right)I}{1+\alpha I}-b\hat{S}-bmI+p\delta I+(\gamma+\beta_2+bm)\\
&\times\left(\frac{\beta\left(\hat{S}+m\right)I}{1+\alpha I}-(p\delta+\gamma)I-\frac{\beta_2 I}{1+\alpha_2 I}\right)\frac{1}{b},\\
\frac{dv}{dt}&=\frac{dI}{dt} \qquad\qquad (\text{A.3})\\
&=\frac{\beta\left(\hat{S}+m\right)I}{1+\alpha I}-(p\delta+\gamma)I-\frac{\beta_2 I}{1+\alpha_2 I}. \qquad\qquad (\text{A.4})
\end{aligned}$$

Substituting $S=u-\frac{(\gamma+\beta_2+bm)v}{b}$, $I=v$ and $\beta m=p\delta+\gamma+\beta_2$ we obtain:

$$\begin{aligned}
\frac{dv}{dt}&=0u+f(v,u)\\
\frac{du}{dt}&=-bu+g(v,u),
\end{aligned} \tag{A.5}$$

where

$$\begin{aligned}
f(u,v)&=-\frac{v\,(-\beta\,b-\beta\,b\alpha_2\,v)\,u}{(1+\alpha\,v)\,(1+\alpha_2\,v)\,b}\\
&-\frac{v}{(1+\alpha\,v)\,(1+\alpha_2\,v)\,b}\left(\left(\beta\,bm\alpha_2+b\gamma\,\alpha\,\alpha_2-\beta\,\alpha_2\,p\delta+bp\delta\,\alpha\,\alpha_2+\beta^2\alpha_2\,m\right)v^2\right.\\
&+\left.\left(bp\delta\,\alpha_2+\beta\,bm-\beta\,bmalpha2+b\gamma\,\alpha_2+\beta^2m-\beta\,p\delta+b\alpha\,\beta\,m\right)v\right),\\
g(u,v)&=-\frac{1}{(1+\alpha\,v)\,(1+\alpha_2\,v)\,b^2}[v((mb^2\gamma\,\alpha\,\alpha_2+2\,\beta^2bm^2\alpha_2+\beta\,\alpha_2\,p^2\delta^2\\
&+\beta^3\alpha_2\,m^2-b\gamma\,p\delta\,\alpha\,\alpha_2+b\gamma\,\alpha\,\alpha_2\,\beta\,m-2\,\beta^2\alpha_2\,mp\delta+bp\delta\,\alpha\,\alpha_2\,\beta\,m\\
&-b^2m\alpha\,\alpha_2\,\beta-\beta^2bm\alpha_2+b^2m^2\beta\,\alpha_2+b^2mp\delta\,\alpha\,\alpha_2-bp^2\delta^2\alpha\,\alpha_2\\
&-2\,\beta\,bm\alpha_2\,p\delta-b^2m\beta\,\alpha_2+b\beta\,\alpha_2\,p\delta)v^2+(b^2m^2\beta-2\,\beta\,bmp\delta-\beta\,b^2m+2\,\beta^2bm^2\\
&-\beta^2bm+\beta\,p^2\delta^2+2\,\beta\,bm\alpha_2\,p\delta-bp\delta\,\alpha\,\beta\,m+\beta^3m^2+\beta\,bp\delta-b^2\alpha\,\beta\,m-2\,\beta^2mp\delta\\
&+b^2m^2\alpha\,\beta+b\alpha\,\beta^2m^2-u\beta\,b^2m\alpha_2-b\beta^2u\alpha_2m+b\beta\,u\alpha_2p\delta-\gamma\,bp\delta\,\alpha_2+\gamma\,\beta\,bm\alpha_2
\end{aligned}$$

$$+ b^2mp\delta\,\alpha_2 - b^2m^2\beta\,\alpha_2 + u\beta\, b^2\alpha_2 - bp^2\delta^2\alpha_2 - \beta^2 bm^2\alpha_2 + b^2m\gamma\,\alpha_2)v - b^2m\beta\, u$$
$$+ u\beta\, b^2 - b\beta^2 um + b\beta\, up\delta)]. \tag{A.6}$$

