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A Model for Host-Multipathogen Interaction

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Abstract. We present a mathematical model for disease dynamics that explores the relationship between ecology and immunology. The model includes various populations of hosts in the presence of two pathogens. Ecological factors include isolation and disease-induced mortality. Immunological factors are immunosuppression and cross-immunity. Via certain assumptions, we reduce the original mathematical model to a simpler model, and we analyze the stability of the extinction equilibrium. We use Matlab to calculate numerical solutions for both the reduced and the full models, paying particular attention to parameters that affect the stability of equilibria, such as the disease transmission rates. We verify the conditions for disease coexistence for the full model. Finally, we explore the behavior of the full model under the assumption that the disease transmission rates change with time, which could account for seasonal variability in transmission rates. We found that varying one disease transmission parameter with respect to time may be enough, at least in some cases, to produce similar dynamics obtained when both transmission rates depend on time.

Keywords: multi-pathogen, immunosuppression, cross-immunity, ecology, immunology

1 Introduction

Most models for host-pathogen interaction have, until recently, included only one pathogen and one host. Certain studies suggest the interaction between different pathogens, for instance, in the case of measles and whooping cough (see [2], pp. 49-51). Hence, researchers are becoming more concerned with models that include multiple pathogens and multiple hosts.

Host-multipathogen models depict the interaction between ecology and immunology. Ecological interactions are observed, for instance, when infection of a host by a particular pathogen results in either isolation (i.e., when a patient is sent home to rest or quarantined) or death, making it either more difficult or even impossible for a different pathogen to infect that host. Immunological interactions may result from either immunosuppression or cross-immunity. In the first case, a host that has been infected by a pathogen has reduced or no immune protection against a second pathogen. In the later case, an infected host has acquired either partial or full immunity against a different pathogen, as may happen when a host is exposed to different strains of a pathogen.

The host-multipathogen model presented here was originally introduced and discussed by Pejman Rohani, Helen J. et al (see [2]). In section 2, we present the model assumptions, parameters, and equations. In section 3, we analyze a reduced version of the model, obtained by assuming that there is no disease-induced mortality and no immune-mediated interaction. In section 4, we analyze the full model, mostly through numerical solutions, and verify the conditions for disease coexistence stated in [2]. In addition, we expand on this analysis by exploring the influence of seasonal variability of the disease transmission parameters in the model dynamics (see [2], p.65, where disease transmission rates are assumed to be higher during school terms and lower at other times of the year).

2 The Model

2.1 Assumptions

The model considers infection by two different pathogens and is based on the following assumptions (summarized from [2], pp. 53-54).

- All newborns are susceptible to both infections.
- Once an individual becomes infected by a pathogen, the individual leaves the susceptible population and enters the exposed population for that pathogen. The exposed individual does not show any symptoms and is not infectious yet, but has entered a latent period of infection. During this period, the individual may contract the second ("competing") disease.
- At the end of the latency period, the individual becomes infectious (can transmit the disease to others), though asymptomatic, and may still become infected with the second pathogen.
- Once symptoms appear, the infected individual enters the convalescent population for the disease. During convalescence, the individual may be in a period of isolation and either temporary cross-immunity or temporary immunosuppression. In either case, there is a probability of contracting the second disease. In addition, the convalescing individual may eventually die or may recover from the disease.
- An individual that has recovered from infection by a particular pathogen is assumed to be immune to that pathogen but may still be susceptible to the second pathogen, if not previously exposed to it.

2.2 Populations

The following are the variables used in the model. The subscript $i = 1, 2$ is used to distinguish between the two diseases (see [2], p.64).

- S_0 = individuals susceptible to both diseases
- E_i = individuals exposed to disease i only
- I_i = infectious individuals with disease i only
- C_i = convalescing individuals with disease i only

- S_i = individuals who have recovered from disease i only
- S_{12} = individuals who are no longer susceptible to either infection; they have been exposed in some way to both infections
- ε_i = individuals exposed to disease i
- $\frac{\lambda_i}{\beta_i}$ = infectious individuals with disease i

Note that the last two types of populations overlap with the previous ones, as they may include individuals who have been infected by both pathogens. We also have

- $N = S_0 + S_{12} + \sum_{i=1}^{2}(E_i + I_i + C_i + S_i)$ = total population

2.3 Parameters

The parameters that appear in the model are the following (as before, $i = 1, 2$; see [2], p.64):

- v = host per capita birth rate (0-1 1/year)
- μ = host per capita death rate (0-1 1/year)
- β_i = transmission rate of disease i (typically 100-2,000 1/year)
- $1/\sigma_i$ = latency period of disease i (typically 1/52-2/52 years)
- $1/\gamma_i$ = infectious period of disease i (typically 1/52-3/52 years)
- $1/\delta_i$ = isolation period of disease i (typically 1/52-4/52 years)
- ρ_i = probability of infection-induced mortality for disease i (0-1)
- ϕ_i = coinfection probability of disease i, after contracting disease $j \neq i$ (0-1)
- ξ_i = temporary immunosuppression or cross-immunity for disease i, after contracting disease $j \neq i$ (≥ 0)
- χ_i = permanent immunosuppression or cross-immunity for disease i, after contracting disease $j \neq i$ (≥ 0)
- ψ_i = differential infection-induced mortality for disease i (0-1)

