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Analysis and Numerical Simulation of Two-strain influenza model considering Quarantine and Cross-immunity

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Abstract

The purpose of this paper is to understand how "the infectious disease model of two influenza virus strains" spreads through the analysis of differential equations and numerical simulations using Matlab. Therefore, we consider the cross-immunity between the two virus strains under different levels of competition and quarantine policy. We find the conditions of stability and existence for equilibrium points. Calculate the basic reproduction number $\Re_i$ of each virus strain respectively and define isolation reproduction number $\Re_q$ of the overall system. If $\Re_q < 1$, both virus strains will die out. Even if any $\Re_i < 1$, subthreshold coexistence can still occur. Finally, through Hopf bifurcation theorem and numerical simulations, we confirmed that the diseases will coexist with oscillation. From numerical results, we find that quarantine may destabilize the dynamics, strong (weak) equal cross-immunity leads to periodic behavior (equilibria), and the dynamics turn periodic as the difference of two cross-immunity exceeds a critical value.

Problem description

Historically, there are many times global influenza pandemics which caused more than one hundred million death. For example, 1918 Spanish flu pandemic (H1N1), 1968 Hong Kong flu pandemic (H3N2), 2009 swine flu pandemic (H1N1). From the cases of influenza in U.S. since 2008 (fig.1), the case become much fewer since covid-19 outbreak, and the epidemic peaks appear in winter, so the behavior of influenza transmission is periodic. The protection against some diseases gained from a former infection of other diseases is called the cross-immunity. For instance, it had been shown that H1N1 and H3N2 has cross-immunity. In [3], Jorge A. Alfaro-Murillo and Sherry Towers consider an influenza model with multiple strains and antigenic drift. Using time-dependent rate of disease transmission which is called seasonal forcing to simulate the seasonal behavior of influenza.

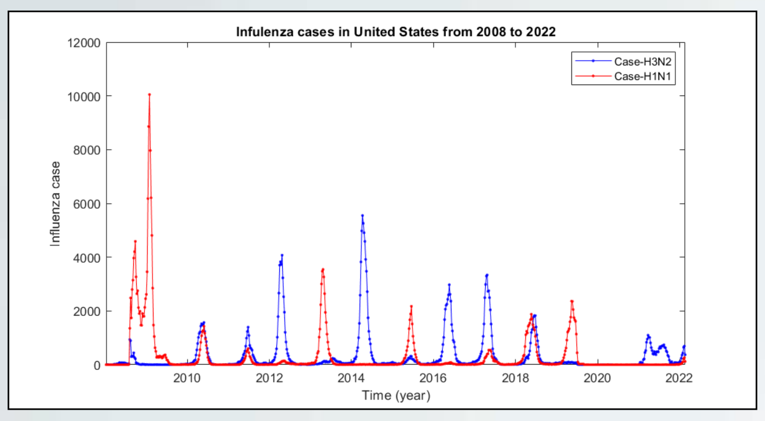

Figure 1. Inflenza case in U.S. form 2008 to 2022

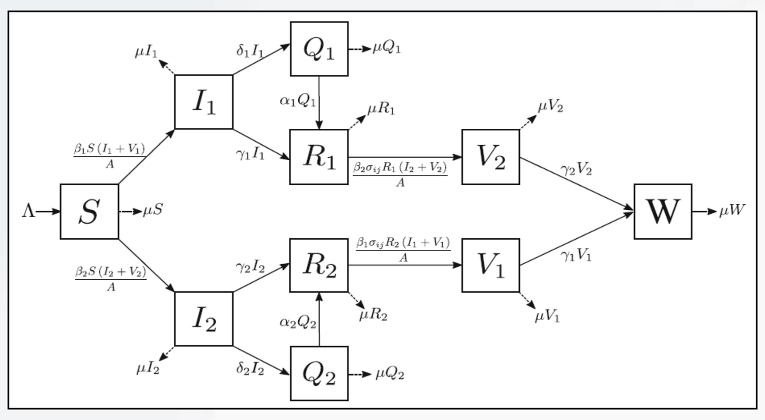

Figure 2. Flow chart of disease transmit

The cross-immunity is determined by the antigenic distance. They found that reduced magnitude of disease outbreaks in tropical regions than in temperate regions and the relationship of the size or time annual major peak of influenza and seasonal forcing. Since the behavior of influenza transmission is seasonality, [4] shows that a periodic solution exists when the transmission rate is periodic in a single-strain model.

