MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **xx**, Number **0xx**, xx **20xx**

doi:10.3934/mbe.2009.xx.xx

pp. **1–xx**

# A NOTE ON THE DYNAMICS OF AN SAIQR INFLUENZA MODEL

ANA LUZ VIVAS

Ph.D Student, Department of Mathematics, New Mexico State University
Las Cruces, NM, USA

CARLOS CASTILLO-CHAVEZ

Mathematical, Computational, and Modeling Sciences Center,
Physical Sciences A, P.O. Box, 871904, Tempe, AZ 85287-1904

ERNEST BARANY

Department of Mathematics, New Mexico State University
Las Cruces, NM, USA

Abstract. There is an extensive literature on the modifications of classical Susceptible-Infected-Recovered (SIR) models, the bread and butter in the study of disease dynamics, that support the concept of recurrent (periodic) outbreaks. In this note we provide an extension motivated by our desire to understand the role of asymptomatics on the dynamics of influenza.

1. **Introduction.** Mathematical models of disease transmission have been widely used and developed for well over a century [13, 14]. They have become standard "tools" in the study of the spread and control of communicable diseases such as measles, tuberculosis, rubella, chicken pox and, one of the most common diseases affecting humans, influenza [1, 3, 10, 20, 2, 5, 15, 21]. Modifications to the $SIR$ (Susceptible-Infectious-Recovered) epidemiological model have been used to model the dynamics of viral infections that provide permanent immunity after recovery. The inclusion of a class of individuals that are isolated after infection has gained increasing mathematical attention [4, 8, 12]. The inclusion of a quarantine class, $Q$, has been shown to grant the so-called $SIQR$ epidemiological model the "ability" to support recurrent outbreaks [7, 17, 18].

2000 *Mathematics Subject Classification.* Primary: 92D40, 34D23; Secondary: 92D25.
*Key words and phrases.* SAIQR influenza model, asymptomatic class, basic reproduction number, endemic equilibrium, Hopf bifurcations.

In this note, we introduce an extension (motivated from the ongoing work on influenza) of the $SIQR$ model through the addition of a class, $A$, of asymptomatic individuals [9]. The corresponding epidemiological model is referred as an $SAIQR$ model. It is assumed that individuals in the $A$ class may be less infectious than those in the $I$ class. The mathematical properties of this model are then studied with the intent to qualify well posedness, illustrate the existence of equilibria and in some special cases derive the conditions for the existence of periodic solutions due to Hopf bifurcations.

2. **The $SAIQR$ model.** For this model the total population of individuals is divided between five compartments: $S(t)$, susceptible individuals; $A(t)$, asymptomatic infectious individuals; $I(t)$, symptomatic infectious individuals; $Q(t)$, isolated (quarantined) individuals and $R(t)$, recovered (immune) individuals. The population recruits new members, into $S(t)$, at a constant rate $\Lambda$, and each class removes individuals from the system at a rate of $\mu$. The transmission coefficient, the average number of effective contacts that lead to a new infection of a susceptible, due to a contact with a symptomatically infectious individual, is denoted by $\beta$. We assume that individuals from the $A$-class are infectious but with reduced per-capita infection rate, $\beta\sigma$, $\sigma \in [0, 1]$. The transferred proportion of individuals from the $S$ to the $I$ class is denoted by $p$ while the proportion transferred from $S$- to the $A$-classes is given by $1 - p$. The per-capita isolation quarantine rate of symptomatically infectious individuals is $\theta$. Further, isolated (quarantined) individuals are assumed to have negligible contacts with member of the overall population. Denoting the per-capita recovery rates for asymptomatic, symptomatic and isolated individuals as $\gamma_1$, $\gamma_2$ and $\gamma_3$, respectively then the above leads to the following system of non-linear ordinary differential equations:

$$\begin{aligned} S' &= \Lambda - \beta S\frac{(I+\sigma A)}{N-Q} - \mu S \\ A' &= (1-p)\beta S\frac{(I+\sigma A)}{N-Q} - (\gamma_1+\mu)A \\ I' &= p\beta S\frac{(I+\sigma A)}{N-Q} - (\gamma_2+\theta+\mu)I \\ Q' &= \theta I - (\gamma_3+\mu)Q \\ R' &= \gamma_1 A + \gamma_2 I + \gamma_3 Q - \mu R, \end{aligned} \tag{1}$$

with initial conditions

$$S(0) = S_0, A(0) = A_0, I(0) = I_0, Q(0) = 0, R(0) = 0.$$

Defining $N := S + A + I + Q + R$ we may conclude that

$$\frac{dN}{dt} = \Lambda - \mu N,$$

and, therefore, that $N(t) \to \Lambda/\mu$ as $t \to \infty$. That is the total population is asymptotically constant. The well-posedness of the model follows from a straight forward application of the classical theory [19].