By [3] the system (A.5) has a center manifold of the form $u = h(v)$. Let $\phi : \mathbb{R} \to \mathbb{R}$ and define the annihilator:

$$N\phi = \phi'(v)(f(v,\phi(v))) + b\phi - g(v,\phi(v))$$
$$= \frac{1}{b^2(1+\alpha v)(1+\alpha_2 v)}[bp\delta\,\alpha\, v^3\alpha_2\beta\, m + b^2m^2\beta\, v^2 - \beta\, v^2b^2m + b^3\phi + b^3\phi\,\alpha\, v$$
$$+ b^3\phi\,\alpha_2 v + b^2m\gamma\,\alpha_2\, v^2 + \phi\,\beta\, vb^2 + vb\phi\,\beta\, p\delta + b^2mp\delta\,\alpha_2 v^2 - \phi\,\beta\, v^2b^2m\alpha_2$$
$$- \gamma\, bp\delta\,\alpha_2 v^2 + b^2m\gamma\,\alpha\, v^3\alpha_2 + \gamma\,\beta\, v^2bm\alpha_2 + b^2m^2\alpha\, v^2\beta - 2\,\beta^2v^2mp\delta - \beta^2v^2bm^2\alpha_2$$
$$+ \beta\, v^2bp\delta b^2v^2\alpha\,\beta\, m + b\alpha\, v^2\beta^2m^2 - bp\delta\,\alpha\, v^2\beta\, m + \beta^3v^2m^2 - 2\,\beta\, v^2bmp\delta + \beta^3v^3\alpha_2 m^2$$
$$+ 2\,\beta^2v^2bm^2 + \beta\, v^2p^2\delta^2 - \beta^2v^2bm - \phi\,\beta\, vb^2m - vb\phi\,\beta^2m + \beta\, v^3b\alpha_2 p\delta - b^2v^3\alpha\,\alpha_2\beta\, m$$
$$- bp^2\delta^2\alpha\, v^3\alpha_2 - 2\,\beta^2v^3\alpha_2 mp\delta + \phi\,\beta\, v^2b^2\alpha_2 - b^2m^2\beta\, v^2\alpha_2 + b^2m^2\beta\, v^3\alpha_2 - \beta\, v^3b^2m\alpha_2$$
$$- \beta^2v^3b\alpha_2 m + 2\,\beta^2v^3bm^2\alpha_2 - bp^2\delta^2v^2\alpha_2 + \beta\, v^3\alpha_2 p^2\delta^2 + b^3\phi\,\alpha\, v^2\alpha_2 - v^2b\phi\,\beta^2m\alpha_2$$
$$+ v^2b\phi\,\beta\, p\delta\,\alpha_2 + b\gamma\,\alpha\, v^3\alpha_2\beta\, m + b^2mp\delta\,\alpha\, v^3\alpha_2 - \gamma\, bp\delta\,\alpha\, v^3\alpha_2 - 2\,\beta\, v^3bm\alpha_2 p\delta$$
$$+ 2\,\beta\, v^2bm\alpha_2 p\delta]. \tag{A.7}$$

Assume that $\phi = a_0v^2 + a_1v^3 + O(v^4)$, then by substituting ϕ and $\frac{d\phi}{dv}$ in the annihilator $N\phi$ and expanding its Taylor series we get:

$$N\phi = \frac{1}{b^2}\Big((\gamma\,\beta\, bm\alpha_2 + b^2mp\delta\,\alpha_2 - b^2m^2\beta\,\alpha_2 + 2\,\beta\, bm\alpha_2\, p\delta + 2\,\beta^2bm^2 + b^2m^2\beta$$
$$- \beta\, b^2m + b^3a_0 - \beta^2bm^2\alpha_2 - 2\,\beta\, bmp\delta + b^2m\gamma\,\alpha_2 - \gamma\, bp\delta\,\alpha_2 - b^2\alpha\,\beta\, m - \beta^2bm$$
$$+ vb\alpha\,\beta^2m^2 + b^2m^2\alpha\,\beta - 2\,\beta^2mp\delta + \beta\, p^2\delta^2 - bp\delta\,\alpha\,\beta\, m - bp^2\delta^2\alpha_2 + \beta\, bp\delta$$
$$+ \beta^3m^2)v^2 - \frac{1}{b^2}[\alpha\,\beta^3m^2 - a_0\,\beta\, b^2 - b^3a_1 - 2\, bp\delta\,\alpha\,\beta\, m - \beta^2bm^2\alpha_2{}^2 - bp^2\delta^2\alpha_2{}^2$$
$$+ mb^2\gamma\,\alpha_2{}^2 - b^2m^2\beta\,\alpha_2{}^2 - b^2\alpha\,\beta\, m - b^2\alpha^2\beta\, m - \alpha\,\beta^2bm + b\alpha^2\beta^2m^2 + b^2m^2\alpha^2\beta$$
$$+ \alpha\,\beta\, p^2\delta^2 + 3\, a_0\,\beta\, b^2m + 3\, a_0\, b\beta^2m + 2\, a_0\, b^2\gamma\,\alpha_2 + 2\, a_0\, b^2\, p\delta\,\alpha_2 - 2\, a_0\,\beta\, b^2m\alpha_2$$
$$- 3\, a_0\, b\beta\, p\delta + 2\, a_0\, b^2\alpha\,\beta\, m - 2\,\alpha\,\beta^2mp\delta + \alpha\,\beta\, bp\delta + b^2mp\delta\,\alpha_2{}^2 + b\gamma\,\alpha_2{}^2\beta\, m$$
$$- b\gamma\, p\delta\,\alpha_2{}^2 + 2\,\beta\, bm\alpha_2{}^2p\delta - bp\delta\,\alpha^2\beta\, m + b^2m^2\alpha\,\beta + 2\, b\alpha\,\beta^2m^2]v^3 + O(v^4)\Big). \tag{A.8}$$

By choosing the coefficients of v^2 and v^3 in order to have $N\phi = O(v^4)$ we obtain that a_0 and a_1 must be the following:

$$a_0 = -\frac{1}{b^3}[b^2m^2\beta + \beta\, bp\delta - b^2\alpha\,\beta\, m + b^2mp\delta\,\alpha_2 - \gamma\, bp\delta\,\alpha_2 + \gamma\,\beta\, bm\alpha_2 - 2\,\beta\, bmp\delta$$
$$- \beta\, b^2m + 2\,\beta^2bm^2 - \beta^2bm + \beta\, p^2\delta^2 + 2\,\beta\, bm\alpha_2\, p\delta - bp\delta\,\alpha\,\beta\, m + \beta^3m^2 - bp^2\delta^2\alpha_2$$
$$- b^2m^2\beta\,\alpha_2 - 2\,\beta^2mp\delta + b^2m\gamma\,\alpha_2 + b\alpha\,\beta^2m^2 + b^2m^2\alpha\,\beta - \beta^2bm^2\alpha_2], \tag{A.9}$$

$$a_1 = \frac{1}{b^3}[\alpha\,\beta^3m^2 - ao\,\beta\, b^2 - 2\, bp\delta\,\alpha\,\beta\, m - \beta^2bm^2\alpha_2 - bp^2\delta^2\alpha_2{}^2 + mb^2\gamma\,\alpha_2^2 - b^2m^2\beta\alpha_2^2$$
$$- b^2\alpha\,\beta\, m - b^2\alpha^2\beta\, m - \alpha\,\beta^2bm + b\alpha^2\beta^2m^2 + b^2m^2\alpha^2\beta + \alpha\,\beta\, p^2\delta^2 + 3\, a_0\,\beta\, b^2m$$
$$+ 3\, a_0\, b\beta^2m + 2\, a_0\, b^2\gamma\,\alpha_2 + 2\, a_0\, b^2\, p\delta\,\alpha_2 - 2\, a_0\,\beta\, b^2m\alpha_2 - 3\, a_0\, b\beta\, p\delta + 2\, a_0\, b^2\alpha\,\beta\, m$$

$$- 2\alpha\beta^2 mp\delta + \alpha\beta bp\delta + b^2 mp\delta\alpha_2{}^2 + b\gamma\alpha_2{}^2\beta m - b\gamma p\delta\alpha_2{}^2 + 2\beta bm\alpha_2{}^2 p\delta$$
$$- bp\delta\alpha^2\beta m + b^2 m^2\alpha\beta + 2b\alpha\beta^2 m^2]. \tag{A.10}$$

Hence $h(v) = a_0 v^2 + a_1 v^3 + O(v^4)$.