In this study, we consider a disease model with quarantine and cross-immunity which is as same as [5]. It has four equilibrium points which are disease-free (E_0), strain 1 survives (E_1), strain 2 survives (E_2) and two strains coexist (E_3). Our problems are the following:

a) The existence condition of each equilibrium point.
b) The stability condition of each equilibrium point.
c) The condition of the behavior of disease transmission becomes periodic.
d) How the behavior changes if we adjust the parameters.

Notation

β_i is the transmission coefficient for strain i. Λ is the rate at which individuals are born into the population. μ is the nature mortality rate. α_i is the rate at which individuals leave quarantine. γ_i is the recovery rate from strain i. δ_i is the rate of quarantine. σ_{ij} is the cross-immunity against strain j following an infection with strain i. $(i, j = 1,2)$

$$
\begin{cases}
\dfrac{dS}{dt} = \Lambda - \sum_{i=1}^{2} \beta_i S \dfrac{(I_i + V_i)}{A} - \mu S \\
\dfrac{dI_i}{dt} = \beta_i S \dfrac{(I_i + V_i)}{A} - (\mu + \gamma_i + \delta_i) I_i \\
\dfrac{dQ_i}{dt} = \delta_i I_i - (\mu + \alpha_i) Q_i \\
\dfrac{dR_i}{dt} = \gamma_i I_i + \alpha_i Q_i - \beta_j \sigma_{ij} R_i \dfrac{(I_j + V_j)}{A} - \mu R_i \\
\dfrac{dV_i}{dt} = \beta_i \sigma_{ij} R_j \dfrac{(I_i + V_i)}{A} - (\mu + \gamma_i) V_i \\
\dfrac{dW}{dt} = \sum_{i=1}^{2} \gamma_i V_i - \mu W \\
A = S + W + \sum_{i=1}^{2} (I_i + V_i + R_i)
\end{cases}
$$

Figure 3. ODE model of disease transmit

Results and discussion

To analyze the stability of equilibrium points, we compute the Jacobian matrices and the eigenvalues. The following theorem summarizes the results for one equilibrium point E_1, and there are similar results for E_2.

Theorem Define

$$f(\Re_1) = \frac{1}{1 + \sigma(\Re_1 - 1)\left(1 + \frac{\delta_2}{\mu + \gamma_2}\right)\left(1 - \frac{\mu(\mu + \alpha_1)}{(\mu + \gamma_1)(\mu + \alpha_1) + \alpha_1 \delta_1}\right)}, \alpha_c(\mu) = \frac{\delta_1}{\Re_1^*}\left(1 - \frac{1}{\Re_1^*}\right) + O(\mu^{\frac{1}{2}})$$

then we have following properties:

(1) If $\Re_2 < f(\Re_1)$ and $\alpha_1 > \alpha_c(\mu)$, then E_1 is locally asymptotically stable.
(2) If $\Re_2 > f(\Re_1)$ and $\alpha_1 < \alpha_c(\mu)$, then E_1 is unstable.
(3) When $\Re_2 < f(\Re_1)$, according to *Hopf bifurcation theorem*, the periodic solutions of period is

$$T = \frac{2\pi}{|Im(\omega_{2,3})|} \approx \frac{2\pi}{\left((\gamma_1 + \delta_1)(\Re_1^* - 1)\right)^{1/2} \mu^{1/2}}$$

appears at $\alpha_1 = \alpha_c(\mu)$, where $\Re_i = \frac{\beta_i}{\mu + \gamma_i + \delta_i}, i = 1, 2$