**Result 2.1**: Let $S_0, A_0, I_0, Q_0, R_0 \geq 0$, $S_0 + A_0 + I_0 + Q_0 + R_0 = N_0$. Then there exits solutions $S(t), A(t), I(t), Q(t), R(t)$ for the dynamical system (1), with initial data $S_0, A_0, I_0, Q_0, R_0$ at time $t = 0$, that are defined for all time $t \geq 0$. In fact, $S(t), A(t), I(t), Q(t), R(t)$ are nonnegative and $S(t) + A(t) + I(t) + Q(t) + R(t) = N$ for all $t$. If $A_0 = 0, I_0 = 0, Q_0 = 0$ then $A(t) \equiv 0$ and $I(t) \equiv 0$. If $I_0 > 0$ and $A_0 > 0$, then $S(t), A(t), I(t), Q(t), R(t)$ are strictly positive for all $t > 0$ and $Q$ is bounded by $\hat{Q} = max\left\{Q_0, \frac{\theta}{\gamma_3+\mu}\right\}$. An outline of the proof is provided in the Appendix.

Since the total population is asymptomatically constant the results in [2], guarantee that the following system

$$\begin{aligned} S' &= \Lambda - \beta S\frac{(I+\sigma A)}{N-Q} - \mu S \\ A' &= (1-p)\beta S\frac{(I+\sigma A)}{N-Q} - (\gamma_1+\mu)A \\ I' &= p\beta S\frac{(I+\sigma A)}{N-Q} - (\gamma_2+\theta+\mu)I \\ Q' &= \theta I - (\gamma_3+\mu)Q, \end{aligned} \tag{2}$$

with $N = \dfrac{\Lambda}{\mu}$, has the same asymptotic qualitative dynamics as those of System (1). Model (2) has two equilibria, the disease free equilibria $E_0 = (\Lambda/\mu, 0, 0, 0)$ and, whenever the disease's basic reproduction number is greater than one, a unique endemic equilibria $E^*(S_\infty(\Re_0), A_\infty(\Re_0), I_\infty(\Re_0), Q_\infty(\Re_0))$.

3. **Basic reproduction number and endemic equilibria.** Linearizing System (2) around $E_0$, yields the following Jacobian matrix

$$J(E_0) = \begin{pmatrix} -\mu & -\beta\sigma & -\beta & 0 \\ 0 & \sigma(1-p)\beta - (\gamma_1 + \mu) & \beta(1-p) & 0 \\ 0 & \sigma p\beta & p\beta - (\gamma_2 + \theta + \mu) & 0 \\ 0 & 0 & \theta & -(\gamma_3 + \mu) \end{pmatrix}.$$

The stability of $E_0$ is determined by the real parts of the eigenvalues of the matrix

$$J_1(E_0) = \begin{pmatrix} \sigma(1-p)\beta - (\gamma_1 + \mu) & \beta(1-p) \\ \sigma p\beta & p\beta - (\gamma_2 + \theta + \mu) \end{pmatrix}.$$

From the eigenvalues of the above matrix we conclude that

$$\Re_0 \equiv \frac{p\beta}{\gamma_2 + \theta + \mu} + \frac{(1-p)\beta\sigma}{\gamma_1 + \mu} \tag{3}$$

and note that the disease-free state is locally asymptotically stable as long as $\Re_0 < 1$. The basic reproduction number ($\Re_0$) is the sum of the additive contributions of the $A$- and $I$-classes to the generation of secondary infections of "influenza" when $S(0) \approx \Lambda/\mu$.

