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ORIGINAL ARTICLE

Stability analysis of an influenza virus model with disease resistance

Nguyen Huu Khanh*

College of Natural Sciences, CanTho University, Viet Nam

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Abstract We study a new model describing the transmission of influenza virus with disease resistance in human. Mathematical analysis shows that dynamics of the spread is determined by the basic reproduction number R_0. If $R_0 \leq 1$, the disease free equilibrium is globally asymptotically stable, and if $R_0 > 1$, the endemic equilibrium is globally asymptotically stable under some conditions. The change of stability of equilibria is explained by transcritical bifurcation. Lyapunov functional method and geometric approach are used for proving the global stability of equilibria. A numerical investigation is carried out to confirm the analytical results. Some effective strategies for eliminating virus are suggested.

2010 Mathematics subject classification: 34D23; 37B25; 92D30

1. Introduction

Influenza, also called the flu, is a disease caused by a virus that affects mainly the nose, throat, bronchi and, occasionally, lungs. The virus can spread from person to person through air by coughs, sneezes or from infected surfaces, and by the direct contact to infected persons. There are three types of influenza virus, namely, A, B, and C. Among these, influenza A viruses are more severe than others for human populations. Mathematical models have provided a useful tool to understand disease dynamics and give out preventive strategies [1,2].

In 2003, Neil and coworkers [3] constructed a mathematical model of influenza transmission simulating the effect of neuraminidase inhibitor therapy on infection rates and transmission of drug-resistant viral strains. They concentrate on numerical investigation without considering the stability of the model. Fraser et al. [4] studied the transmission model of influenza A (H1N1) in the human population, but they did not include cross-species transmission. Coburn [5] presented a complex model for transmission of three species (birds, pigs and human). In [1], Pongsumpun considered the model for the transmission of Swine flu, a new strain of type A influenza virus, with different probability of the patients who have symptomatic and asymptomatic infections. Recently, Zhou and Guo [2] ana-

* Tel.: +84 908791280.
E-mail address: nhkhanh@ctu.edu.vn
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lyzed an influenza model with vaccination. However, many articles did not concern with disease resistance in human.

The stability of epidemic models has been studied in many papers [6–8]. Many authors paid attention to local stability of equilibria. Recently, the study of epidemic models mainly concerns global asymptotic stability. The most successful approaches to the problem are the direct Lyapunov method [9–13] and the geometric method [14,15].

In this paper, we consider a new SEIR model depicting the transmission of influenza virus with disease resistance in human. In the model, a person in exposed group or infected group can come back to susceptible group without treatment. This describes realistic modeling of treatment. The model is given by a system of four differential equations depending on parameters. By using the method of next generation matrix [16], we found a threshold R_0 called basic reproduction number. In general, when $R_0 \leq 1$, the disease dies out and when $R_0 > 1$, the disease persists in the population. If we suppose that the endemic equilibrium also exists for $R_0 < 1$, although it is not true, then the bifurcation occurring in the model can be explained as a transcritical bifurcation. Several various methods are used to determine the stability of equilibria. We concentrate our study on the globally stable stability of equilibria. This is obtained by Lyapunov functional approach and geometric approach. A numerical investigation is carried out by Mathematica software and AUTO software package confirming theoretical results.

The paper is organized as follows. In the next section, we introduce the structure of the transmission model, equilibria and basic reproduction number. Section 3 deals with the local stability of equilibria. In Section 4, we prove the global stability of equilibria by Lyapunov functional approach and geometric approach. Some numerical simulations are given in Section 5. Finally, Section 6 summarizes this work.

2. The model and its basic properties

2.1. The structure of the model

We consider the transmission of influenza virus among the people. The total population, size $N(t)$, is divided into four distinct epidemiological subclasses of individuals which are susceptible, exposed, infectious and recovered, with sizes denoted by $\overline{S}(t), \overline{E}(t), \overline{I}(t), \overline{R}(t)$, respectively. In exposed group, there are people who have been in contact with an infected individual but uninfected. Besides, infectious group has people infected but become exposed without treatment. We assume that the environment is homogeneous and natural death rates have common rate μ.

The model is given by a system of ordinary differential equations:

$$\begin{aligned}
\frac{d\overline{S}}{dt} &= \Lambda - \gamma \overline{S}(t)\frac{\overline{E}(t)+\overline{I}(t)}{N(t)} + c\overline{E}(t) + b\overline{I}(t) \\
&\quad + \alpha \overline{R}(t) - \mu \overline{S}(t) \\
\frac{d\overline{E}}{dt} &= \gamma \overline{S}(t)\frac{\overline{E}(t)+\overline{I}(t)}{N(t)} - (c+\varepsilon+\mu)\overline{E}(t) \\
\frac{d\overline{I}}{dt} &= \varepsilon \overline{E}(t) - (\beta+b+\mu)\overline{I}(t) \\
\frac{d\overline{R}}{dt} &= \beta \overline{I}(t) - (\alpha+\mu)\overline{R}(t),
\end{aligned} \tag{1}$$

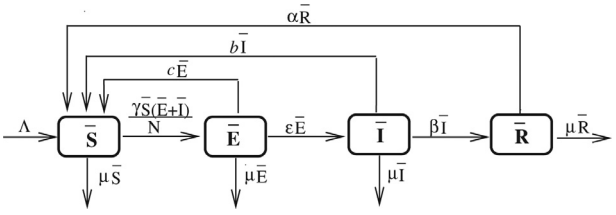

Figure 1 Transfer diagram of the model (1).

where Λ is a constant recruitment of susceptible human, γ is the contact rate of virus transmission, c is the rate at which the exposed human become to be susceptible human without treatment, b is the rate at which the infectious human become to be the susceptible human without treatment, $\varepsilon = 1/\mathrm{IIP}$ where IIP is the intrinsic incubation period of virus, α is the rate at which the recovered human become to be the susceptible human again, β is the rate at which the infectious human become to be the recovered human, and μ is the natural death rate of the human population. Fig. 1 shows the transfer diagram of the model (1).