2.4 Equations

The host-multipathogen model is a system of 14 ordinary differential equations defined as follows (see [2], p.63):

$$\frac{dS_0}{dt} = \upsilon N - (\lambda_1 + \lambda_2)\frac{S_0}{N} - \mu S_0 \tag{1}$$

$$\frac{dE_1}{dt} = \lambda_1 \frac{S_0}{N} - \phi_2 \lambda_2 \frac{E_1}{N} - (\sigma_1 + \mu)E_1 \tag{2}$$

$$\frac{dE_2}{dt} = \lambda_2 \frac{S_0}{N} - \phi_1 \lambda_1 \frac{E_2}{N} - (\sigma_2 + \mu)E_2 \tag{3}$$

$$\frac{dI_1}{dt} = \sigma_1 E_1 - \phi_2 \lambda_2 \frac{I_1}{N} - (\gamma_1 + \mu)I_1 \tag{4}$$

$$\frac{dI_2}{dt} = \sigma_2 E_2 - \phi_1 \lambda_1 \frac{I_2}{N} - (\gamma_2 + \mu)I_2 \tag{5}$$

$$\frac{dC_1}{dt} = \gamma_1 I_1 - \xi_2 \phi_2 \lambda_2 \frac{C_1}{N} - (\delta_1 + \mu)C_1 \tag{6}$$

$$\frac{dC_2}{dt} = \gamma_2 I_2 - \xi_1 \phi_1 \lambda_1 \frac{C_2}{N} - (\delta_2 + \mu)C_2 \tag{7}$$

$$\frac{dS_1}{dt} = (1 - \rho_1)\delta_1 C_1 - \chi_2 \lambda_2 \frac{S_1}{N} - \mu S_1 \tag{8}$$

$$\frac{dS_2}{dt} = (1 - \rho_2)\delta_2 C_2 - \chi_1 \lambda_1 \frac{S_2}{N} - \mu S_2 \tag{9}$$

$$\frac{dS_{12}}{dt} = (1-\rho_1)(1-\rho_2)\left(\lambda_2 \frac{\phi_2 E_1 + \phi_2 I_1 + \xi_2 \phi_2 C_1}{N} + \lambda_1 \frac{\phi_1 E_2 + \phi_1 I_2 + \xi_1 \phi_1 C_2}{N}\right)$$
$$+(1 - \psi_2 \rho_2)\chi_2 \lambda_2 \frac{S_1}{N} + (1 - \psi_1 \rho_1)\chi_1 \lambda_1 \frac{S_2}{N} - \mu S_{12} \tag{10}$$

$$\frac{d\varepsilon_1}{dt} = \lambda_1 \frac{S_0}{N} + \phi_1 \lambda_1 \frac{E_2}{N} + \phi_1 \lambda_1 \frac{I_2}{N} + \xi_1 \phi_1 \lambda_1 \frac{C_2}{N} + \chi_1 \lambda_1 \frac{S_2}{N} - (\sigma_1 + \mu)\varepsilon_1 \tag{11}$$

$$\frac{d\varepsilon_2}{dt} = \lambda_2 \frac{S_0}{N} + \phi_2 \lambda_2 \frac{E_1}{N} + \phi_2 \lambda_2 \frac{I_1}{N} + \xi_2 \phi_2 \lambda_2 \frac{C_1}{N} + \chi_2 \lambda_2 \frac{S_1}{N} - (\sigma_2 + \mu)\varepsilon_2 \tag{12}$$

$$\frac{d\lambda_1}{dt} = \beta_1 \sigma_1 \varepsilon_1 - (\gamma_1 + \mu)\lambda_1 \tag{13}$$

$$\frac{d\lambda_2}{dt} = \beta_2 \sigma_2 \varepsilon_2 - (\gamma_2 + \mu)\lambda_2 \tag{14}$$

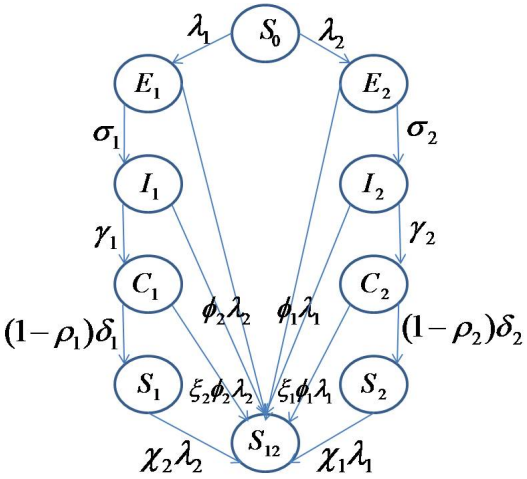

Figure 1: Flow Diagram for the Host-Multipathogen Model

We summarize the flow along the non-overlapping populations of the model in Figure 1. We include the parameters associated with each transition. Notice that an individual follows a vertical path of populations, on either the left side or right side of the diagram, while he or she is only infected with one pathogen. The moment an individual becomes exposed to both infections, even if they have recovered from the first infection, he or she transitions into the S_{12} population. Individuals in the S_{12} population may have recovered from both diseases, or may still be exposed or infectious with one or both diseases (see [2], p. 64). Thus, S_{12} individuals may be included in the ε_1, ε_2, λ_1, or λ_2 populations, continuing to play a role in disease transmission.

In addition to the flow depicted in Figure 1, newborn individuals enter the susceptible population S_0 only, and anyone may die from either natural death or from infection-induced death.

3 The Reduced Model

If we let $Z_i = E_i + I_i + C_i + S_i + S_0$ $(i = 1, 2)$, and assume that there is no disease-induced mortality ($\rho_1 = \rho_2 = 0$), no immunosuppression/cross-immunity ($\xi_i = \chi_i = 1, i = 1, 2$), and that the probability of coinfection is 1 ($\phi_i = 1, i = 1, 2$), we can reduce the original host-multipathogen model to obtain the following model (see [2], pp. 64-65).

