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Cross-immunity-induced backward bifurcation for a model of transmission dynamics of two strains of influenza

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ABSTRACT

A new deterministic model for the transmission dynamics of two strains of influenza is designed and used to qualitatively assess the role of cross-immunity on the transmission process. It is shown that incomplete cross-immunity could induce the phenomenon of backward bifurcation when the associated reproduction number is less than unity. The model undergoes competitive exclusion (where Strain i drives out Strain j to extinction whenever $\mathcal{R}_{0i} > 1 > \mathcal{R}_{0j}$; $i, j = 1, 2, i \neq j$). For the case where infection with one strain confers complete immunity against infection with the other strain, it is shown that the disease-free equilibrium of the model is globally-asymptotically stable whenever the reproduction number is less than unity. In the absence of cross-immunity, the model can have a continuum of co-existence endemic equilibria (which is shown to be globally-asymptotically stable for a special case). When infection with one strain confers incomplete immunity against the other, numerical simulations of the model show that the two strains co-exist, with Strain i dominating (but not driving out Strain j), whenever $\mathcal{R}_{0i} > \mathcal{R}_{0j} > 1$.

1. Introduction

One of the important problems in mathematical epidemiology is the study of the transmission dynamics of diseases with multiple strains in the presence of partial or complete immunity. Consequently, the mathematical modeling of diseases with multiple pathogen strains, such as dengue fever, HIV/AIDS, influenza, malaria and West Nile virus, has received considerable attention (see, for instance, [1–11] and some of the references therein). These studies have, in general, focused on the determination of threshold condition(s) for the co-existence of the strains, as well as the evaluation of the role of cross-immunity (defined as a scenario where infection with one strain confers partial or complete protection against infection with another strain) in the transmission dynamics of the disease strains.

In a multi-strain dynamics situation, infection by one or more of the strains may modify the sensitivity to infection by the other strains [4,7–9,12]. Some of the main questions of epidemiological interest, in the studies of modeling multi-strain dynamics, are:

(i) which strain(s) will dominate in the long run (i.e., does competitive exclusion phenomenon occurs)?
(ii) under what conditions will the strains co-exist?
(iii) what is the effect of cross-immunity (partial or complete) on the multi-strain dynamics?

These questions could be addressed using the threshold quantity known as the *basic reproduction number* of the disease [6,13,14], which represents the average number of secondary cases generated by a typical infected individual in a completely

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susceptible population. Earlier studies has estimated that the reproduction number of the 1918–1919 influenza pandemic and other seasonal strains of influenza ranged between 1.5 and 5.4 [4,9,15–20].

Using an SIQR deterministic model for the dynamics of two strains of influenza in the presence of isolation of symptomatic cases, Nuno et al. [7] showed that cross-immunity and host isolation could induce sustained periodic oscillations. Bremermann and Thieme [21] show the phenomenon of competitive exclusion (where the strain with the largest reproduction number persists and eliminates the remaining strains) in a simple model with multiple strains (similar results were obtained in [8,22–24]). Gumel [9] shows co-existence of two strains (avian and mutant) of influenza when their reproduction numbers exceed unity using a model for the transmission dynamics of avian and human influenza strains in the presence of isolation (the model in [9] does not undergo competitive exclusion).

The aim of this study is to rigorously assess the role of cross-immunity on the transmission dynamics of two strains of influenza in a population. To achieve this objective, a new deterministic model (which extends the model in [7]) will be designed.

The paper is organized as follows. The extended model is formulated in Section 2 and analyzed in Section 3.

2. Formulation of a mathematical model

The model is based on the transmission dynamics of two strains of influenza. The total population at time t, denoted by $N(t)$, is subdivided into susceptible ($S(t)$); exposed to strain i ($i = 1, 2$) (E_i); infectious with strain i (I_i); recovered from strain i (R_i); recovered from strain i and exposed to strain j ($i, j = 1, 2\, i \neq j$) (E_{ij}); recovered from strain i and infectious with strain j (I_{ij}); and individuals recovered from infection with both strains (M), so that

$$N(t) = S(t) + E_1(t) + I_1(t) + R_1(t) + E_2(t) + I_2(t) + R_2(t) + E_{12}(t) + I_{12}(t) + E_{21}(t) + I_{21}(t) + M(t).$$