We assume that the total size of population $N(t)$ is constant, that is $N(t) = N$. Then $\overline{S}(t) + \overline{E}(t) + \overline{I}(t) + \overline{R}(t) = N$.

Let $S(t) = \frac{\overline{S}(t)}{N}$, $E(t) = \frac{\overline{E}(t)}{N}$, $I(t) = \frac{\overline{I}(t)}{N}$, $R(t) = \frac{\overline{R}(t)}{N}$. We obtain the reduced system

$$\begin{aligned}
\frac{dS}{dt} &= \mu - \gamma S(t)(E(t)+I(t)) + cE(t) + bI(t) \\
&\quad + \alpha R(t) - \mu S(t) \\
\frac{dE}{dt} &= \gamma S(t)(E(t)+I(t)) - (c+\varepsilon+\mu)E(t) \\
\frac{dI}{dt} &= \varepsilon E(t) - (\beta+b+\mu)I(t) \\
\frac{dR}{dt} &= \beta I(t) - (\alpha+\mu)R(t),
\end{aligned} \tag{2}$$

with the condition $S(t) + E(t) + I(t) + R(t) = 1$.

It follows from the system (2) that $(S+E+I+R)' = \Lambda - \mu(S+E+I+R) = \Lambda - \mu$. Then $\limsup_{t\to\infty}(S+E+I+R) \leq \frac{\Lambda}{\mu}$. Therefore, the feasible region for system (2) is $\Omega = \{(S,E,I,R) : S > 0, E \geq 0, I \geq 0, R \geq 0, S+E+I+R \leq \frac{\Lambda}{\mu}\}$.

It is easy to verify that the region Ω is positively invariant with respect to system (2).

2.2. Equilibria

To find equilibria, we set the right-hand side of the system (2) equals zero. Then we get two equilibria in the coordinate (S,E,I,R):

(i) Disease free equilibrium $P_0(1,0,0,0)$. It is seen that the equilibrium P_0 always exists.

(ii) Disease endemic equilibrium $P_1(S^*,E^*,I^*,R^*)$ with positive components:

$$S^* = \frac{1}{R_0},$$

$$E^* = \frac{(\alpha+\mu)(\beta+b+\mu)G_1}{G_2},$$

$$I^* = \frac{\varepsilon(\alpha+\mu)G_1}{G_2},$$

$$R^* = \frac{\beta\varepsilon G_1}{G_2},$$

where $R_0 = \frac{\gamma(\beta+b+\mu+\varepsilon)}{(\beta+b+\mu)(c+\varepsilon+\mu)}$,

$$G_1 = (\beta+b+\varepsilon+\mu)\gamma - (\beta+b+\mu)(c+\varepsilon+\mu), \quad (3)$$

$$G_2 = \gamma(\beta+b+\varepsilon+\mu)[\beta\varepsilon + (\alpha+\mu)(\beta+b+\varepsilon+\mu)]. \quad (4)$$

When $R_0 > 1$, we have $G_1 > 0$. This implies the equilibrium P_1 exists as $R_0 > 1$.

2.3. Basic reproduction number

This section presents the basic reproduction number, denoted by R_0, that is the number of secondary cases which one case would produce in a completely susceptible population. We use the method of next generating matrix to determinate the expression for R_0 [16]. The model (2) always has a disease free equilibrium $P_0(1, 0, 0, 0)$. Let $x = (E, I, S, R)^\top$. Then the model (2) can be written as

$$\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x),$$

where

$$\mathcal{F}(x) = \begin{pmatrix} \gamma S(E+I) \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

$$\mathcal{V}(x) = \begin{pmatrix} (c+\varepsilon+\mu)E \\ -\varepsilon E + (\beta+b+\mu)I \\ -\mu + \gamma S(E+I) - cE - bI - \alpha R + \mu S \\ -\beta I + (\alpha+\mu)R \end{pmatrix}.$$

We can get

$$F = \begin{pmatrix} \gamma & \gamma \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} c+\varepsilon+\mu & 0 \\ -\varepsilon & \beta+b+\mu \end{pmatrix}.$$

The next generation matrix for the model (2) is

$$FV^{-1} = \begin{pmatrix} \frac{\gamma(\beta+b+\mu+\varepsilon)}{(\beta+b+\mu)(c+\varepsilon+\mu)} & \frac{\gamma}{(\beta+b+\mu)} \\ 0 & 0 \end{pmatrix}.$$

The spectral radius of matrix FV^{-1} is $\rho(FV^{-1}) = \frac{\gamma(\beta+b+\mu+\varepsilon)}{(\beta+b+\mu)(c+\varepsilon+\mu)}$. According to the Theorem 2 in [16], the basic reproduction number of the system (2) is $R_0 = \frac{\gamma(\beta+b+\mu+\varepsilon)}{(\beta+b+\mu)(c+\varepsilon+\mu)}$.