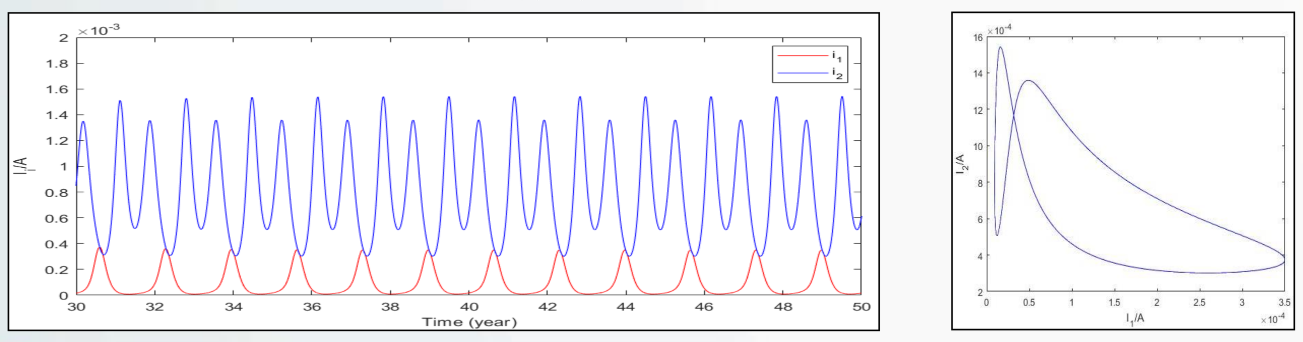

Figure 4. The periodic behavior of disease transmit and its phase-plane plot.

From the function $f(\Re_1)$ in the theorem, we can define function $g(\Re_2)$ in a similar way, and then we can plot a bifurcation diagram (figure 5). In figure 5, the first quadrant of $(\Re_1, \Re_2)$-plane is divided into four regions. In the region $\{(\Re_1, \Re_2)| 0 < \Re_1, \Re_2 < 1\}$, two strains both die out (E_0). In the region I (II), the strain 1(strain 2) survives ($E_1(E_2)$). In the region III, two strains would coexist. Then by using the bifurcation diagram and the reproduction numbers $\Re_1$ and $\Re_2$, we can predict the dynamics of two strains system

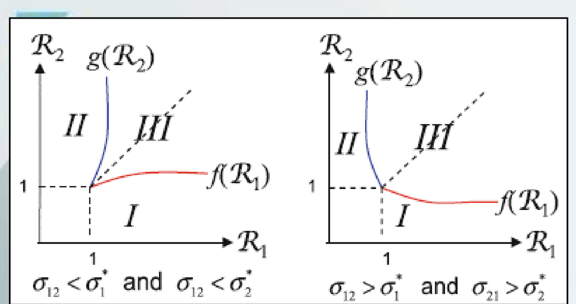

Figure 5. The regions of stability.

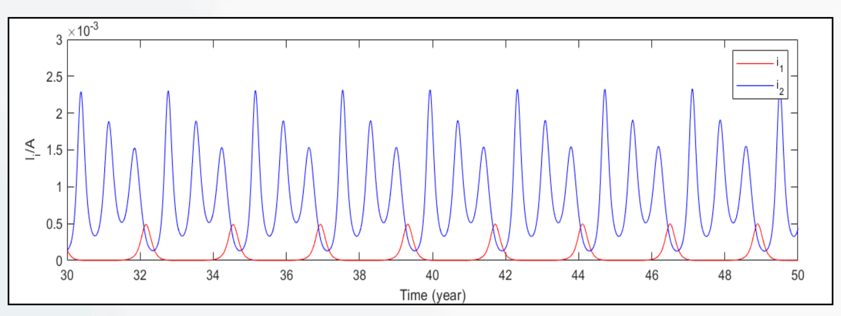

Figure 6. The subthreshold coexistence.

