On A Model For The Cross Protection Of Two Infectious Diseases

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Abstract

This paper studies the effects of the spread of two similarly transmitted infectious diseases with cross protection in an unvaccinated population using a basic SEIR model with vital dynamics (births and deaths). A basic Mathematical model is built-up to study the joint transmission dynamics of diseases in the population. The equilibriums of these models as well as their stabilities are studied. Specifically, the stability results for disease-free and endemic steady states are proven. Finally, numerical simulations of the models are carried out with Matlab / Mathematica to study the behavior of the solutions in different regions of the parameter space.

Keywords: cross protection, infectious diseases, disease-free and endemic equilibria, numerical simulations, joint modeling

1. Introduction

Infectious diseases have accompanied humanity since the beginnings of history and are still of major concern. The discovery of penicillin, other antibiotics and the rise of vaccination programmes have not always succeeded in the extinction of infectious diseases while new ones are ever appearing, like recently H7N9 to name just one. Thus, the modelling of the dynamic of infectious diseases processes is as important as ever, not only to understand the nature of diseases but also to help formulating appropriate vaccination strategies to fight the spread [1]. From Daniel Bernoulli's analysis of smallpox [2], mathematical modelling of infectious diseases has increased over the past four decades. He was, noticeably, the first to express the proportion of susceptible individuals of an endemic infection in terms of the force of infection (the annual rate of acquiring an infection) and life expectancy. Hundreds of mathematical models have proven particularly powerful in the study of the effects of bacterial, parasitic and viral pathogens.

Formerly, by the use of relatively simple models for capturing only the most critical biological mechanisms much understanding has been gained. Mathematical models and computer simulations have become useful in analyzing the spread and control of infectious diseases. Together, they build and test theories that are involved with complex biological systems related disease, getting quantitative conjectures, determining parameter sensitivities and estimating parameters from data. Many mathematical models have been proposed in the literature describing the behaviour of two or more diseases [4, 5]. Some work considers models with two diseases such as HIV and tuberculosis [6-10] or described two strains of one disease present in the population [11-15]. The results in this studies support the view that when the competing infections provide complete protection for each other, the infection with the largest R_0 will force the other strain to extinction, although a rapid life cycle may allow short-term dominance. In this paper, we explore this evolutionary paradigm using a basic SEIR model.

The outline of the paper is as follows. In Section 2, we formulate a basic joint disease model and discuss its mathematical and epidemiological feasibility. The threshold conditions for the existence and uniqueness equilibria are derived and the local and global asymptotically stability of equilibria are proved in Sections 3, while Section 4 is devoted to numerical simulations. In Section 5, we summarise the findings and conclusions.

2. Description of Epidemiological Model

Compartmental models (for example, Anderson and May, [16]) may be used to model and describe the dynamics of infectious diseases in order to gain the understanding of the qualitative behaviour of the system. The purpose of this paper is to consider a model that models two strains or infections with cross immunity. These can be two different diseases with similar mode of transmission or two strains of the same disease. We assume homogeneous mixing in the population, that is, all members of the population interact with one another to the same degree. Using a compartmental modelling approach as shown in Figure 1, the host population is divided into six disjoint epidemiological classes at time t.
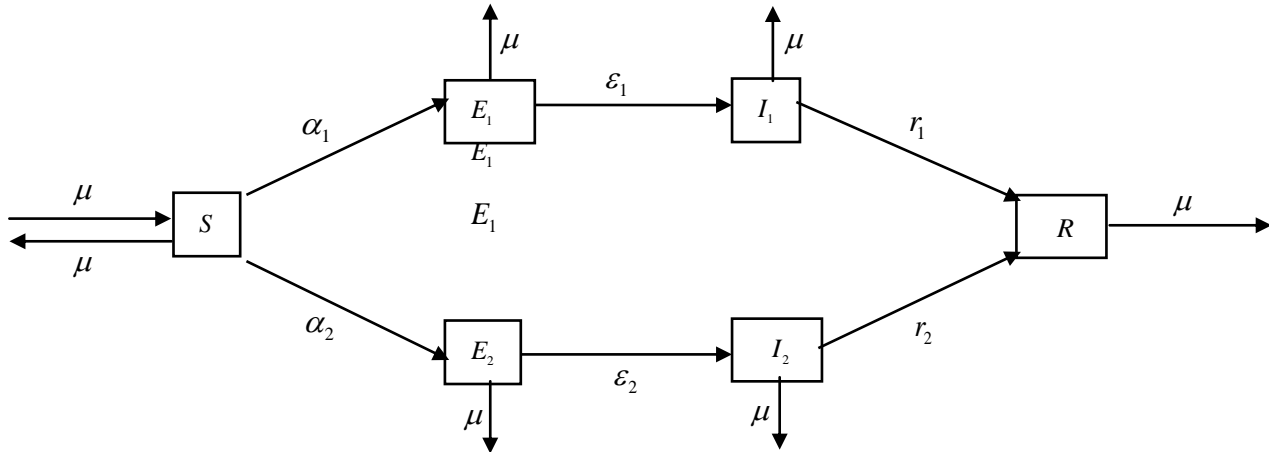
Figure 1: Schematic representation of the flow of hosts through the compartments for the joint-disease model.