Note that when $R_0 > 1$ then $G_1 = (\beta+b+\varepsilon+\mu)\gamma - (\beta+b+\mu)(c+\varepsilon+\mu) > 0$ and the endemic equilibrium P_1 exists.

3. Local stability and bifurcation of equilibria

3.1. Local stability of the disease free equilibrium

Theorem 1. *P_0 is locally asymptotically stable if $R_0 < 1$. Whereas, P_0 is unstable if $R_0 > 1$.*

Proof. The Jacobian matrix at P_0 is given by

$$J_{P_0} = \begin{pmatrix} -\mu & -\gamma+c & -\gamma+b & \alpha \\ 0 & \gamma-(c+\varepsilon+\mu) & \gamma & 0 \\ 0 & \varepsilon & -(\beta+b+\mu) & 0 \\ 0 & 0 & \beta & -(\alpha+\mu) \end{pmatrix}.$$

Eigenvalues of the above matrix are

$$\lambda_1 = -\mu, \quad \lambda_2 = -(\alpha+\mu),$$
$$\lambda_3 = -\frac{1}{2}\left(L + \sqrt{L^2+4G_1}\right),$$
$$\lambda_4 = -\frac{1}{2}\left(L - \sqrt{L^2+4G_1}\right).$$

where $L = \beta+b+c+\varepsilon+2\mu-\gamma > 0$, $G_1 = (\beta+b+\varepsilon+\mu)\gamma - (\beta+b+\mu)(c+\varepsilon+\mu)$.

Eigenvalues λ_1, λ_2 and λ_3 are always negative. If $R_0 < 1$, then $G_1 < 0$. It implies $\lambda_4 < 0$. Therefore, P_0 is locally asymptotically stable. Whereas, for $R_0 > 1$ then $\lambda_4 > 0$ and P_0 is unstable. □

3.2. Local stability of the endemic equilibrium

The local stability of the endemic equilibrium P_1 is proved by the Routh-Hurwitz criterion.

Theorem 2. *The endemic equilibrium P_1 of the system (2) is locally asymptotically stable in Ω for $R_0 > 1$.*

Proof. The Jacobian matrix at P_1 is given by

$$J_{P_1} = \begin{pmatrix} -\gamma(E^*+I^*)-\mu & -\gamma S^*+c & -\gamma S^*+b & \alpha \\ \gamma(E^*+I^*) & \gamma S^* - (c+\varepsilon+\mu) & \gamma S^* & 0 \\ 0 & \varepsilon & -(\beta+b+\mu) & 0 \\ 0 & 0 & \beta & -(\alpha+\mu) \end{pmatrix}.$$

The characteristic equation is

$$\lambda^4 + a_3\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0,$$

with

$$a_3 = (\alpha+\beta+b+c+\varepsilon+2\mu-\gamma) + 2\mu + \gamma[G_2 + (\alpha+\mu)(L_1+\varepsilon)]\frac{G_1}{G_2},$$

$$a_2 = \mu(L_1+L_2) + (\alpha+\mu+L_1)[\mu+L_2+\gamma(E^*+I^*-S^*)],$$

$$a_1 = (\alpha+\mu)\gamma(L_1+\varepsilon)^2[(\beta+\mu)\varepsilon + (\alpha+2\mu)L_1 + (\alpha+\mu)(\varepsilon+\mu)]\frac{G_1}{G_2} + (\alpha+\mu)\mu(\mu L_1 + \varepsilon L_2),$$

$$a_0 = \gamma(E^*+I^*)[\varepsilon\mu(\alpha+b+\mu) + \alpha(\alpha+\mu)L_1],$$

where $L_1 = \beta+b+\mu$, $L_2 = c+\varepsilon+\mu$ and G_1, G_2 are given by Eqs. (3) and (4).

From the Routh-Hurwitz criterion, the endemic equilibrium P_1 is locally stable when

$$a_0 > 0, a_1 > 0, a_3 > 0 \quad \text{and} \quad a_1a_2a_3 - a_1^2 - a_0a_3^2 > 0.$$

It is easy to see that $a_0 > 0, a_1 > 0, a_3 > 0$. By using Mathematica software, the condition $a_1a_2a_3 - a_1^2 - a_0a_3^2 > 0$ is satisfied for $R_0 > 1$. □

4. Global stability of equilibria

4.1. Global stability of the disease free equilibrium

We use Lyapunov function to prove the global stability of the disease free equilibrium.

Theorem 3. *If $R_0 \le 1$, then the free disease equilibrium P_0 of the system (2) is globally asymptotically stable in Ω.*

Proof. We construct the following Lyapunov function:

$$W(t) = (S - 1 - \ln S) + E + a_1 I + a_2 R.$$

where $a_1 = \frac{L_2}{L_1+\varepsilon}$, $0 < a_2 \le \frac{\sigma_{\min}+\mu(1-S_{\max})}{\beta S_{\max}}$, $\sigma_{\min} = (c+b+\alpha)\cdot \min\{E, I, R\}$, $L_1 = \beta + b + \mu$ and $L_2 = c + \varepsilon + \mu$.