3.1 Equations

$$\frac{dS_0}{dt} = \upsilon N - (\lambda_1 + \lambda_2)\frac{S_0}{N} - \mu S_0 \tag{15}$$

$$\frac{dZ_1}{dt} = \upsilon N - \lambda_2 \frac{Z_1}{N} - \mu Z_1 \tag{16}$$

$$\frac{dZ_2}{dt} = \upsilon N - \lambda_1 \frac{Z_2}{N} - \mu Z_2 \tag{17}$$

$$\frac{dS_{12}}{dt} = \lambda_2 \frac{Z_1 - S_0}{N} + \lambda_1 \frac{Z_2 - S_0}{N} - \mu S_{12} \tag{18}$$

$$\frac{d\varepsilon_1}{dt} = \lambda_1 \frac{Z_2}{N} - (\sigma_1 + \mu)\varepsilon_1 \tag{19}$$

$$\frac{d\varepsilon_2}{dt} = \lambda_2 \frac{Z_1}{N} - (\sigma_2 + \mu)\varepsilon_2 \tag{20}$$

$$\frac{d\lambda_1}{dt} = \beta_1 \sigma_1 \varepsilon_1 - (\gamma_1 + \mu)\lambda_1 \tag{21}$$

$$\frac{d\lambda_2}{dt} = \beta_2 \sigma_2 \varepsilon_2 - (\gamma_2 + \mu)\lambda_2 \tag{22}$$

3.2 Analysis

We perform a brief analysis of the reduced system of equations by seeking an equilibrium of the form $N = S_0$, that is, a disease-free equilibrium. First, we notice that $N = Z_1 + Z_2 - S_0 + S_{12}$. If we require also that $Z_1 = Z_2 = N = S_0$, then $N = S_0 + S_{12} \Rightarrow S_{12} = 0$. Solving for the equilibria of this system we obtain

from equation 15: $0 = (\upsilon - \mu)S_0 - (\lambda_1 + \lambda_2) \Rightarrow S_0 = \frac{\lambda_1 + \lambda_2}{\upsilon - \mu}$,

from equation 16: $0 = (\upsilon - \mu)S_0 - \lambda_2 \Rightarrow \lambda_2 = (\upsilon - \mu)S_0 = \lambda_1 + \lambda_2 \Rightarrow \boldsymbol{\lambda_1 = 0} \Rightarrow S_0 = \frac{\lambda_2}{\upsilon - \mu}$,

from equation 17: $0 = (\upsilon - \mu)S_0 - \lambda_1 \Rightarrow \lambda_1 = (\upsilon - \mu)S_0 \Rightarrow \boldsymbol{\lambda_2 = 0} \Rightarrow \mathbf{S_0 = 0}$.

From the last four equations, we see that the above results imply that $\varepsilon_1 = \varepsilon_2 = 0$. Hence, the equilibrium obtained is the trivial (extinction) equilibrium.

With the above assumptions, we have two decoupled systems: $(Z_1, \varepsilon_2, \lambda_2)$ and $(Z_2, \varepsilon_1, \lambda_1)$. Let us look at $(Z_1, \varepsilon_2, \lambda_2)$. The equations can be written as

$$\frac{dZ_1}{dt} = (\upsilon - \mu)Z_1 - \lambda_2 \tag{23}$$

$$\frac{d\varepsilon_2}{dt} = \lambda_2 - (\sigma_2 + \mu)\varepsilon_2 \tag{24}$$

$$\frac{d\lambda_2}{dt} = \beta_2 \sigma_2 \varepsilon_2 - (\gamma_2 + \mu)\lambda_2 \tag{25}$$

The Jacobian matrix for this system is

$$\begin{pmatrix} \upsilon - \mu & 0 & -1 \\ 0 & -(\sigma_2 + \mu) & 1 \\ 0 & \beta_2 \sigma_2 & -(\gamma_2 + \mu) \end{pmatrix},$$

which has eigenvalues

$$\eta_1 = \upsilon - \mu,$$
$$\eta_2 = \tfrac{1}{2}(-2\mu - \gamma_2 - \sigma_2 - \sqrt{(\gamma_2 - \sigma_2)^2 + 4\beta_2\sigma_2}),$$
$$\eta_3 = \tfrac{1}{2}(-2\mu - \gamma_2 - \sigma_2 + \sqrt{(\gamma_2 - \sigma_2)^2 + 4\beta_2\sigma_2}).$$

The (hyperbolic) equilibrium is stable if all eigenvalues of the Jacobian matrix are negative (see [3], Chapter 1 and sections 2.6-2.8). That is, the equilibrium is stable if $\upsilon - \mu < 0$ and