The $SAIQR$ model can be thought of as a family of models parameterized by $\sigma$ and $p$, that is $\mathcal{M}(\sigma, p)$. The asymptomatic class is not present when $p = 1$ and $\sigma = 0$. $\mathcal{M}(0, 1)$ corresponds to the classical SIQR model with

$$\Re_0 = \frac{\beta}{\gamma_2 + \theta + \mu}.$$

The importance of $\Re_0$ in the control of disease dynamics is evident from the extensive efforts to estimate its value for various diseases [6] and its role in the study of the long-term dynamics of infections diseases [10].

The simulation of the solutions of System (1), for different $\Re_0$ values, shows for example, that at the beginning of an outbreak, the population from the infections class actually decreases (Figure 1) before it takes off. This last simulation highlights the effect of the inclusion of an asymptomatic class.

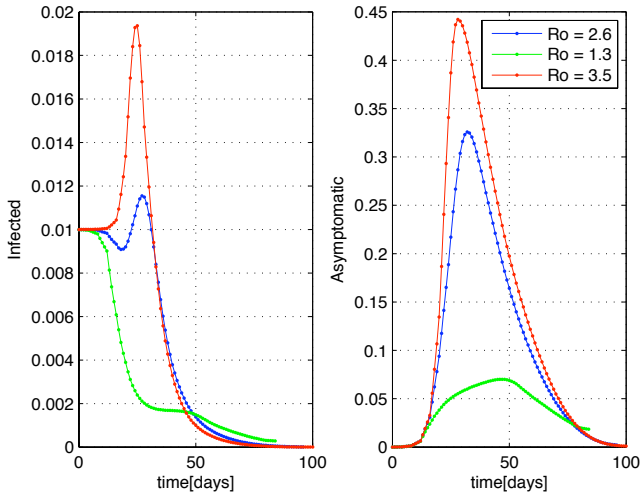


FIGURE 1. Infections and asymptomatic individuals for $p = 0.3$. When $\Re_0 = 2.6$ and $\Re_0 = 3.5$ we can observe that the number of asymptomatic individuals has a peak around the 30 day of the spread of the disease. If $\Re_0 = 1.3$ and $\Re_0 = 2.6$ the number of infectious is decreasing at the beginning of the spread of the disease.

We collect the conditions for stability below (outlines of proofs for each are provided in the Appendix):

**Result 3.1**: If $\Re_0 < 1$ the disease free equilibrium point $E_0 = (\Lambda/\mu, 0, 0, 0)$ for System (2) is locally asymptotically stable. If $\Re_0 > 1$ then $E_0$ is unstable.

**Result 3.2**: If $\Re_0 \leq 1$, the disease free equilibrium point $E_0 = (\Lambda/\mu, 0, 0, 0)$ is globally asymptotically stable.

The endemic equilibrium point $E^*(S_\infty(\Re_0), A_\infty(\Re_0), I_\infty(\Re_0), Q_\infty(\Re_0))$ for System (2) is given by

$$\begin{aligned} S_\infty(\Re_0) &= \frac{\Lambda(1-\frac{ab}{c})}{\mu(1-\frac{ab}{c}\Re_0)} \\ A_\infty(\Re_0) &= (1-p)\mu\frac{ab}{cd}\frac{\Lambda(1-\Re_0)}{\mu(1-\frac{ab}{c}\Re_0)} \\ I_\infty(\Re_0) &= \frac{b}{\theta}\frac{\Lambda(1-\Re_0)}{\mu(1-\frac{ab}{c}\Re_0)} \\ Q_\infty(\Re_0) &= \frac{\Lambda(1-\Re_0)}{\mu(1-\frac{ab}{c}\Re_0)} \end{aligned} \tag{4}$$

where $a = \gamma_2 + \theta + \mu$, $b = \gamma_3 + \mu$, $c = p\mu\theta$ and $d = \gamma_1 + \mu$.

i) $S_\infty(\Re_0)$, $A_\infty(\Re_0)$, $I_\infty(\Re_0)$ and $Q_\infty(\Re_0)$ are positive iff $\Re_0 > 1$.

ii) $S_\infty(\Re_0) + A_\infty(\Re_0) + I_\infty(\Re_0) + Q_\infty(\Re_0) < \Lambda/\mu$.