The derivative of $W(t)$ along the solution curves of (2) in $\mathbb{R}^4_+$ is given by the expression:

$$\begin{aligned} W'(t) &= S'\left(1 - \frac{1}{S}\right) + E' + a_1 I' + a_2 R' \\ &= [\mu - \gamma S(E+I) + cE + bI + \alpha R - \mu S]\left(1 - \frac{1}{S}\right) \\ &\quad + [\gamma(E+I) - L_2 E] + a_1[\varepsilon E - L_1 I] \\ &\quad + a_2[\beta I - (\alpha+\mu)R], \end{aligned}$$

or

$$\begin{aligned} W'(t) &= [\mu + cE + bI + \alpha R - \mu S]\left(1 - \frac{1}{S}\right) \\ &\quad + \gamma(E+I) - (L_2 - a_1\varepsilon)E - a_1 L_1 I \\ &\quad + a_2\beta I - a_2(\alpha+\mu)R. \end{aligned} \tag{5}$$

Since $a_1 = \frac{L_2}{L_1+\varepsilon}$ then we have $L_2 - a_1\varepsilon = a_1 L_1 = \frac{L_1 L_2}{L_1+\varepsilon}$. Note that $\gamma = \frac{L_1 L_2}{L_1+\varepsilon} R_0$. Substituting these conditions into (5) we get

$$\begin{aligned} W'(t) &= -[\mu + bE + cI + \alpha R - \mu S]\left(\frac{1}{S} - 1\right) \\ &\quad - \frac{L_1 L_2}{L_1+\varepsilon}(1 - R_0)(E+I) + a_2\beta(1 - S - E - R) \\ &\quad - a_2(\alpha+\mu)R = -[\mu + bE + cI \\ &\quad + \alpha R - (\mu + a_2\beta)S]\left(\frac{1}{S} - 1\right) \\ &\quad - \frac{L_1 L_2}{L_1+\varepsilon}(1 - R_0)(E+I) - a_2\beta E - a_2(\alpha+\beta+\mu)R. \end{aligned}$$

Because $0 < a_2 \le \frac{\sigma_{\min}+\mu(1-S_{\max})}{\beta S_{\max}}$ we have $\mu + bE + cI + \alpha R - (\mu + a_2\beta)S \ge 0$. Thus, $W'(t)$ is negative if $R_0 \le 1$. Note that, $W'(t) = 0$ if and only if $S = 1$, $E = I = R = 0$. Hence, the invariant set $\{(S, E, I, R) \in \Omega : W'(t) = 0\}$ is the singleton $\{P_0\}$, where P_0 is the disease free equilibrium point. Therefore, by the LaSalle's Invariance Principle [17], P_0 is globally stable in the set Ω when $R_0 \le 1$. This completes the proof. □

4.2. Global stability of the endemic equilibrium

This section presents the stability of the endemic equilibrium P_1. The global stability under some conditions is examined by Lyapunov functional method and geometric approach.

4.2.1. Lyapunov functional approach

Theorem 4. *If $R_0 > 1$, then the unique endemic equilibrium P_1 is globally asymptotically stable, provided that* $\max\{b, c, \alpha\} \le cE^* + bI^* + \alpha R^*$.

Proof. We define a Lyapunov function V as follows:

$$\begin{aligned} V(S, E, I, R) &= \left(S - S^* - S^* \ln\frac{S}{S^*}\right) + \left(E - E^* - E^* \ln\frac{E}{E^*}\right) \\ &\quad + k\left(I - I^* - I^* \ln\frac{I}{I^*}\right), \end{aligned}$$

where $k = \frac{\gamma S^* I^*}{\varepsilon E^*}$.

The derivative of V along the solution curves of (2) is given by

$$\begin{aligned} V' &= S'\left(1 - \frac{S^*}{S}\right) + E'\left(1 - \frac{E^*}{E}\right) + kI'\left(1 - \frac{I^*}{I}\right) \\ &= [\mu - \gamma S(E+I) + bE + cI + \alpha R - \mu S]\left(1 - \frac{S^*}{S}\right) \\ &\quad + [\gamma S(E+I) - (c+\varepsilon+\mu)E]\left(1 - \frac{E^*}{E}\right) \\ &\quad + k[\varepsilon E - (\beta+b+\mu)I]\left(1 - \frac{I^*}{I}\right). \end{aligned}$$

Using

$$\begin{aligned} \mu &= \gamma S^*(E^* + I^*) + \mu S^* - (cE^* + bI^* \\ &\quad + \alpha R^*),\ (c+\varepsilon+\mu)E^* = \gamma S^* E^* + \gamma S^* I^*, \end{aligned}$$

we get

$$\begin{aligned} V' &= \left[\gamma S^*(E^* + I^*) + 2\mu S^* - \mu S - \gamma S^*(E^* + I^*)\frac{S^*}{S} - \mu S^* \frac{S^*}{S}\right. \\ &\quad \left. + \gamma S^* E + \gamma S^* I\right] + [c(E - E^*) + b(I - I^*) + \alpha(R - R^*)]\left(1 - \frac{S^*}{S}\right) \\ &\quad + \left[-(c+\varepsilon+\mu)E - \gamma E^* S - \gamma E^* \frac{SI}{E} + (\gamma S^* E^* + \gamma S^* I^*)\right] \\ &\quad + \left[k\varepsilon E - k(\beta+b+\mu)I - k\varepsilon I^* \frac{E}{I} + k(\beta+b+\mu)I^*\right]. \end{aligned}$$