$$\begin{aligned}
&-2\mu - \gamma_2 - \sigma_2 + \sqrt{(\gamma_2 - \sigma_2)^2 + 4\beta_2\sigma_2} < 0 \\
\Leftrightarrow\ &\sqrt{(\gamma_2 - \sigma_2)^2 + 4\beta_2\sigma_2} < 2\mu + \gamma_2 + \sigma_2 \\
\Leftrightarrow\ &(\gamma_2 - \sigma_2)^2 + 4\beta_2\sigma_2 < (2\mu + \gamma_2 + \sigma_2)^2 \\
\Leftrightarrow\ &\gamma_2^2 - 2\gamma_2\sigma_2 + \sigma_2^2 + 4\beta_2\sigma_2 < 4\mu^2 + 4\mu\gamma_2 + 4\mu\sigma_2 + \gamma_2^2 + 2\gamma_2\sigma_2 + \sigma_2^2 \\
\Leftrightarrow\ &4\beta_2\sigma_2 < 4\gamma_2\sigma_2 + 4\mu^2 + 4\mu\gamma_2 + 4\mu\sigma_2 \\
\Leftrightarrow\ &\tfrac{\beta_2\sigma_2}{\gamma_2\sigma_2 + \mu^2 + \mu\gamma_2 + \mu\sigma_2} < 1 \\
\Leftrightarrow\ &R_0^2 = \tfrac{\beta_2\sigma_2}{(\mu+\sigma_2)(\mu+\gamma_2)} < 1.
\end{aligned}$$

The quantity R_0^i is defined to be the basic reproductive ratio for disease i (see [2], p.54). R_0^i can be interpreted as the average number of secondary infections produced by introducing a single infected individual with disease i into a population of susceptibles (see [1], p. 247).

3.3 Numerical Solutions

We use Matlab's ode23 function to calculate numerical solutions to the reduced model. The goal is to verify the conditions for stability of the trivial equilibrium and explore the different possible behaviors of the model according to the value of R_0^2. Initial values used are $Z_1(0) = 50,000, \varepsilon_2(0) = 10, \lambda_2(0) = 0$.

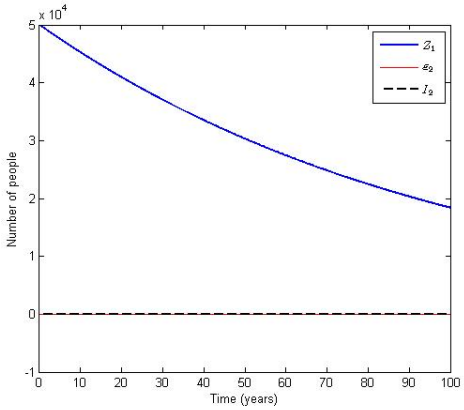

Figure 2: $\upsilon = 0.01, \mu = 0.02, \sigma_2 = 45.625, \gamma_2 = 95, \beta_2 = 70; R_0^2 = 0.7364$

Figure 2 shows an example were the trivial equilibrium is stable. Notice that $R_0^2 < 1$ and $\upsilon - \mu < 0$. Susceptible, exposed, and infectious individuals decrease to zero as time increases.

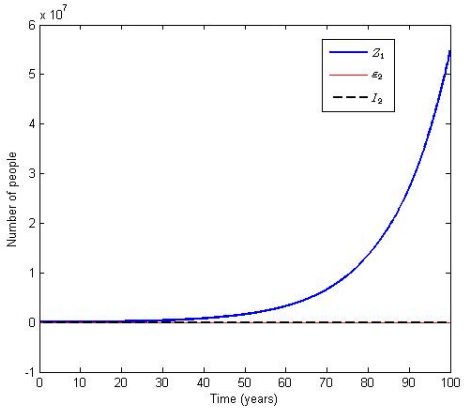

Figure 3: $\upsilon = 0.09, \mu = 0.02, \sigma_2 = 45.625, \gamma_2 = 95, \beta_2 = 70, R_0^2 = 0.7364$

In Figure 3 we see an example where the trivial equilibrium is unstable. Susceptible individuals increase with time, while the exposed and infectious populations go to zero. In this case $R_0^2 < 1$ but $\upsilon - \mu > 0$.

In Figures 4 and 5 the value of $R_0^2 > 1$, and hence the populations of exposed and infectious individuals increase.

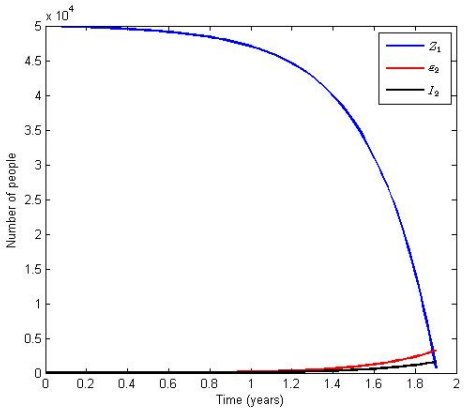

Figure 4: $\upsilon = 0.01, \mu = 0.02, \sigma_2 = 45.625, \gamma_2 = 90, \beta_2 = 100, R_0^2 = 1.1104$

In Figure 5 we see that the population of susceptible individuals increases for a while and then begins to decrease towards zero. The results observed here suggest that the increase in the population of susceptible individuals will occur, at least for some time, whenever $\upsilon - \mu > 0$.

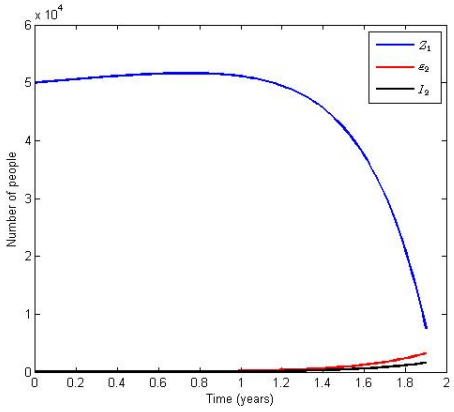

Figure 5: $\upsilon = 0.09, \mu = 0.02, \sigma_2 = 45.625, \gamma_2 = 90, \beta_2 = 100, R_0^2 = 1.1104$