The Jacobian matrix for System (2) at $E^*(S_\infty(\Re_0), A_\infty(\Re_0), I_\infty(\Re_0), Q_\infty(\Re_0))$ is

$$J(E^*) = \begin{pmatrix} -A-\mu & -\sigma\beta & -B & D \\ (1-p)C & \sigma(1-p)B - E & (1-p)B & -(1-p)D \\ pA & \sigma pB & pB - F & -pD \\ 0 & 0 & \theta & -G \end{pmatrix}$$

where

$$\begin{aligned} A &= \beta\frac{I_\infty(\Re_0) + \sigma A_\infty(\Re_0)}{N - Q_\infty(\Re_0)} \\ B &= \beta\frac{S_\infty(\Re_0)}{N - Q_\infty(\Re_0)} \\ C &= \beta\frac{S_\infty(\Re_0)(I_\infty(\Re_0) + \sigma A_\infty(\Re_0))}{N - Q_\infty(\Re_0)} \\ D &= \beta\frac{S_\infty(\Re_0)(I_\infty(\Re_0) + \sigma A_\infty(\Re_0))}{(N - Q_\infty(\Re_0))^2}, \end{aligned}$$

and

$$E = \gamma_1 + \mu, \qquad F = \gamma_2 + \theta + \mu, \qquad G = \gamma_3 + \mu.$$

**Result 3.3**: If $\Re_0 > 1$ System (2) has an uniquely determined nonnegative endemic equilibrium point given by (4). This endemic equilibrium $E^*$ is "usually" locally asymptotically stable. The generation of periodic solutions via a Hopf bifurcation is possible as parameters are varied. An outline of the proof is in the Appendix.

The characteristic polynomial, associated with the local stability of $E^*$, is

$$P(\lambda;\xi) = p_0(\xi) + p_1(\xi)\lambda + p_2(\xi)\lambda^2 + p_3(\xi)\lambda^3 + p_4(\xi)\lambda^4, \tag{5}$$

where $\xi$ denotes the model's parameter vector.

The stability of the endemic equilibrium is tied to the roots of (5). It is at this point that we make the decision to explore the region of parameter space that is relevant in the study of the dynamics of influenza. Specifically we observe that the average life-expectancy $(1/\mu)$ is in the order of decades while $1/\gamma_1$, $1/\gamma_2$ $1/\gamma_3$ and $1/\theta$ are in order of days. Hence, we can safely assume that $\mu$ is much smaller than $\gamma_1, \gamma_2, \gamma_3$ and $\theta$. Taking into account these differences in time scales (longevity versus the infectious period) plus the fact that the functions $p_i(\xi)$ for $(i = 0, ...4)$ are analytic functions in $\xi$, we proceed to generate series expansion for the coefficients of the characteristic polynomial near $\mu = 0$. In the limiting case, $\mu = 0$, Polynomial (5) becomes

$$P(\lambda;\xi) = \gamma_1\gamma_3(\gamma_2+\theta)\lambda + \gamma_3(\gamma_2+\theta)\lambda^2 + (\gamma_1+\gamma_2+\gamma_3+\theta)\lambda^3 + \lambda^4. \tag{6}$$

4. **An example.** We set $\gamma = \gamma_1 = \gamma_2 = \gamma_3$ and $\theta = k\gamma$ where $k \geq 3$.

The exact algebraic expressions for the roots are extremely complex and therefore we proceed to postulate specific relations between the recovery and the isolation rates. Specifically, we let $\gamma = \gamma_1 = \gamma_2 = \gamma_3$ and let the isolation rate be proportional to the recovery rate, $\theta = k\gamma$. Since $1/\theta \in [1, 7]$ then $k \geq 3$. Under these assumptions Polynomial (6) becomes

$$p(\lambda, \gamma, k) = \gamma^3(1+k) + \gamma^2(1+k)\lambda + \gamma(3+k)\lambda^2 + \lambda^3,$$

which has an interesting structure, a cubic in both $\lambda$ and $\gamma$. When $k = 3$, it reduces to the simple cubic polynomial

$$p(\lambda, \gamma) = 4\gamma^3 + 4\gamma^2\lambda + 6\gamma\lambda^2 + \lambda^3,$$

from where we see that the eigenvalues depend on the parameter $\gamma$. The real parts of the eigenvalues $\lambda_i(\xi)$ determine the stability of the endemic equilibrium and as parameters are varied, we will show the real part of the complex eigenvalues changes sign. Computer calculations allows us to conclude that there is a negative real eigenvalue $\lambda_1(\xi)$ and two complex conjugate eigenvalues $\lambda_2(\xi)$, $\bar{\lambda}_2(\xi)$. Figure 2, provides the graphs for $Re(\lambda_2)$ that include the possibility of a change in sign (for small values of $\gamma$). We conclude that a Hopf bifurcation is possible. In fact, we see that $Re(\lambda_2)$ is very small for some $\gamma$ values and negative for $\gamma \geq 0.047$. Hence, the existence of lightly damped oscillations approaching the endemic equilibrium naturally emerge. This qualitative behavior (slowly damped oscillations) captures "biologically" recurring epidemics. Figure 3, provides the graph for infectious and asymptomatic classes where this behavior is observed.