The expression for V' can be rewritten in the following form:

$$\begin{aligned} V' &= \mu S^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) \\ &\quad + \gamma S^* E^*\left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) \\ &\quad + \gamma S^* I^*\left(3 - \frac{S^*}{S} - \frac{S}{S^*}\frac{I}{I^*}\frac{E^*}{E} - \frac{I^*}{I}\frac{E}{E^*}\right) \\ &\quad + [c(E - E^*) + b(I - I^*) + \alpha(R - R^*)]\left(1 - \frac{S^*}{S}\right) \\ &\quad + \left(\gamma\frac{S^* I^*}{E^*} - k\varepsilon\right)I^*\frac{E}{I} + [\gamma S^* - (c+\varepsilon+\mu) + k\varepsilon]E \\ &\quad + [\gamma S^* - k(\beta+b+\mu)]I - \gamma S^* I^* + k(\beta+b+\mu)I^*. \end{aligned}$$

Since $k = \frac{\gamma S^* I^*}{\varepsilon E^*}$ and $\varepsilon E^* = (\beta+b+\mu)I^*$, we have

$$\begin{aligned} &\gamma\frac{S^* I^*}{E^*} - k\varepsilon = 0, \quad \gamma S^* - (c+\varepsilon+\mu) + k\varepsilon = 0, \\ &\gamma S^* I^* - k(\beta+b+\mu)I^* = 0. \end{aligned}$$

Now, V' has a new form

$$V' = -\mu S^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right) - \gamma S^* E^*\left(\frac{S}{S^*} + \frac{S^*}{S} - 2\right)$$
$$+ -\gamma S^* I^*\left(\frac{S^*}{S} + \frac{S}{S^*}\frac{I}{I^*}\frac{E^*}{E} + \frac{I^*}{I}\frac{E}{E^*} - 3\right)$$
$$+[c(E-E^*) + b(I-I^*) + \alpha(R-R^*)]\left(1 - \frac{S^*}{S}\right).$$

Let $k = cE^* + bI^* + \alpha R^*$. We have

$$[c(E-E^*) + b(I-I^*) + \alpha(R-R^*)]\left(1 - \frac{S^*}{S}\right)$$
$$= [(cE + bI + \alpha R) - (cE^* + bI^* + \alpha R^*)]\frac{S-S^*}{S}$$
$$\leq [k(E+I+R) - k]\frac{S-S^*}{S} = [k(1-S) - k]\frac{S-S^*}{S}$$
$$\leq -k\frac{(S-S^*)^2}{S} \leq 0.$$

Applying the comparison between the arithmetical and the geometrical means, we can conclude that $V'(t) \leq 0$ for all (S, E, I), and the strict equality $V'(t) = 0$ holds only for $S = S^*, E = E^*, I = I^*$. Hence, the invariant set $\{(S, E, I) \in \Omega : V'(t) = 0\}$ is the singleton $\{P_1\}$, where P_1 is the endemic equilibrium point. Therefore, by the LaSalle's Invariance Principle [17], P_1 is globally stable in the set Ω when $R_0 > 1$. This completes the proof. □

Theorem 5. *If $R_0 > 1$ and $\alpha = b = c$ then the endemic equilibrium P_1 is globally asymptotically stable.*

Proof. The proof of Theorem 5 is the same as in Theorem 4. For $\alpha = b = c$, we have
$[c(E-E^*) + b(I-I^*) + \alpha(R-R^*)](1 - \frac{S^*}{S}) =$
$-\alpha\frac{(S-S^*)^2}{S} \leq 0$. □

4.2.2. Geometric approach

In the following, we will discuss the global stability of the endemic equilibrium P_1 when $R_0 > 1$ using the geometric approach. Firstly, we present some preliminaries on the geometric approach to global dynamics [14]. Consider the autonomous dynamical system:

$$\dot{x} = f(x), \tag{6}$$

where $f : D \to \mathbb{R}^n$, $D \subset \mathbb{R}^n$ open set and simply connected and $f \in C^1(D)$.

Let $Q(x)$ be an $\binom{n}{2} \times \binom{n}{2}$ matrix value function that is C^1 on D and consider

$$B = Q_f Q^{-1} + QJ^{[2]}Q^{-1},$$

where the matrix Q_f is $(q_{ij}(x))_f = (\partial q_{ij}(x)/\partial x)^\top \cdot f(x) = \nabla q_{ij} \cdot f(x)$, and $J^{[2]}$ is the second additive compound matrix of the Jacobian matrix J, i.e. $J(x) = Df(x)$. Consider the Lozinskiĭ measure μ of B with respect to a vector norm $|\cdot|$ in $\mathbb{R}^{\binom{n}{2}}$ (see [18]), that is

$$\mu(B) = \lim_{h\to 0^+}\frac{|I + hB| - 1}{h}.$$

Define a quantity $\bar{q}_2$ as

$$\bar{q}_2 = \limsup_{t\to\infty}\sup_{x_0\in K}\frac{1}{t}\int_0^t \mu(B(x(s, x_0)))ds.$$

We will apply the following:

Theorem 6 (see [14]). *Assume that D is simply connected, and*

(H$_1$) There exists a compact absorbing set $K \subset D$,
(H$_2$) The system (6) has a unique equilibrium $\tilde{x}$ in D,

then the unique equilibrium $\tilde{x}$ of (6) is globally asymptotically stable in D if $\bar{q}_2 < 0$.