Appendix B. Hopf bifurcation

To analyze the behavior of the solutions of (3) when $s = 0$ we make a change of coordinates $x = S - S_2$, $y = I - I_2$, to obtain a new equivalent system to (3) with an equilibrium in (0, 0) in the x–y plane. Under this change the system becomes in:

$$\frac{dx}{dt} = \frac{a_{11}x + a_{12}y + c_1 xy + c_2 y^2 + c_7}{1 + \alpha y + \alpha I_2},$$
$$\frac{dy}{dt} = \frac{a_{21}x + a_{22}y + c_3 xy + c_4 xy^2 + c_5 y^2 + c_6 y^3 + c_8}{(1 + \alpha y + \alpha I_2)(1 + \alpha_2 y + \alpha_2 I_2)} \tag{B.1}$$

where:

$$a_{11} = -b - \beta_1 I_2 - b\alpha I_2 \tag{B.2}$$
$$a_{12} = -2bm\alpha I_2 + bm\alpha - b\alpha S_2 + 2p\delta\alpha I_2 + p\delta - bm - \beta_1 S_2 \tag{B.3}$$
$$c_1 = -b\alpha - \beta_1 \tag{B.4}$$
$$c_2 = -bm\alpha + p\delta\alpha \tag{B.5}$$
$$a_{21} = -I_2(-\beta_1 - \beta_1\alpha_2 I_2) \tag{B.6}$$
$$a_{22} = -2p\delta\alpha I_2 + 2\beta_1\alpha_2 S_2 I_2 - 3p\delta\alpha\alpha_2 I_2{}^2 - 2\gamma\alpha I_2$$
$$- 2\gamma\alpha_2 I_2 - 2p\delta\alpha_2 I_2 - 2\beta_2\alpha I_2 - 3\gamma\alpha\alpha_2 I_2{}^2 - \gamma - p\delta - \beta_2 + \beta_1 S_2 \tag{B.7}$$
$$c_3 = 2\beta_1\alpha_2 I_2 + \beta_1 \tag{B.8}$$
$$c_4 = \beta_1\alpha_2 y^2 \tag{B.9}$$
$$c_5 = -3p\delta\alpha\alpha_2 I_2 - 3\gamma\alpha\alpha_2 I_2 - p\delta\alpha + \beta_1\alpha_2 S_2 - \gamma\alpha - \gamma\alpha_2 - p\delta\alpha_2 - \beta_2\alpha \tag{B.10}$$
$$c_6 = -p\delta\alpha\alpha_2 - \gamma\alpha\alpha_2 \tag{B.11}$$
$$c_7 = -(\beta_1 S_2 I_2 - bm\alpha I_2 + bS_2 - p\delta I_2 - p\delta\alpha I_2{}^2 + b\alpha S_2 I_2 + bmI_2 - bm + bm\alpha I_2{}^2) \tag{B.12}$$
$$c_8 = -I_2[p\delta\alpha I_2 + p\delta + p\delta\alpha_2 I_2 + \gamma\alpha_2 I_2 - \beta_1\alpha_2 S_2 I_2 + \gamma\alpha I_2 + \beta_2\alpha I_2$$
$$+ \gamma + \gamma\alpha\alpha_2 I_2{}^2 - \beta_1 S_2 + \beta_2 + p\delta\alpha\alpha_2 I_2{}^2]. \tag{B.13}$$

But from the equations for the equilibrium point we can prove that $c_7 = c_8 = 0$, so the system we will work on is

$$\frac{dx}{dt} = \frac{a_{11}x + a_{12}y + c_1 xy + c_2 y^2}{1 + \alpha y + \alpha I_2},$$
$$\frac{dy}{dt} = \frac{a_{21}x + a_{22}y + c_3 xy + c_4 xy^2 + c_5 y^2 + c_6 y^3}{(1 + \alpha y + \alpha I_2)(1 + \alpha_2 y + \alpha_2 I_2)}. \tag{B.14}$$