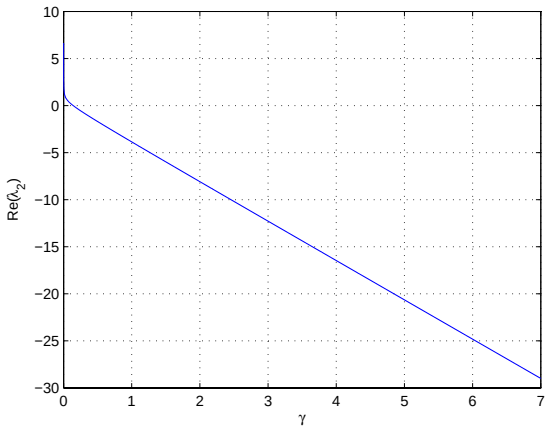


FIGURE 2. Real part of $\lambda_2(\gamma)$, where $\lambda_2$ is a complex eigenvalue of the Jacobian matrix. A change of sign from positive to negative is observed for a small value of the parameter $\gamma \approx 0.047$.

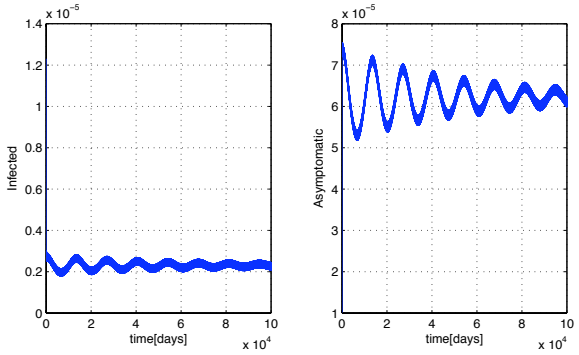


FIGURE 3. Lightly damped oscillations approaching the endemic equilibrium, $\gamma_1 = \gamma_2 = \gamma_3 \approx 0.045$.

5. **Discussion.** Over the past few decades there has been several mathematical studies aimed at identifying key mechanism responsible for disease recurrent outbreaks. Hethcote and Levin [11] reviewed the role of non-linear incidence rates, cross-immunity and delays as mechanism capable of supporting periodic outbreaks. The review paper of Hethcote [10], provides a comprehensive mathematical work carried out over the 80's and 90's. In his review, the impact of quarantine or isolation as a mechanism capable of generating mathematically sustained oscillations is also addressed.

In this note, we look at the simplest epidemiological model that incorporates the dynamics of an asymptomatic class. Further, as it was done in Castillo-Chavez et all [2], we considered the differences in demographic and epidemiological scales that are typical of influenza dynamics in our study of the possibility that an epidemiological model that includes $A$ and $Q$ classes can support sustained oscillations.

We have carried out the standard local analysis of a SAIQR model and shown that when $\Re_0 > 1$, its unique endemic state can become de-stabilized as parameters are varied. We have observed that the real part of the pair of complex conjugate eigenvalues crosses zero as the mean incubation period distribution in the asymptomatic infectious and quarantined classes (all assumed to be the same) changes.

The upshot of this model is that critical neglected epidemiological classes and intervention measures can indeed be capable of supporting (mathematically speaking) recurrent periodic outbreaks.