These classes are: the susceptible class s, exposed to the strain $i(E_i)$, infected with the strain $i(I_i)$, recovered from both diseases R. We assume that each individual can be infected with one of two diseases, however with the restriction that an individual can only be infected with one disease at the same time; this property holds for several diseases [3]. We assume that an individual can be susceptibles, exposed, infected or recovered (or immune) and because of the presence of two diseases, each individual can be in six compartments as shown in Figure 1.

We assume that nobody dies due to infection. Recovered individuals do not flow back into the susceptible compartment, as life-long immunity is assumed. The deaths balance the births, so that the population size N is constant. Let α_i denote the effective contact rate for which an individual becomes infected with strain $i(i=1,2)$; let ε_i denote the effective leaving rate for which an individual leaves the class E_i to the class $I_i(i=1,2)$ and let r_i denote the effective recovery rate for which individuals recover and then move from class $I_i(i=1,2)$ to the class R. Biologically exposed individuals are not capable of transmitting the disease and as already described in [17], taking these effectives' transmission rates to be independent of the population size N for human diseases has been shown to be a plausible assumption [3]. We assume that susceptible may become infected only through contacts with an infectious individual at a rate $\alpha_i I_i / N, i=1,2$. Susceptible individuals are infected with strain 1 or strain 2 entering classes E_1 and E_2, respectively. The transfer out of the epidemiological classes are given by $\varepsilon_i E_i$ and $r_i I_i$, so that $1/\varepsilon_i$ is the average period of exposure for strain $i(i=1,2)$ and $1/r_i$ is the average infectious period for strain $i(i=1,2)$.

The joint SEIR model is obtained by 'translating' the compartmental model proposed above into mathematical terms. It consists of six coupled, nonlinear ordinary differential equations:

$$\frac{dS}{dt} = \mu\big(N - S(t)\big) - \alpha_1 I_1(t) S(t)/N - \alpha_2 I_2(t) S(t)/N,$$

$$\frac{dE_1}{dt} = \alpha_1 I_1(t) S(t)/N - (\varepsilon_1 + \mu) E_1(t),$$

$$\frac{dI_1}{dt} = \varepsilon_1 E_1(t) - (r_1 + \mu) I_1(t),$$

$$\frac{dE_2}{dt} = \alpha_2 I_2(t) S(t)/N - (\varepsilon_2 + \mu) E_2(t),$$ (2.1)

$$\frac{dI_2}{dt} = \varepsilon_2 E_2(t) - (r_2 + \mu) I_2(t),$$

$$\frac{dR}{dt} = r_1 I_1(t) + r_2 I_2(t) - \mu R(t),$$

with $t \geq 0$, subjected to the initial conditions:

$$S(0) = S_{(0)} \geq 0, E_1(0) = E_{1(0)} \geq 0, I_1(0) = I_{1(0)} \geq 0, E_2(0) = E_{2(0)} \geq 0, I_2(0) = I_{2(0)} \geq 0, R(0) = R_{(0)} \geq 0 \quad (2.2)$$

and

$$N = S(t) + E_1(t) + I_1(t) + E_2(t) + I_2(t) + R(t) \quad \text{for all} \quad t \geq 0. \quad (2.3)$$