If we denote system (3) as $(S, I)' = f(S, I)$ and system (B.1) as $(x, y)' = F(x, y)$, $f = (f_1, f_2)$, $F = (F_1, F_2)$ then

$$F(x, y) = f(x + S_2, y + I_2),$$

and

$$\frac{\partial F_i}{\partial x}(x, y) = \frac{\partial f_i}{\partial S}(x + S_2, y + I_2)\frac{\partial S}{\partial x}(x, y) + \frac{\partial f_i}{\partial I}(x + S_2, y + I_2)\frac{\partial I}{\partial x}(x, y) = \frac{\partial f_i}{\partial S}(x + S_2, y + I_2)$$
$$\frac{\partial F_i}{\partial y}(x, y) = \frac{\partial f_i}{\partial S}(x + S_2, y + I_2)\frac{\partial S}{\partial y}(x, y) + \frac{\partial f_i}{\partial I}(x + S_2, y + I_2)\frac{\partial I}{\partial y}(x, y) = \frac{\partial f_i}{\partial S}(x + S_2, y + I_2).$$

So, the Jacobian matrix of (61) $DF(0,0)$ in the equilibrium is equal to the Jacobian matrix of system (3) $Df(S_1, I_1)$. We can also compute the partial derivatives of system (B.1) and (61) to prove that they are equal, i.e.,

$$Df(S_2, I_2) = DF(0,0). \tag{B.15}$$

Therefore the system (61) and (3) are equivalent and we can work with system (61). The Jacobian matrix $DF(0,0)$ of (61) is:

$$DF(0,0) = \begin{bmatrix} \dfrac{a_{11}}{1+\alpha I_2} & \dfrac{a_{12}}{(1+\alpha I_2)} \\ \dfrac{a_{21}}{(1+\alpha_2 I_2)\,(1+\alpha I_2)} & \dfrac{a_{22}}{(1+\alpha_2 I_2)\,(1+\alpha I_2)} \end{bmatrix}. \tag{B.16}$$

So system (61) can be rewritten as

$$\frac{dx}{dt} = \frac{a_{11}x}{1+\alpha I_2} + \frac{a_{12}y}{1+\alpha I_2} + G_1(x,y) \tag{B.17}$$

$$\frac{dy}{dt} = \frac{a_{21}x}{(1+\alpha I_2)\,(1+\alpha_2 I_2)} + \frac{a_{22}y}{(1+\alpha I_2)\,(1+\alpha_2 I_2)} + G_2(x,y) \tag{B.18}$$

where

$$G_1 = \frac{1}{(1+\alpha y+\alpha I_2)(1+\alpha I_2)}\{[(1+\alpha I_2)c_1 - a_{11}\alpha]xy + [c_2(1+\alpha I_2) - \alpha a_{12}]y^2\} \tag{B.19}$$

$$\begin{aligned} G_2 = {} & \frac{1}{(1+\alpha y+\alpha I_2)(1+\alpha_2 y+\alpha_2 I_2)(1+\alpha I_2)(1+\alpha_2 I_2)}\{[c_3(1+\alpha I_2)(1+\alpha_2 I_2) \\ & - a_{21}(\alpha_2+\alpha+2\alpha\alpha_2 I_2)]xy + [c_4(1+\alpha I_2)(1+\alpha_2 I_2) - a_{21}\alpha\alpha_2]xy^2 \\ & + [c_5(1+\alpha I_2)(1+\alpha_2 I_2) - a_{22}(\alpha_2+\alpha+2\alpha\alpha_2 I_1)]y^2 + [c_6(1+\alpha I_2)(1+\alpha_2 I_2) - a_{22}\alpha\alpha_2]y^3\}. \end{aligned} \tag{B.20}$$

We need the normal form of the system (61). The eigenvalues of $DF(0,0)$ when $s_2 = 0$ and (i), (ii) are satisfied are:

$$\Lambda i, -\Lambda i.$$

With complex eigenvector

$$v = \begin{pmatrix} -1 \\ \dfrac{-\Lambda i(1+\alpha I_2) + a_{11}}{a_{12}} \end{pmatrix}, \qquad \bar{v} = \begin{pmatrix} -1 \\ \dfrac{\Lambda i(1+\alpha I_2) + a_{11}}{a_{12}} \end{pmatrix}.$$