**Appendix. Proof of Result 2.1**:

The right hand side of System (1) is continuously differentiable and hence it is locally Lipschitz, and therefore there exits a unique solution $S(t), A(t), I(t), Q(t), R(t)$ to System (1) with the initial data $S_0, A_0, I_0, Q_0, R_0$ that is defined on a maximal forward interval of existence [19]. Consider the set $\Omega \subset \mathbb{R}^5$ defined by

$$\Omega = \{(S, A, I, R, Q) : 0 \leq S + A + I + Q + R \leq \frac{\Lambda}{\mu}\},$$

we show that

i) Since $I(0) \geq 0$ and $A(0) \geq 0$ from System (1) we have that

$$\begin{aligned} I(t) &\geq I_0 \exp \int_0^\infty \left[ p\beta S \frac{1}{N-Q} - (\gamma_2 + \theta + \mu) \right] dt \\ A(t) &\geq A_0 \exp \int_0^\infty \left[ (1-p)\beta\sigma \frac{S}{N-Q} - (\gamma_1 + \mu) \right] dt \\ Q(t) &= \left[ Q_0 + \int_0^t \theta I(\zeta) e^{(\gamma_3+\mu)(\zeta - t_0)} d\zeta \right] e^{(\gamma_3+\mu)(t_0 - t)} \\ R(t) &= \left[ R_0 + \int_0^t (\gamma_1 A(\zeta) + \gamma_2 I(\zeta) + \gamma_3 Q(\zeta)) e^{\mu(\zeta - t_0)} d\zeta \right] e^{\mu(t_0 - t)}, \end{aligned}$$

then $S(t) \geq 0$, $A(t) \geq 0$, $I(t) \geq 0$, $Q(t) \geq 0$, $R(t) \geq 0$ for all $t > 0$.

ii) $Q$ is bounded by $\hat{Q} = max \left\{ Q_0, \frac{\theta}{\gamma_3 + \mu} \right\}$. The last statement will be established if we show that $Q(t) \leq \kappa$ for all $t \geq 0$ and that $\kappa \geq \frac{\theta}{\gamma_3+\mu}$ if $Q_0 \leq \kappa$. Suppose that the above inequalities do not hold then there exists a time $t_1$ with $Q'(t_1) > 0$ and $Q(t_1) > \kappa$. From the Q-equation in System (1) we have

$$\frac{dQ(t_1)}{dt} = \theta I(t_1) - (\gamma_3 + \mu) Q(t_1) \leq \theta (I(t_1) - 1) \leq 0,$$

since $(I(t_1) - 1) < 0$ and $\theta > 0$. This contradiction implies that $Q(t) < \kappa$ for all $t \geq 0$. Suppose now that $Q(0) > \kappa \geq \frac{\theta}{\gamma_3+\mu}$. In order to show that $Q(t) \leq Q(0)$ for all $t \geq 0$ we assume that the last inequality does not hold. Hence there exists a time $t_2 > 0$ such that $Q(t_2) \geq Q(0)$ and $Q'(t_2) > 0$.

However since $Q(t_2) > \frac{\theta}{\gamma_3+\mu}$, then

$$Q'(t_2) = \theta I(t_2) - (\gamma_3 + \mu)Q(t_2) \leq \theta(I(t_2) - 1) \leq 0,$$

but $Q'(t_2) > 0$. Hence we have reach a contradiction and $Q(t)$ is bounded from above by $\hat{Q}$ , where $\hat{Q} = max\left\{Q_0, \frac{\theta}{\gamma_3 + \mu}\right\}$.

**Proof of Result 3.1**: The stability of the disease free equilibrium point depends on the signs of the real parts of the eigenvalues of the Jacobian matrix $J(E_0)$. $-\mu$ and $-(\gamma_3 + \mu)$ are two eigenvalues of $J(E_0)$. Conditions $trace(J_1(E_0)) < 0$ and $det(J_1(E_0)) > 0$ is equivalent to $\Re_0 < 1$, hence this guarantee the asymptotic stability of the disease-free equilibrium. If $\Re_0 > 1$ implies that $E_0$ is unstable. see [19] for more mathematical details.

**Proof of Result 3.2**: Define a Liapunov function $L$ over $\Omega_0 \in \Omega$ as follows, $L(\mathbf{x}) = \sigma(\gamma_2 + \theta + \mu)A + (\gamma_1 + \mu)I$, for $\mathbf{x} \in \Omega_0$. Hence $L$ satisfies

i) $L \in C^1(\Omega_0)$, $L(\Lambda/\mu, 0, 0, 0) = 0$ and $L(\mathbf{x}) > 0$ if $\mathbf{x} \neq E_0$.

ii) $\frac{dL}{dt} < (\gamma_1 + \mu)(\gamma_2 + \theta + \mu)(I + \sigma A)\left[\Re_0 - 1\right] < 0$ if $\Re_0 < 1$, for all $\mathbf{x} \in \Omega_0$, $\mathbf{x} \neq E_0$,

then $E_0$ is globally asymptotically stable if $\Re_0 < 1$.