4 The Full Model

4.1 Stability

According to Pejman Rohani, Helen J. et al ([2], p. 54), the disease coexistence state requires $R_0^i > 1$ and $R_0^j > \frac{R_0^i}{1+a_i(R_0^i-1)}$, where

$$a_i = \frac{1}{\sigma_i+\mu}\{\phi\mu + \frac{\sigma_i}{\gamma_i+\mu}(\phi\mu + \frac{\gamma_i}{\delta_i+\mu}(\xi\phi\mu + \chi(1-\rho_i)\delta_i))\}$$

and $R_0^i = \frac{\beta_i\sigma_i}{(\mu+\sigma_i)(\mu+\gamma_i)}, i, j = 1, 2, j \neq i.$

4.2 Numerical Solutions

The following parameter values, based on values provided by Pejman Rohani, Helen J. et al [2] in the study of measles ($i = 1$) and whooping cough ($i = 2$), were used for the calculation of numerical solutions: $\mu = 0.02, \sigma_1 = \sigma_2 = 45.625, \delta_1 = 365/7, \delta_2 = 365/14, \gamma_1 = 73, \gamma_2 = 365/14, \beta_1 = 1250, \beta_2 = 446$. In addition, the last two parameters were varied in order to explore bifurcations, that is, the change in stability of the disease coexistence state. Other parameter values used are provided with each of the following figures. Initial values used were $S_0(0) = 50,000, E_i(0) = 10, I_i(0) = C_i(0) = S_i(0) = S_{12}(0) = 0, \varepsilon_i(0) = \lambda_i(0) = 0.2, i = 1, 2.$

In Figure 6, we see that the populations for both diseases increase with time, which is consistent with the fact that the conditions for disesase coexistence are satisfied. Also, if we look closer at the behavior of the populations (for instance, the exposed individuals), we notice that the infections run mostly out-of-phase.

Figure 7 depicts a similar situation, except that the coinfection parameters were set to 1. The graph suggests that both diseases will run more in-phase with each other for larger coinfection probabilities.

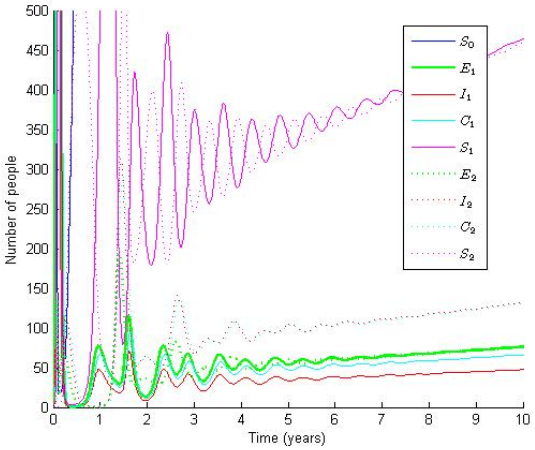

Figure 6: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, R_0^1 = 17.1111, R_0^2 = 17.0862, \frac{R_0^2}{1+a_2(R_0^2-1)} = 0.2479, \frac{R_0^1}{1+a_1(R_0^1-1)} = 0.2477.$

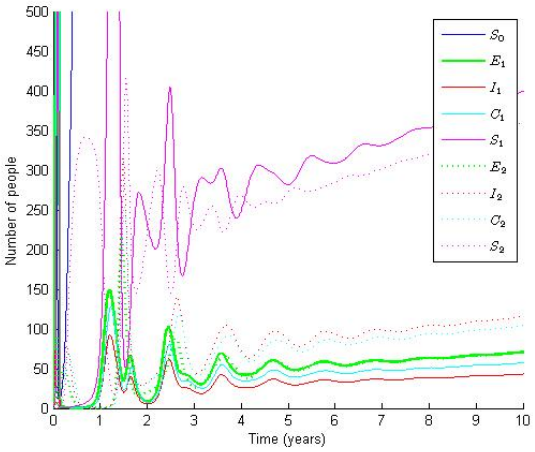

Figure 7: $\upsilon = 0.09, \phi_i = 1, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, R_0^1 = 17.1111, R_0^2 = 17.0862, \frac{R_0^2}{1+a_2(R_0^2-1)} = 0.2478, \frac{R_0^1}{1+a_1(R_0^1-1)} = 0.2476.$

Figure 8 suggests that having at least one low probability of coinfection brings back the out-of-phase behavior for the infections. This result seems to imply that the real life coinfection probabilities for measles and/or whooping cough are low, since these two diseases tend to run out-of-phase (see [2], pp. 51-52).

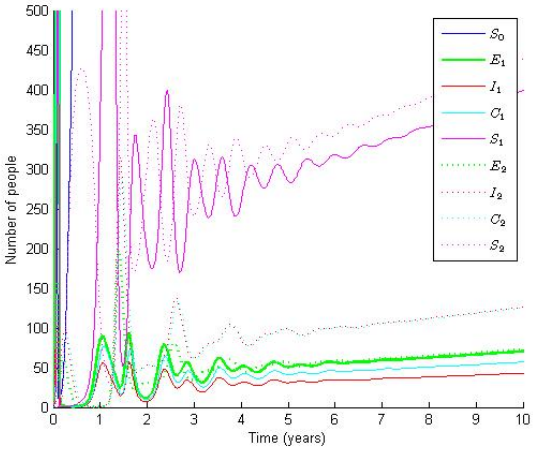

Figure 8: $\upsilon = 0.09, \phi_1 = 0.06, \phi_2 = 1, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, R_0^1 = 17.1111, R_0^2 = 17.0862, \frac{R_0^2}{1+a_2(R_0^2-1)} = 0.2478, \frac{R_0^1}{1+a_1(R_0^1-1)} = 0.2477.$

In Figure 9 we see a case where there is strong permanent croos-immunity for the two infections. The figure depicts an interesting situation, where, during the first few years, one of the diseases is clearly dominant over the competing disease for certain periods of time. The out-of-phase behavior is quite pronounced as well.