Using the Jordan Canonical form of matrix $DF(0,0)$ and the procedure in [10, p. 107,108] we use the change of variable $u = x$, $v = \frac{a_{11}}{\Lambda(1+\alpha I_2)} + \frac{a_{12}y}{\Lambda(1+\alpha I_2)}$, to obtain the following equivalent system:

$$\begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} 0 & \Lambda \\ -\Lambda & 0 \end{pmatrix}\begin{pmatrix} u \\ v \end{pmatrix} + \begin{pmatrix} H_1(u,v) \\ H_2(u,v) \end{pmatrix} \tag{B.21}$$

where

$$H_1(u,v) = -\frac{((-a_{12}c_1 + a_{11}c_2)\,u + (-\Lambda c_2\alpha I_2 + \Lambda a_{12}\alpha - \Lambda c_2)\,v)\,((\Lambda + \Lambda\alpha I_2)\,v - a_{11}u)}{a_{12}\left(\left(\alpha\Lambda + \Lambda\alpha^2 I_2\right)v + a_{12} - \alpha a_{11}u + a_{12}\alpha I_2\right)} \tag{B.22}$$

$$H_2(u,v) = -\frac{1}{h(u,v)}\left[(\Lambda(1+\alpha I_2)v - a_{11}u)\left(A_1v^2 + A_2uv + A_3v + A_4u^2 + A_5u\right)\right]. \tag{B.23}$$

And:

$$\begin{aligned} A_1 = {} & \Lambda^2\,(1+\alpha I_2)^2\,[-a_{12}c_6\alpha_2 I_2{}^2\alpha - a_{11}c_2\alpha_1 I_2{}^2\alpha_2{}^2 - a_{11}c_2\alpha I_2\alpha_2 \\ & - a_{12}c_6\alpha I_2 + a_{11}a_{12}\alpha\alpha_2{}^2 I_2 + a_{11}a_{12}\alpha\alpha_2 + a_{12}a_{22}\alpha\alpha_2 \end{aligned}$$