The model to be considered is given by the following deterministic system of non-linear differential equations (where a dot represents differentiation with respect to t; and all associated parameters are non-negative for all $t \geq 0$):

$$\begin{aligned}
\dot{S} &= \Pi + \xi M - \frac{\beta_1 S(\eta_1 E_1 + I_1)}{N} - \frac{\beta_2 S(\eta_2 E_2 + I_2)}{N} - \frac{\beta_{12} S(\eta_{12} E_{12} + I_{12})}{N} - \frac{\beta_{21} S(\eta_{21} E_{21} + I_{21})}{N} - \mu S,\\
\dot{E_1} &= \frac{\beta_1(\eta_1 E_1 + I_1)}{N} S + \frac{\beta_{21}(\eta_{21} E_{21} + I_{21})}{N} S - \sigma_1 E_1 - \mu E_1,\\
\dot{I_1} &= \sigma_1 E_1 - \gamma_1 I_1 - \mu I_1 - \delta_1 I_1,\\
\dot{R_1} &= \gamma_1 I_1 - \theta_2 \frac{\beta_2 R_1(\eta_2 E_2 + I_2)}{N} - \theta_2 \frac{\beta_{12} R_1(\eta_{12} E_{12} + I_{12})}{N} - \mu R_1,\\
\dot{E_2} &= \frac{\beta_2(\eta_2 E_2 + I_2)}{N} S + \frac{\beta_{12}(\eta_{12} E_{12} + I_{12})}{N} S - \sigma_2 E_2 - \mu E_2,\\
\dot{I_2} &= \sigma_2 E_2 - \gamma_2 I_2 - \mu I_2 - \delta_2 I_2,\\
\dot{R}_2 &= \gamma_2 I_2 - \theta_1 \frac{\beta_1 R_2(\eta_1 E_1 + I_1)}{N} - \theta_1 \frac{\beta_{21} R_2(\eta_{21} E_{21} + I_{21})}{N} - \mu R_2,\\
\dot{E_{12}} &= \theta_2 \frac{\beta_2 R_1(\eta_2 E_2 + I_2)}{N} + \theta_2 \frac{\beta_{12} R_1(\eta_{12} E_{12} + I_{12})}{N} - \sigma_{12} E_{12} - \mu E_{12},\\
\dot{I_{12}} &= \sigma_{12} E_{12} - \gamma_{12} I_{12} - \mu I_{12} - \delta_{12} I_{12},\\
\dot{E_{21}} &= \theta_1 \frac{\beta_1 R_2(\eta_1 E_1 + I_1)}{N} + \theta_1 \frac{\beta_{21} R_2(\eta_{21} E_{21} + I_{21})}{N} - \sigma_{21} E_{21} - \mu E_{21},\\
\dot{I_{21}} &= \sigma_{21} E_{21} - \gamma_{21} I_{21} - \mu I_{21} - \delta_{21} I_{21},\\
\dot{M} &= \gamma_{12} I_{12} + \gamma_{21} I_{21} - \xi M - \mu M,
\end{aligned} \tag{1}$$

where Π is the recruitment rate into the community, ξ is the rate of loss of natural immunity by recovered individuals, β_i (where $i = 1, 2$ here and elsewhere below) is the infection rate with strain i, β_{ij} ($i, j = 1, 2$; $i \neq j$) represents the transmission rate for individuals who recovered from strain i but exposed to strain j and μ is the natural death rate. The modification parameters $\eta_i < 1$ accounts for the assumed reduction of exposed individuals (those in the E_i classes) in relation to infectious individuals (in the I_i classes); the parameters η_{ij} are similarly defined.

Furthermore, σ_i is the transition rate of individuals exposed with strain i (i.e., those in the E_i class) to the corresponding infectious (I_i) class (the parameters σ_{ij} are similarly defined). The parameters γ_i and δ_i represent, respectively, the recovery rates and disease-induced death rate of individuals infected with strain i (the parameters γ_{ij} and δ_{ij} are defined similarly). The modification parameters $0 \leq \theta_i \leq 1$ account for the assumed reduction of susceptibility to strain j of individuals who recovered from strain i (i.e., $0 \leq \theta_i \leq 1$) captures the cross-immunity of individuals who recovered from one strain against acquiring infection with the other. These parameters are described in Table 1, and a flow diagram of the model is depicted in Fig. 1.