Theorem 7. *For $R_0 > 1$, system (7) admits an unique endemic equilibrium which globally asymptotically stable, provided that* $\max\{\alpha, b\} \leq c, 2\alpha < b + c$.

Proof. Because $S(t) + E(t) + I(t) + R(t) = 1$, it is sufficient to consider the following three-dimensional subsystem:

$$\frac{dS}{dt} = \mu - \gamma S(t)(E(t) + I(t)) + cE(t) + bI(t)$$
$$+\alpha(1 - S(t) - E(t) - I(t)) - \mu S(t)$$
$$\frac{dE}{dt} = \gamma S(t)(E(t) + I(t)) - (c + \varepsilon + \mu)E(t)$$
$$\frac{dI}{dt} = \varepsilon E(t) - (\beta + b + \mu)I(t) \tag{7}$$

The Jacobian matrix of the system (7) is

$$J = \begin{pmatrix} -\gamma(E+I) - (\alpha+\mu) & -\gamma S - \alpha + b & -\gamma S - \alpha + c \\ \gamma(E+I) & \gamma S - (c+\varepsilon+mu) & \gamma S \\ 0 & \varepsilon & -(\beta+b+\mu) \end{pmatrix}.$$

The associated second compound matrix is given by

$$J^{[2]} = \begin{pmatrix} -\gamma(E+I) + \gamma S - (\alpha+c+\varepsilon+2\mu) & \gamma S & \gamma S + \alpha - c \\ \varepsilon & -\gamma(E+I) - (\alpha+\beta+b+2\mu) & -\gamma S - \alpha + b \\ 0 & \gamma(E+I) & \gamma S - (\beta+b+c+2\mu) \end{pmatrix}.$$

We set the matrix function Q by $Q = \text{diag}\{1, \frac{E}{I}, \frac{E}{I}\}$. Then $Q_f Q^{-1} = \text{diag}\{0, \frac{E'}{E} - \frac{I'}{I}, \frac{E'}{E} - \frac{I'}{I}\}$. We obtain

$$B = Q_f Q^{-1} + QJ^{[2]}Q^{-1} = \begin{pmatrix} -\gamma(E+I) + \gamma S - (a+c+\varepsilon+2\mu) & \gamma\frac{SI}{E} & (\gamma S + \alpha - c)\frac{I}{E} \\ \frac{\varepsilon E}{I} & \frac{E'}{E} - \frac{I'}{I} - \gamma(E+I) - (\alpha+\beta+b+2\mu) & -\gamma S - \alpha + b \\ 0 & \gamma(E+I) & \frac{E'}{E} - \frac{I'}{I} + \gamma S - (\beta+b+c+2\mu) \end{pmatrix}.$$

The matrix B can be written in block form

$$B = \begin{pmatrix} B_{11} & B_{12} \\ B_{21} & B_{22} \end{pmatrix},$$

where

$$B_{11} = -\gamma S(E+I) + \gamma S - (\alpha + c + \varepsilon + 2\mu),$$
$$B_{12} = \begin{pmatrix} \gamma\frac{SI}{E} & \gamma S + \alpha - c \end{pmatrix},$$

$$B_{21} = \begin{pmatrix} \frac{\varepsilon E}{I} \\ 0 \end{pmatrix}, \quad B_{22} = \begin{pmatrix} \frac{E'}{E} - \frac{I'}{I} - \gamma(E+I) - (a+\beta+b+2\mu) \\ \gamma(E+I) \end{pmatrix}$$

$$\begin{pmatrix} -\gamma S - \alpha + b \\ \frac{E'}{E} - \frac{I'}{I} + \gamma S - (\beta + b + c + 2\mu) \end{pmatrix}.$$

The vector norm $|\cdot|$ in $\mathbb{R}^3$ can be chosen as $|(u, v, w)| = \max\{|u|, |v| + |w|\}$.

Let μ denote the Lozinskiĭ measure with respect to this norm. Then we can obtain

$$\mu(B) \leq \sup\{g_1, g_2\},$$

with

$$g_1 = \mu_1(B_{11}) + |B_{12}|, \quad g_2 = \mu_1(B_{22}) + |B_{21}|,$$

where $|B_{12}|$, $|B_{21}|$ are matrix norms with respect to the L^1 vector norm and μ_1 denotes the Lozenskiĭ measure with respect to the L^1 norm. Specifically,

$$\mu_1(B_{11}) = -\gamma(E+I) + \gamma S - (\alpha + c + \varepsilon + 2\mu),$$

$$|B_{12}| = \max\left\{ \left|\gamma \frac{SI}{E}\right|, \left|(\gamma S + \alpha - c)\frac{I}{E}\right| \right\}, |B_{21}| = \varepsilon \frac{E}{I},$$

$$\mu_1(B_{22}) = \frac{E'}{E} - \frac{I'}{I} - (\beta + b + 2\mu) + \max\{-\alpha, \gamma S - c + |-\gamma S - \alpha + b|\}.$$

Because of the condition $\alpha \leq c$, it follows $|B_{12}| = \gamma \frac{SI}{E}$.