$$
\begin{aligned}
&- a_{11}c_2{\alpha_2}^2 I_2 - a_{12}c_6\alpha_2 I_2 - a_{11}c_2\alpha_2 - a_{12}c_6]\\
A_2 &= -\Lambda\ (1+\alpha I_2)\,[a_{11}a_{12}c_1{\alpha_2}^2\alpha {I_2}^2 + {a_{12}}^2c_4\alpha_2{I_2}^2\alpha - 2\,a_{12}a_{11}c_6\alpha_2{I_2}^2\alpha\\
&- 2\,c_2\alpha{I_2}^2{\alpha_2}^2{a_{11}}^2 + a_{12}\alpha{\alpha_2}^2{a_{11}}^2 I_2 - 2\,a_{12}a_{11}c_6\alpha I_2 - 2\,c_2\alpha I_2\alpha_2{a_{11}}^2\\
&+ {a_{12}}^2c_4\alpha I_2 + a_{11}a_{12}c_1\alpha_2\alpha I_2 + a_{11}a_{12}c_1{\alpha_2}^2 I_2 + {a_{12}}^2c_4\alpha_2 I_2 - 2\,a_{12}a_{11}c_6\alpha_2 I_2\\
&- 2\,{a_{11}}^2c_2{\alpha_2}^2 I_2 + {a_{12}}^2c_4 - 2\,{a_{11}}^2c_2\alpha_2 - 2\,a_{12}a_{11}c_6 + a_{11}a_{12}c_1\alpha_2 + a_{12}\alpha\alpha_2{a_{11}}^2\\
&- {a_{12}}^2\alpha a_{21}\alpha_2 + 2\,a_{12}a_{11}a_{22}\alpha\alpha_2]\\
A_3 &= \Lambda\ (1+\alpha I_2)\,a_{12}[-a_{12}c_5\alpha{I_2}^2\alpha_2 + a_{12}a_{11}\alpha_1{\alpha_2}^2{I_2}^2 + 2\,a_{12}a_{22}\alpha\alpha_2 I_2\\
&+ 2\,a_{12}a_{11}\alpha\alpha_2 I_2 - a_{12}c_5\alpha I_2 + a_{12}a_{22}\alpha + a_{11}a_{12}\alpha - a_{12}c_5\alpha_2 I_2 + a_{12}a_{22}\alpha_2\\
&- 2\,a_{11}c_2\alpha{I_2}^2\alpha_2 - a_{11}c_2\alpha I_2 - a_{11}c_2 - a_{11}c_2{\alpha_2}^2{I_2}^2 - 2\,a_{11}c_2\alpha_2 I_2]\\
A_4 &= -a_{11}[-{a_{12}}^2c_4\alpha_2 I_2 - a_{11}a_{12}c_1\alpha_2\alpha I_2 + c_2\alpha I_2\alpha_2{a_{11}}^2 - {a_{12}}^2c_4\alpha_2{I_2}^2\alpha\\
&- {a_{12}}^2c_4\alpha I_2 - {a_{12}}^2c_4 + {a_{12}}^2\alpha a_{21}\alpha_2 - a_{12}a_{11}a_{22}\alpha\alpha_2 - a_{11}a_{12}c_1{\alpha_2}^2\alpha{I_2}^2\\
&+ a_{12}a_{11}c_6 + {a_{11}}^2c_2{\alpha_2}^2 I_2 + a_{12}a_{11}c_6\alpha_2{I_2}^2\alpha + {a_{11}}^2c_2\alpha_2 - a_{11}a_{12}c_1\alpha_2\\
&+ a_{12}a_{11}c_6\alpha_2 I_2 + a_{12}a_{11}c_6\alpha I_2 + c_2\alpha{I_2}^2{\alpha_2}^2{a_{11}}^2 - a_{11}a_{12}c_1{\alpha_2}^2 I_2]\\
A_5 &= a_{12}[2\,{a_{11}}^2c_2\alpha_2 I_2 + {a_{11}}^2c_2\alpha I_2 + {a_{12}}^2\alpha a_{21} + {a_{11}}^2c_2{\alpha_2}^2{I_2}^2 - a_{12}a_{11}a_{22}\alpha_2\\
&- a_{12}a_{11}a_{22}\alpha - {a_{12}}^2c_3\alpha_2 I_2 - {a_{12}}^2c_3\alpha I_2 + a_{11}a_{12}c_5 + {a_{12}}^2\alpha_2 a_{21} - a_{12}a_{11}c_1\\
&+ 2\,{a_{12}}^2\alpha a_{21}\alpha_2 I_2 - a_{12}a_{11}c_1{\alpha_2}^2{I_2}^2 - a_{12}a_{11}c_1\alpha I_2 - 2\,a_{12}a_{11}c_1\alpha_2 I_2\\
&+ a_{11}a_{12}c_5\alpha_2 I_2 + a_{11}a_{12}c_5\alpha I_2 - {a_{12}}^2c_3\alpha{I_2}^2\alpha_2 - {a_{12}}^2c_3 + a_{11}a_{12}c_5\alpha{I_2}^2\alpha_2\\
&- 2\,a_{12}a_{11}a_{22}\alpha\alpha_2 I_2 - 2\,a_{12}a_{11}c_1\alpha{I_2}^2\ alpha_2 - a_{12}a_{11}c_1\alpha{I_2}^3{\alpha_2}^2 + 2\,{a_{11}}^2c_2\alpha{I_2}^2\alpha_2\\
&+ {a_{11}}^2c_2\alpha{I_2}^3{\alpha_2}^2 + {a_{11}}^2c_2]\\
h(u,v) &= \Lambda\ (1+\alpha I_2)^2\,a_{12}[\left(\alpha\Lambda + \Lambda\,\alpha^2 I_2\right)v + a_{12} - \alpha a_{11}u + a_{12}\alpha I_2]\\
&\times\ [(\alpha_2\Lambda + \alpha_2\Lambda\,\alpha I_2)\,v + a_{12} - \alpha_2 a_{11}u + \alpha_2 I_2 a_{12}]\,(1+\alpha_2 I_2)\,.
\end{aligned}
$$

Let

$$
\begin{aligned}
\bar{a}_2 &= \frac{1}{16}[(H_1)_{uuu} + (H_1)_{uvv} + (H_2)_{uuv} + (H_2)_{vvv}] + \frac{1}{16(-\Lambda)}[(H_1)_{uv}((H_1)_{uu} + (H_1)_{vv})\\
&- (H_2)_{uv}((H_2)_{uu} + (H_2)_{vv}) - (H_1)_{uu}(H_2)_{uu} + (H_1)_{vv}(H_2)_{vv}].
\end{aligned} \tag{B.24}
$$