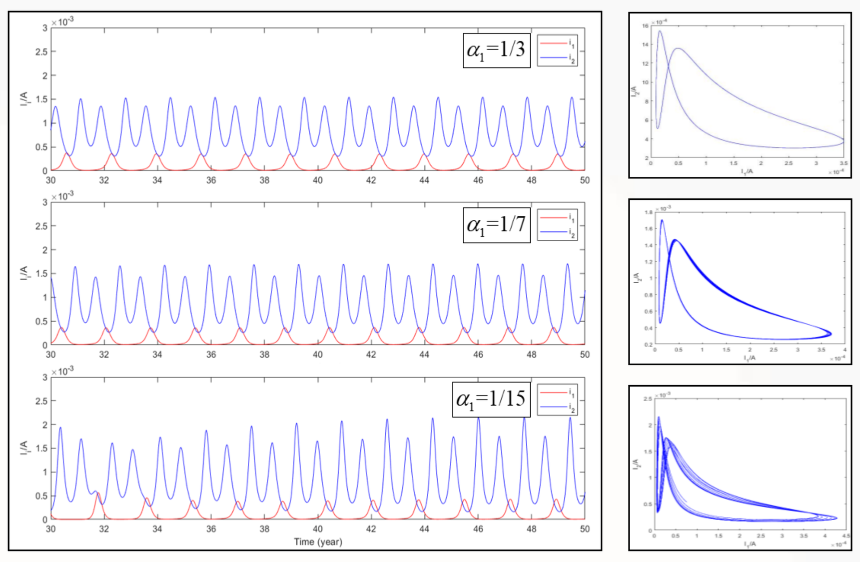

Figure 7. Adjusting the quarantine period (α)

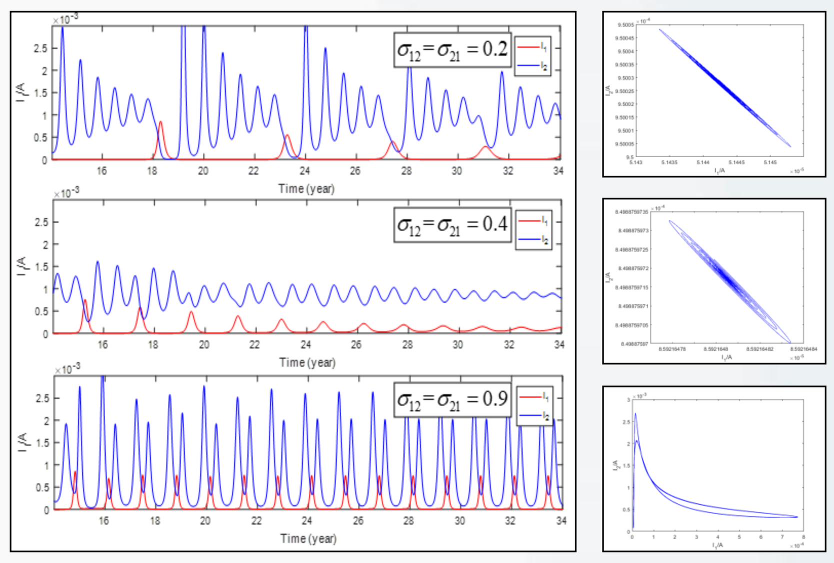

Figure 8. Adjusting the cross-immunity $(\sigma_1 = \sigma_2)$

From the numerical simulation (figure 4), we can find the behavior of disease transmission is periodic in some conditions, and this periodic behavior is the same as influenza transmission. Then we use the numerical simulation to observe how the dynamics change when adjusting parameters. The endemic peaks become higher as the infective rate increases. During the process of adjusting the infective rate, we find that the subthreshold coexistence (figure 6) occurs possibly when $\Re_1$ or $\Re_2$ is smaller than 1. Figure 7 shows that the epidemic peaks become higher and the periodic behavior becomes irregular when the length of the quarantine period increases. For the cross-immunity, we consider whether two cross-immunity are equal or not. First, in figure 8, the equal cross-immunity case shows that strong cross-immunity destabilizes the system and weak cross-immunity may lead the system to a stable equilibrium point. Second, in figure 9, if two cross-immunity is not equal, then the behavior of disease transmission changes from becoming a stable equilibrium point to a periodic oscillation when the difference of two cross-immunity is larger than some value. In other words, the dynamics turns periodic when $\sigma_{12} - \sigma_{21} > \varepsilon$, for some $\varepsilon \in \mathbb{R}^+$.