Since (7) is uniformly persistent, there exists $T > 0$ such that $S(t) \leq \frac{b+c-2\alpha}{2\gamma}$ for $t > T$. Moreover, from the conditions $\max\{\alpha, b\} \leq c, 2\alpha < b + c$ we can include that $\gamma S - c + |-\gamma S - \alpha + b| \leq -\alpha$. Therefore, $\mu_1(B_{22}) = \frac{E'}{E} - \frac{I'}{I} - (\beta + b + 2\mu) - \alpha$. We have

$$g_1 = -\gamma(E+I) + \gamma S - (\alpha + c + \varepsilon + 2\mu) + \gamma \frac{SI}{E}.$$

It follows from (7) that $\frac{E'}{E} = \gamma S + \gamma \frac{SI}{E} - (c + \varepsilon + \mu)$, then we have

$$g_1 = \frac{E'}{E} - (\alpha + \mu) - \gamma(E+I) \leq \frac{E'}{E} - (\alpha + \mu),$$

$$g_2 = \varepsilon \frac{E}{I} + \frac{E'}{E} - \frac{I'}{I} - (\beta + b + 2\mu) - \alpha.$$

Based on Eqs. (7) we have $\frac{I'}{I} = \varepsilon \frac{E}{I} - (\beta + b + \mu)$. It implies

$$g_2 = \frac{E'}{E} - (\alpha + \mu).$$

Therefore

$$\mu(B) \leq \frac{E'}{E} - (\alpha + \mu).$$

Thus, for $t > T$ we have

$$\frac{1}{t}\int_0^t \mu(B)ds \leq \frac{1}{t}\log\frac{E'(t)}{E(t)} + \frac{1}{t}\int_0^T \mu(B)ds - (\alpha + \mu)\frac{t-T}{t},$$

which implies $\bar{q}_2 < 0$. This completes the proof. □

5. Numerical simulation

In this section, we carry out a numerical investigation for the system (2) to illustrate the analytic results obtained above. Numerical results are displayed in the following figures (see Fig. 2 and Fig. 3).

Fig. 2 shows time series of solutions of the model as $R_0 \leq 1$. For $\alpha = 0.35, \beta = 0.5, b = 0.025, c = 0.35, \varepsilon = 0.15, \gamma = 0.1$, and $\mu = 0.015$, we have $R_0 = 0.248112 < 1$. In this case, the disease free equilibrium P_0 is globally asymptotically stable. With the initial condition $(S(0), E(0), I(0), R(0)) = (0.002, 0.006, 0.003, 0.001)$, the exposed component $E(t)$ and the infectious component $I(t)$ of solutions tends to 0 as t approaches to $+\infty$. This implies that the disease dies out.

Fig. 3 indicates time series of solutions of the model as $R_0 > 1$. For $\alpha = 0.35, \beta = 0.33, b = 0.025, c = 0.35, \varepsilon = 0.1, \gamma = 0.5$, and $\mu = 0.075$, we have $R_0 = 1.17386 > 1$. In this case, the endemic equilibrium is globally asymptotically stable. With the initial condition $(S(0), E(0), I(0), R(0)) = (0.01, 0.01, 0.01, 0.01)$ the exposed component $E(t)$ goes to the positive value 0.1124 and the infectious component $I(t)$ approaches to the positive value 0.02849 as t tends to $+\infty$. This means that the disease remains in the population.

The change of local stability of the equilibria P_0 and P_1 can be explained by the transcritical bifurcation where two equilibria collide and interchanges their stability [8]. By using AUTO software package, one can detect the transcritical bifurcation

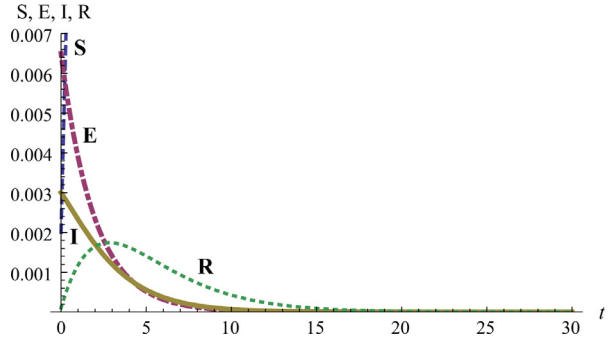

Figure 2 Time series of solutions of the model (2) as $R_0 \leq 1$.

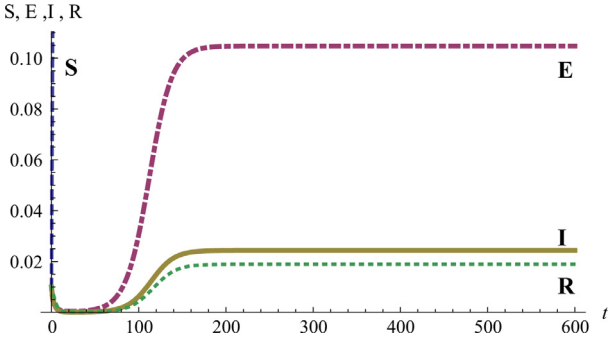

Figure 3 Time series of solutions of the model (2) as $R_0 > 1$.