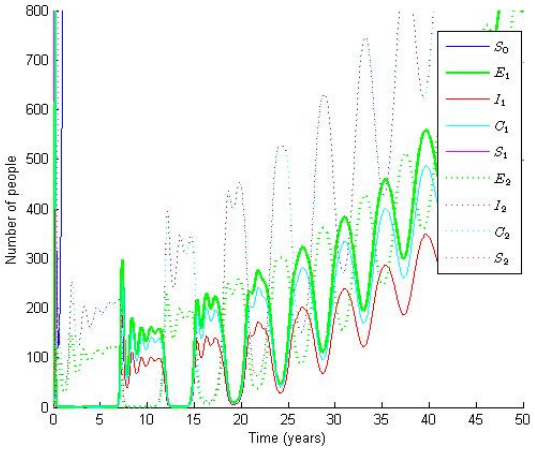

Figure 9: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, R_0^1 = 17.1111, R_0^2 = 17.0862, \frac{R_0^2}{1+a_2(R_0^2-1)} = 6.9810, \frac{R_0^1}{1+a_1(R_0^1-1)} = 6.9846.$

The next figures represent cases where the disease coexistence conditions are not satisfied. In Figure 10 we see a case where the disease transmission rates are low. The values of R_0^i are both greater than 1, and $R_0^2 > \frac{R_0^1}{1+a_1(R_0^1-1)}$, but $R_0^1 < \frac{R_0^2}{1+a_2(R_0^2-1)}$.

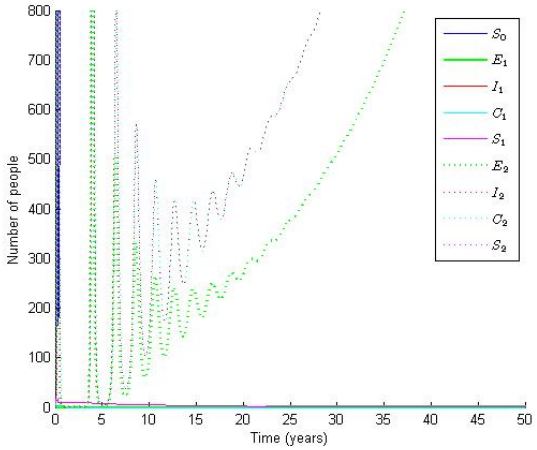

Figure 10: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, \beta_1 = 100, \beta_2 = 200, R_0^1 = 1.3689, R_0^2 = 7.6620, \frac{R_0^2}{1+a_2(R_0^2-1)} = 4.7903, \frac{R_0^1}{1+a_1(R_0^1-1)} = 1.3249.$

For Figure 11, the values of R_0^i are still both greater than 1, $R_0^1 > \frac{R_0^2}{1+a_2(R_0^2-1)}$, but $R_0^2 < \frac{R_0^1}{1+a_1(R_0^1-1)}$. We notice in the last two cases that the population of infected individuals that remains seems to be determined by the value of R_0^j that is greater than $\frac{R_0^i}{1+a_i(R_0^i-1)}, j \neq i$.

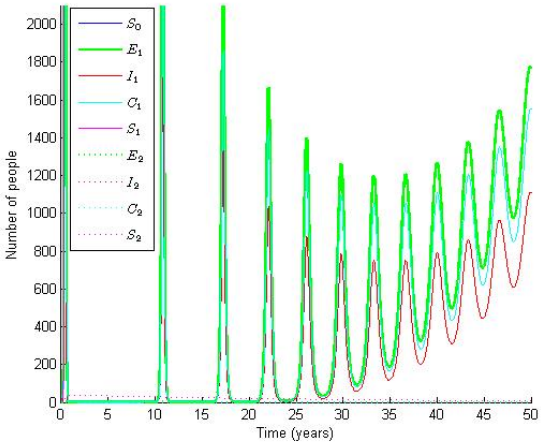

Figure 11: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, \beta_1 = 180, \beta_2 = 50, R_0^1 = 2.4640, R_0^2 = 1.9155, \frac{R_0^2}{1+a_2(R_0^2-1)} = 1.7697, \frac{R_0^1}{1+a_1(R_0^1-1)} = 2.1772.$

For the case in Figure 12, the disease transmission rates were set very low. Here $R_0^2 > 1$, but $R_0^1 < 1$.

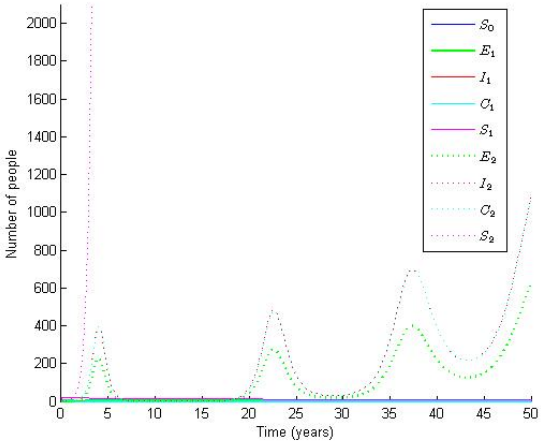

Figure 12: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, \beta_i = 30, R_0^1 = 0.4107, R_0^2 = 1.1493, \frac{R_0^2}{1+a_2(R_0^2-1)} = 1.1341, \frac{R_0^1}{1+a_1(R_0^1-1)} = 0.4337.$

The case depicted by Figure 13 is very similar to that of Figure 12, except that now $R_0^2 < 1$, and $R_0^1 > 1$. These last two cases suggest that the value of R_0^i that is greater than one will determine which of the two diseases will remain.