**Proof of Result 3.3**: To determine if a Hopf bifurcations occurs, we use a Lemma in which Hurwitz determinants are included. In our case ($n = 4$), Hurwitz determinants depend on the following matrix

$$\mathbf{L_4}(\xi) = \begin{pmatrix} p_1(\xi) & p_2(\xi) & 0 & 0 \\ p_3(\xi) & p_2(\xi) & p_1(\xi) & p_0(\xi) \\ 0 & p_4(\xi) & p_3(\xi) & p_2(\xi) \\ 0 & 0 & 0 & p_4(\xi) \end{pmatrix}$$

and are defined as follows

$$D_1(\xi) = det(L_1(\xi)), D_2(\xi) = det(L_2(\xi)), D_3(\xi) = det(L_3(\xi)), D_4(\xi) = det(L_4(\xi)),$$

where

$$\mathbf{L_1}(\xi) = p_1(\xi),$$

$$\mathbf{L_2}(\xi) = \begin{pmatrix} p_1(\xi) & p_0(\xi) \\ p_3(\xi) & p_2(\xi) \end{pmatrix},$$

$$\mathbf{L_3}(\xi) = \begin{pmatrix} p_1(\xi) & p_0(\xi) & 0 \\ p_3(\xi) & p_2(\xi) & p_1(\xi) \\ 0 & p_4(\xi) & p_3(\xi) \end{pmatrix},$$

The Routh-Hurwitz criteria can be stated in terms of their polynomials. Specifically, when $p_0(\xi) > 0$ the polynomial $p(\lambda, \xi)$ has all roots with negative real parts if and only if

$$D_1(\xi) > 0, D_2(\xi) > 0, D_3(\xi) > 0, D_4(\xi) > 0.$$

Since $D_4(\xi) = p_4(\xi)D_3(\xi)$ and in our case $p_4(\xi) = 1$, the Routh-Hurwitz conditions can be rewritten in this case as

$$p_0(\xi) > 0, D_1(\xi) > 0, D_2(\xi) > 0, D_3(\xi) > 0.$$

We use the following lemma, as a criteria for the possibility of a Hopf bifurcations [16].

**Lemma**: Assume that there is a smooth curve of equilibria $(x(\xi), \xi)$ with $x(\xi_0) = x_0$. For system (2), there is a simple Hopf bifurcation if

**(i):** $p_0(\xi_0) > 0, D_1(\xi_0) > 0, D_2(\xi_0) > 0, D_3(\xi) = 0.$

**(ii):** $dD_3(\xi_0)/d\xi \neq 0.$

Condition $D_3(\xi) = 0$ is equivalent to

$$p_1(\xi)p_2(\xi)p_3(\xi) - p_1^2(\xi) - p_0(\xi)p_3^2(\xi) = 0$$

and in the limited case ($\mu = 0$), since $p_0(\xi) = 0$ then

$$p_2(\xi)P_3(\xi) - p_1(\xi) = 0.$$

The last equation represents the surface where a Hopf bifurcation can occurs. Condition $dD_3(\xi_0)/d\xi \neq 0$ is equivalent to

$$\begin{aligned} dD_3(\xi_0)/d\xi = &[(\gamma_2+\theta)(\gamma_1+\gamma_3)+\gamma_1\gamma_3][\gamma_3(\gamma_2+\theta)][(\gamma_1+\gamma_2+\gamma_3+\theta)]+ \\ &\gamma_1\gamma_3(\gamma_2+\theta)+[\gamma_1+\gamma_2+\gamma_3+\theta)^2]+[\gamma_1\gamma_3(\gamma_2+\theta)][(\gamma_2+\theta)] \\ &-2[\gamma_1\gamma_3(\gamma_2+\theta)][(\gamma_2+\theta)(\gamma_1+\gamma_3)+\gamma_1\gamma_3] \\ &\neq 0, \end{aligned}$$

which is certainly true for the set of parameters $\xi$ and therefore a Hopf bifurcation occurs.