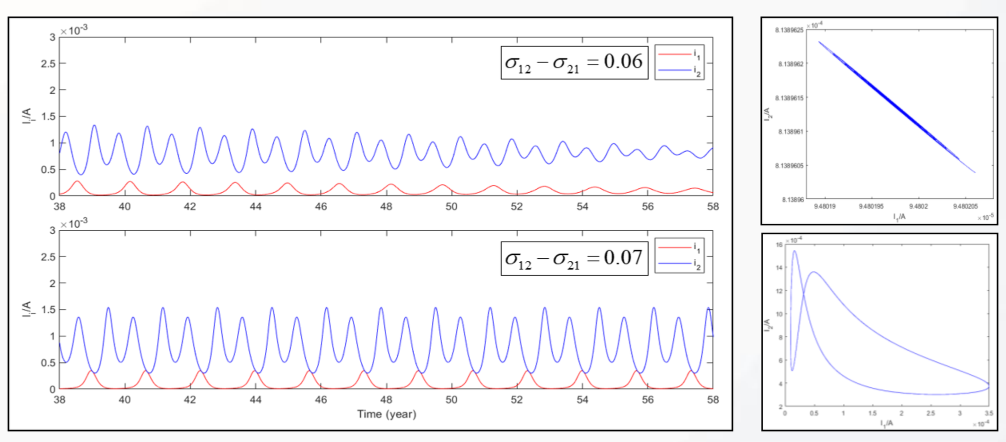

Figure 9. Adjusting the cross-immunity $(\sigma_1 \neq \sigma_2)$

Conclusions

By analyzing the Jacobian matrix, we find the condition of existence and stability for each equilibrium point. The oscillatory coexistence is established via Hopf bifurcation and confirmed by numerical simulations. When computing the coexistence equilibria, we find that subthreshold coexistence may occur even if $\Re_1 < 1$ or $\Re_2 < 1$. The quarantine policy seems effective, but the numerical result shows that this could destabilize flu dynamics and create uncertainty. In recent years, much fewer cases of influenza due to the pandemic of covid-19, the policies like wearing masks and quarantine which are equivalent to adding quarantine to system may accumulate susceptible class and potentially result in the future flu outbreak. When two diseases which have cross-immunity transmit in an area, they would compete with each other and it is helpful to control disease. For symmetric cross-immunity, then the stronger cross-immunity is, the more stable dynamic is. The sufficiently different cross-immunity means strong competition and makes dynamics seasonally periodic. For the future tasks, we would extend the model to many aspects of epidemiology modeling, such as seasonality in transmission rate, individual difference of infective rate, age-structure, and possibility of coinfection. Finally, we could research the influenza dynamics with this model since the periodic oscillation in numerical simulation is similar to the influenza cases.

References

[1] CDC, National, regional, and state level outpatient illness and viral surveillance, Cdc.gov, 2020. [Online]
[2] Hillaire, Marine LB, et al. "Cross-protective immunity against influenza pH1N1 2009 viruses induced by seasonal influenza A (H3N2) virus is mediated by virus-specific T-cells." Journal of General Virology 92.10 (2011)
[3] J. A. Alfare-Murillo, S. Towers, and Z. Feng, "A deterministic model for influenza infection with multiple strains and antigenic drift," Journal of Biological Dynamics, vol. 7, pp 191-211, Dec. 2013.
[4] J. L. Aron and I. B. Schwartz, "Seasonality and period-doubling bifurcations in an epidemic model," Journal of Theoretical Biology, vol. 110, pp. 665–679, Oct. 1984.
[5] M. Nu˜no, Z. Feng, M. Martcheva, and C. Castillo-Chavez, "Dynamics of two-strain influenza with isolation and partial cross-immunity," SIAM Journal on Applied Mathematics, vol. 65, pp. 964–982, Jan. 2005.
[6] F. Brauer, C. Castillo-Ch´avez, and Z. Feng, Mathematical models in epidemiology. Springer, 2019.