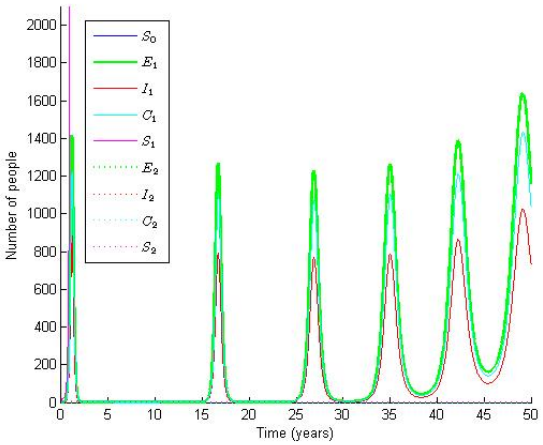

Figure 13: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, \beta_1 = 100, \beta_2 = 30, R_0^1 = 1.3689, R_0^2 = 0.7662, \frac{R_0^2}{1+a_2(R_0^2-1)} = 0.7827, \frac{R_0^1}{1+a_1(R_0^1-1)} = 1.3249.$

Figure 14 shows a disease-free state, where the populations of all exposed, infectious, and convalescent individuals decrease to zero. Here we have $R_0^1 < 1$ and $R_0^2 < 1$. This case helps verify that when the basic reproductive number for a disease is less than one, the number of individuals infected with that disease will decrease to zero.

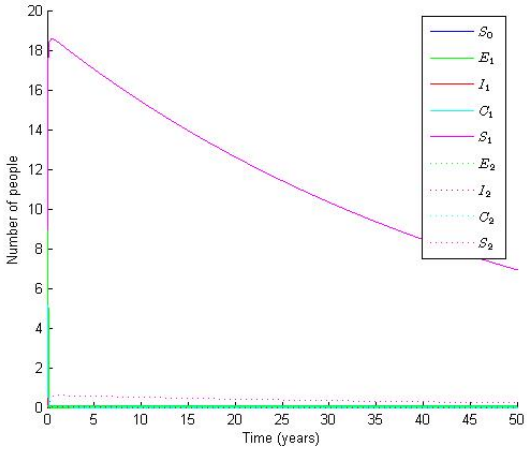

Figure 14: $\upsilon = 0.09, \phi_i = 0.06, \xi_i = 2, \rho_i = 0.1, \chi_i = 0.1, \psi_i = 0.2, \beta_1 = 60, \beta_2 = 20, R_0^1 = 0.8213, R_0^2 = 0.7662, \frac{R_0^2}{1+a_2(R_0^2-1)} = 0.7827, \frac{R_0^1}{1+a_1(R_0^1-1)} = 0.8348.$

Next, we experiment with the disease transmission rate parameters β_i by making them vary with time, in order to simulate seasonality effects in disease transmission. First, we let $\beta_1 = 1250 + 1000\sin(2\pi t)$ and keep $\beta_2 = 446$. All of the other parameter values were taken the same as in the case shown in Figure 6. In that case, both diseases coexisted, but the infectious populations were both increasing. In this case, the infections run markedly out-of-phase and with sharp spikes in the numbers of infectious individuals. In time, both populations are increasing on average, but the diseases alternate between each other. The first half of the year belongs to disease 1, and the second half belongs to disease 2.

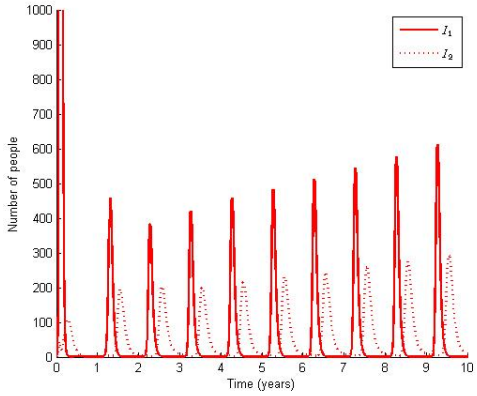

Figure 15: $\upsilon = 0.09, \phi_i = 1, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, \beta_1 = 1250 + 1000\sin(2\pi t), \beta_2 = 446.$

Now, we let $\beta_1 = 1250$ and $\beta_2 = 446 + 400\sin(2\pi t)$, and keep all other parameters the same as in the previous case. We observe on Figure 16 that the populations still increase and decrease sharply each year, with now disease 2 dominating most of the year, but with both diseases running almost identically for roughly the second half of the year. Contrary to the previous case, the diseases do not run separately, but towards the middle of each year they both have high numbers of infectious individuals.