**Acknowledgements.** This project has been supported by grants from the National Science Foundation (NSF - Grant DMPS-0838705), the National Security Agency (NSA - Grant H98230-09-1-0104), the Alfred P. Sloan Foundation; and the President and Provost Offices at Arizona State University. Special thanks to Xiaohong Wang for her valuable contributions.

## REFERENCES

[1] F. Brauer and C. Castillo-Chavez, "Mathematical Models in Population Biology and Epidemiology," Texts in Applied Mathematics, 40, Springer-Verlag, New York, 2001.

[2] C. Castillo-Chavez and H. R. Thieme, *Asymptotically authonomous epidemic models, mathematical pulation dynamics: Analysis of heterogeneity* O. Orino, D. Axelrod, M. Kimmel, M. Langlais, Eds. **1** (1995), 33–50.

[3] C. Castillo-Chavez, H.W. Hethcote, V. Andreasen, S.A. Levin and W.M. Liu, *Epidemiological models with age structure, proportionate mixing, and cross-immunity* Journal of Mathematical Biology, Springer, **40** (1989), 233–258.

[4] C. Castillo-Chavez, C. Castillo-Garsow and A.A. Yakubu, *Mathematical models of isolation and quarantine* JAMA, American Medical Association, **290** (2003), 2876–2877.

[5] N.J. Cox and Subbarao, *Global epidemiology of influenza: Past and present* Annu. Rev. Med. **51** (2000), 407-421.

[6] P. Van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold en- demic equilibria for compartmental models of disease transmission* Mathematical Biosciences **180** (2002), 29-48.

[7] Z. Feng, "A Mathematical Model for the Dynamics of Childhood Diseases Under the Impact of Isolation," Ph.D thesis, Arizona State University, 1994.

[8] Z. Feng and H. Thieme, *Recurrent outbreaks of childhood diseases revisited: The impact of isolation*, Math. Biosc. and Eng. **129** (1995), 93–130.

[9] A. Flahault, X. De Lamballerie, T. Hanslik and N. SAlez, *Symptomatic infections less frequent with H1N1pdm than with seasonal strains*, URL http://knol.google.com/k/symptomatic-infections-less-frequent-with-h1n1pdm-than-with-seasonal-strains PLoS Curr Influenza **28** (2009).

[10] H. W. Hethcote, *The mathematic of infectious diseases*, SIAM review, **42**(2000), 599–653.

[11] H.W. Hethcote and S.A. Levin, *Periodicity in epidemiological models*, Levin, Hallman, gross (Eds), Springer-Verlag. Applied Mathematical Ecology. **18**(1989), 193–211.

[12] H. W. Hethcote, M. Zhien and L.Shengbing, *Effects of quarentine in six endemic models for infectious diseases*, John A. Jacquez memorial volume. Math. Biosci. **180** (2002), 141–160.

[13] W. O. Kermack and A.G. McKendrick, *Contributions to the mathematical theory of epidemics*, Proc. Royal Soc. London, **115**(1927), 700–721.

[14] W. O. Kermack and A.G. McKendrick, *Contributions to the mathematical theory of epidemics, part II*, Proc. Royal Soc. London, **138**(1932), 55–83.

[15] S. A. Levin , J. Dushoff and J. B. Plotkin, *Evolution and persistence of influenza A and other diseases*, Math. Biosc. and Eng. **188** (2004), 17–28.

[16] W. M. Liu, *Criterion of Hopf bifurcations without using eigenvalues*, Journal of Mathematical Analysis and Applications, (1994).

[17] E. Mustafa, "Epidemic in Structered Populations with Isolation and Cross-immunity," Ph.D thesis, Arizona State University, 2007.

[18] M. Nuno, "A Mathematical Model for the Dynamics of Influenza at the Population and Host Level," Ph.D thesis, Cornell University, 2005.

[19] L. Perko, "Differential Equations and Dynamical Systems," Springer, 2000.

[20] H. Thieme, "Mathematics in Population Biology," Princeton series in Theoritical and Computational Biology, Princeton University Press, Princeton, NJ, 2003.

[21] R. J. Webby, *Are we ready for pandemic influenza*, Science, **302** (2003), 1519-1522.

*E-mail address*: alvivasm@nmsu.edu

*E-mail address*: ccchavez@asu.edu

*E-mail address*: ebarany@nmsu.edu