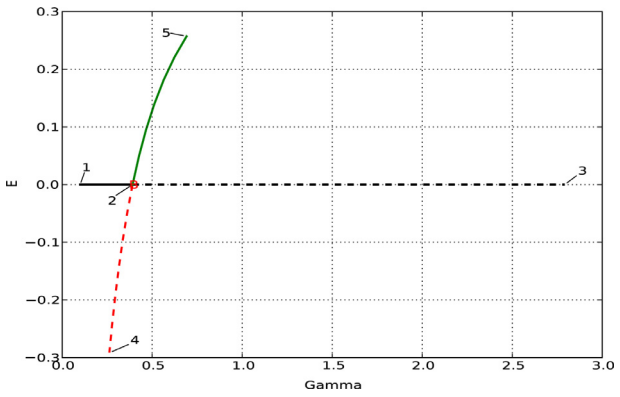

Figure 4 Bifurcation diagram of the model (2) in the plane (γ, E).

in the model. For $\alpha = 0.35$, $\beta = 0.5$, $b = 0.025$, $c = 0.35$, $\varepsilon = 0.15$, $\mu = 0.005$, let γ vary then we get a transcritical bifurcation occurring at the value $\gamma = 0.351872$. The bifurcation diagram is given in Fig. 4 . In the figure, the line passing through the solution 1, 2 and 3 is the curve of disease free equilibrium, and the line containing the solution 4, 2 and 5 is the curve of endemic equilibrium. The solid line is for stable equilibria and the dashed line is for unstable equilibria. Transcritical bifurcation occurs at the solution 2, corresponding to $R_0 = 1$. We also obtain the same bifurcation when other parameters are varied.

6. Conclusions

In this paper, a proposed model for infectious diseases of influenza virus with resistance in human is introduced and studied. The basic reproduction number R_0 is the threshold condition that determines the propagation dynamics. When $R_0 \leq 1$, the system has only a disease free equilibrium P_0 which is globally stable. It implies that the disease dies out eventually. When $R_0 > 1$, the system has a unique endemic equilibrium P_1, which is globally stable under some conditions. This shows that the disease persists in the population and tends to a positive steady state. The local bifurcation, occurring at $R_0 = 1$, is explained by the transcritical bifurcation. The global stability of system has been proved by using the Lyapunov function method as well as geometric approach. As results indicate that spread of disease is very sensitive to contact parameter γ and transform parameters β, b and c. The transmission will slow down if the value of γ is decreasing, and β, b and c are increasing (see Fig. 4). This shows the way to reduce the spread of influenza virus.

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References

[1] P. Pongsumpun, I.M. Tang, Mathematical model of the symptomatic and symptomatic infections of Swine flu, Int. J. Math. Models Meth. Appl. Sci. 2 (5) (2011) 247–254.
[2] X. Zhou, Z. Guo, Analysis of an influenza A (H1N1) epidemic model with vaccination, Arab. J. Math. 1 (2012) 267–282.
[3] M.F. Neil, M. Susan, et al., A population dynamic model for evaluating the potential spread of drug-resistant influenza virus infections during community-based use of antivirals, J. Antimicrob. Chemother. 51 (2003) 977–990.
[4] C. Fraser, A.D. Christl, et al., Pandemic potential of a strain of influenza A(H1N1): early finding, Science 324 (2009) 1557–1561.
[5] B.J. Coburn, Multi-Species Influenza Models with Recombination, Ph.D. dissertation Coral Gables, University of Miami, FL, 2009.
[6] E. Beretta, V. Capasso, On the general structure of epidemic systems, Global asymptotic stability, Comput. Math. Appl. 12A (1986) 677–694.
[7] W.O. Kermack, A.G. McKendrick, Contribution to mathematical theory of epidemics, Proc. R. Soc. A 115 (1927) 700–721.
[8] Z. Ma, J. Zhou, J. Wu, Modeling and Dynamics of Infectious Diseases, World Scientific Publishing, 2009.
[9] A.M. Lyapunov, The General Problem of the Stability of Motion, Taylor and Francis, London, 1992.
[10] A. Korobeinikon, G.C. Wake, Lyapunov functions and global stability for SIR, SIRS, and SIS epidemiological models, Appl. Math. Lett. 15 (2002) 955–960.
[11] A. Korobeinikov, Lyapunov functions and global properties for SEIR and SEIS epidemic models, Math. Med. Biol. 21 (2004) 75–83.
[12] M.Y. Li, J.S. Muldowney, Global stability for the SEIR model in epidemiology, Math. Biosci. 125 (1995) 155–164.
[13] L.X. Yang, X. Yang, Q. Zhu, L. Wen, A computer virus model with graded cure rates, Nonlin. Anal. Real World Appl. 14 (2013) 414–422.
[14] M.Y. Li, J. Muldowney, A geometric approach to global stability problems, SIAM J. Math. Anal. 27 (4) (1996) 1070–1083.
[15] X. Zhou, J. Cui, Analysis of stability and bifurcation for an SEIR epidemic model with saturated recovery rate, Commun. Nonlin. Sci. Numer. Simulat. 16 (2011) 4438–4450.
[16] P. Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002) 29–48.
[17] J.P. Salle, The Stability of Dynamical System, SIAM, Philadelphia, PA, 1976.
[18] R.H. Martin, Logarithmic norms and projections applied to linear different differential systems, J. Math. Anal. Appl. 45 (1974) 432–454.