Then

$$
\begin{aligned}
\bar{a}_2 &= \frac{3\left(\left(-c_1\Lambda\,v\alpha^2 I_2 + \Lambda\,v a_{11}\alpha^2 - a_{12}c_1\alpha I_2 + a_{11}c_2\alpha I_2 - c_1\Lambda\,v\alpha - a_{12}c_1 + a_{11}c_2\right)a_{12}{a_{11}}^2\alpha\right)}{8\,(a_{12}+\alpha\Lambda\,v)^4\,(1+\alpha_1 I_2)^3}\\
&- \frac{(-3\,a_{11}c_2 - 3\,a_{11}c_2\alpha I_2 + 2\,a_{12}a_{11}\alpha + a_{12}c_1 + a_{12}c_1\alpha_1 I_2)\,\alpha\Lambda^2}{8\,(1+\alpha I_2)\,{a_{12}}^3}\\
&- \frac{1}{8\Lambda\ (1+\alpha I_2)^4\,{a_{12}}^4\,(1+\alpha_2 I_2)^3}[2\,a_{11}A_5\alpha\Lambda + 6\,a_{11}A_5\alpha\Lambda\,\alpha_2 I_2 + 2\,a_{11}A_5\alpha^2\Lambda\,I_2\\
&+ 4\,a_{11}A_5\alpha^2\Lambda\,{I_2}^2\alpha_2 + 2\,a_{11}A_5\alpha_2\Lambda - {a_{11}}^2A_3\alpha - 2\,{a_{11}}^2A_3\alpha\alpha_2 I_2 - {a_{11}}^2A_3\alpha_2 - a_{11}A_2a_{12}\\
&- a_{11}A_2a_{12}\alpha_2 I_2 - a_{11}A_2a_{12}\alpha I_2 - a_{11}A_2a_{12}\alpha{I_2}^2\alpha_2 + A_4\Lambda\,a_{12} + A_4\Lambda\,a_{12}\alpha_2 I_2\\
&+ 2\,A_4\Lambda\,a_{12}\alpha I_2 + 2\,A_4\Lambda\,a_{12}\alpha{I_2}^2\alpha_2 + A_4\Lambda\,a_{12}\alpha^2{I_2}^2 + A_4\Lambda\,a_{12}\alpha^2{I_2}^3\alpha_2]
\end{aligned}
$$

$$
\begin{aligned}
&+\ \frac{3}{8}\frac{(-A_1 a_{12} - A_1 a_{12}\alpha_2 I_2 + A_3\alpha\Lambda + 2\,A_3\alpha\Lambda\,\alpha_2 I_2 + A_3\alpha_2\Lambda)}{(1+\alpha I_2)^2\,{a_{12}}^4\,(1+\alpha_2 I_2)^3}\\
&-\ \frac{1}{16\Lambda}\left[-2\,\frac{\Lambda\,(-2\,a_{11}c_2 - 2\,a_{11}c_2\alpha I_2 + a_{12}a_{11}\alpha + a_{12}c_1 + a_{12}c_1\alpha I_2)}{{a_{12}}^4\,(1+\alpha I_2)^2}\right.\\
&-\ 2\,\frac{(A_5\Lambda + A_5\Lambda\,\alpha I_2 - a_{11}A_3)\,(-a_{11}A_5 + A_3\Lambda + A_3\Lambda\,\alpha I_2)}{\Lambda^2\,(1+\alpha I_2)^6\,{a_{12}}^6\,(1+\alpha_2 I_2)^4}\\
&\left.-4\,\frac{(-a_{12}c_1 + a_{11}c_2)\,{a_{11}}^2 A_5}{{a_{12}}^5\,(1+\alpha I_2)^4\,\Lambda\,(1+\alpha_2 I_2)^2}4\,\frac{(-c_2\alpha I_2 + a_{12}\alpha - c_2)\,\Lambda^2 A_3}{{a_{12}}^5\,(1+\alpha I_2)^2\,(1+\alpha_2 I_2)^2}\right].
\end{aligned}
\tag{B.25}
$$

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