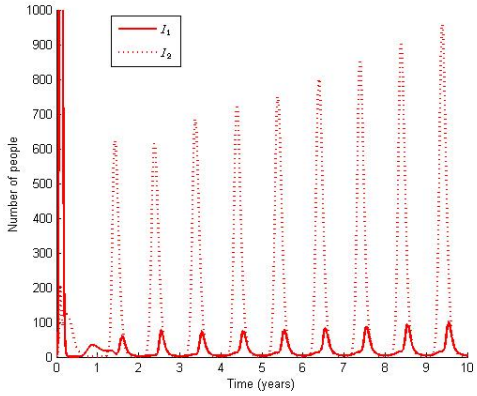

Figure 16: $\upsilon = 0.09, \phi_i = 1, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, \beta_1 = 1250, \beta_2 = 446 + 400\sin(2\pi t)$.

Lastly, we let $\beta_1 = 1250 + 1000\sin(2\pi t)$ and $\beta_2 = 446 + 400\sin(2\pi t)$, so the transmission rates for both diseases are now affected by seasonality, and we keep all other parameters the same as before. We observe that Figure 17 is extremely similar to Figure 15, indicating that, at least in some situations, it may be enough to have only one of the transmission rates be affected by seasonal effects in order to produce similar results to those obtained when both transmission rates depend on seasonal effects.

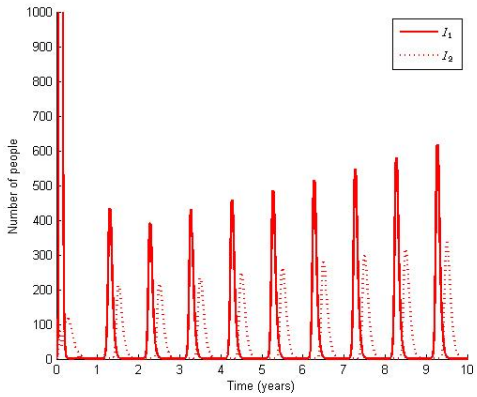

Figure 17: $\upsilon = 0.09, \phi_i = 1, \xi_i = 2, \rho_i = 0.1, \chi_i = 4.7, \psi_i = 0.2, \beta_1 = 1250 + 1000\sin(2\pi t), \beta_2 = 446 + 400\sin(2\pi t)$.

5 Summary

We have considered and performed analysis on a model for host-multipathogen interactions that takes into account two competing pathogens and populations of susceptibles, exposed, infectious, convalescing, and recovered individuals for each disease.

The model can be reduced by removing all ecological and immune interactions between the two pathogens. We analyzed the trivial (extinction) equilibrium for the reduced model. The conditions for stability of the trivial equilibrium were determined and corroborated through numerical solutions. We verified that the condition on the basic reproductive number for the reduced model agrees with the corresponding condition for the full model.

Analysis of the full model was performed via numerical solutions. We verified the conditions for disease coexistence stated in [2] and varied parameters such as the coinfection probabilities, the immunosuppression/cross-immunity, and disease transmission rates, among others that affect the stability of the disease coexistence state.

Among the main findings, we have that lower coinfection probabilities will produce more out-of-phase behavior between the two diseases (see Figures 6, 7, and 8). In other words, once the first disease has established itself in the population, there will be very little chance, at least for some time, for the second disease to spread. Since measles and whooping cough run mostly out-of-phase from each other, we believe that the coinfection probabilities for at least one of these two diseases is low. Similar dynamics were observed in the case where there was strong cross-immunity (which affects individuals who have recovered from at least one of the diseases) for both diseases, except that the out-of-phase behavior was much more pronounced for the first few years of infection (see Figure 9).

Figures 10 and 11 suggest that the value of R_0^j that is greater than $\frac{R_0^i}{1+a_i(R_0^i-1)}, j \neq i$ determines which of the two diseases will remain in the population, given that both values of R_0^i are greater than 1. On the other hand, we see in Figures 12 through 13 that, if at least one of the $R_0^i s$ is less than 1, the disease that will remain is the one whose basic reproductive ratio is greater than 1. Figure 14 shows that when both $R_0^i s$ are less than 1, the populations of infected individuals for both diseases will decrease to zero, and the dynamics reach a disease-free state.

Finally, we considered seasonal effects in the disease transmission rates. We used a sine function to let each disease transmission rate parameter vary with time. First, we let each parameter vary individually (Figures 15 and 16), then we let both vary together (Figure 17). In all cases, the dynamics depicted annual sharp increase and decline in the number of infectious individuals for both diseases. The results also led us to the conjecture that, at least in some cases, seasonal effects on the transmission rate of one disease may be enough to produce similar outcomes to those obtained when both transmission rates depend on seasonal factors.

6 Future Work

In order to further the analysis of the reduced model, a different steady state may be sought by making a weaker assumption than $Z_1 = Z_2 = N = S_0$. More simulations should be performed on both the reduced and full model to further explore the effects of the parameters on the stability of equilibria, i.e., to perform a more thorough bifurcation analysis. A computer package, such as Mathematica or Maple, along with appropriate hardware, should be used to attempt to find and

analyze the remaining equilibria for both models. In addition, seasonal variability of disease transmission rates should be explored further in order to determine conditions where time dependence of one disease transmission parameter produces similar results to those obtained when both disease transmission parameters are dependent on time.

7 References

[1] Edelstein - Keshet, L. Mathematical Models in Biology. McGraw-Hill, 1988.
[2] Pejman Rohani, H. J., Wearing, D.A., and Yunxin Huang. 'Understanding Host-Multipathogen Systems: Modeling the Interaction Between Ecology and Immunology'. From Chapter Three of Ostfeld, R.S., Keesing, F., and Eviner, V.T. Infectious Disease Ecology. Princeton University Press, 2008.
[3] Perko, L. Differential Equations and Dynamical Systems. 2^{nd}ed. Springer, 1996.