Because of equation (2.3), the final equation in (2.1) is redundant. We reformulate the model in terms of proportions by setting, $s = S/N, e_1 = E_1/N, i_1 = I_1/N, e_2 = E_2/N, i_2 = I_2/N$ and $r = R/N$. Using proportions, the model equations become

$$\frac{ds(t)}{dt} = \mu\big(1 - s(t)\big) - \alpha_1 i_1(t) s(t) - \alpha_2 i_2(t) s(t),$$

$$\frac{de_1}{dt} = \alpha_1 i_1(t) s(t) - (\varepsilon_1 + \mu) e_1(t),$$

$$\frac{di_1}{dt} = \varepsilon_1 e_1(t) - (r_1 + \mu) i_1(t),$$ (2.4)

$$\frac{de_2}{dt} = \alpha_2 i_2(t) s(t) - (\varepsilon_2 + \mu) e_2(t),$$

$$\frac{di_2}{dt} = \varepsilon_2 e_2(t) - (r_2 + \mu) i_2(t),$$

in the domain

$$F = \left\{ (s, e_1, i_1, e_2, i_2) \in \mathrm{R}_+^5 \,\big|\, s + e_1 + i_1 + e_2 + i_2 \leq 1 \right\}, \quad (2.5)$$

as the epidemiologically feasible region of interest. In what follows is a theorem that states that the above set is positively invariant with respect to (2.4) under the assumptions placed on the model.

Theorem 2.1. *If* $s(0) \geq 0$, $e_1(0) \geq 0$, $i_1(0) \geq 0$, $e_2(0) \geq 0$, $i_2(0) \geq 0$, *the solutions* $s(t)$, $e_1(t)$, $i_1(t)$, $e_2(t)$, $i_2(t)$ *of system* (2.4) *are positive for* $t \geq 0$. *For system* (2.4), *the region* F *is positively invariant and all solutions starting in* F *do not leave* F.

Following a similar argument as in [13] which is given in the appendix, it is shown that $\hat{n}(t)$ is bounded and all solutions starting in F do not leave F, where $\hat{n}(t) = s(t) + e_1(t) + i_1(t) + e_2(t) + i_2(t) = 1 - r(t)$. Therefore, the proposed model is mathematically and epidemiologically well posed since all feasible solutions of the system (2.4) enter the region F. Hence, F is positively invariant and it is sufficient to consider solutions of system (2.4) in F. Existence, uniqueness and continuation results for system (2.4) hold in this region. We denote by ∂F and $\overset{\circ}{F}$ the boundary and interior of F in R_+^5, respectively.

3. Analysis of Epidemiological Model

3.1 Basic Reproductive Number

Analyzing an epidemiological model in order to gain some biological insight into the parameters in the model can be done using the basic reproductive number, R_0 [16]. For many simple homogeneous models (e.g. SIS, SIR,

SIRS, SEIR, SEIRS, MSEIR, etc.), the basic reproductive number can be intuitively expressed by the product of the contact rate, the average fraction surviving the pre-infectious period (if this is included in the model) and by the average infectious period. We now show how the mathematical expression R_0 is obtained for model (2.4). Mathematically, it is defined as the spectral radius of the next generation matrix [18, 19]. This is done by investigating de_1/dt, di_1/dt, de_2/dt and di_2/dt, since they measure the virulence of the infection in the model (2.4). For each of the infected states (here e_1, i_1, e_2 and i_2), we define:

F_k: the rate of appearance of new infections in compartment k,

V_k: the rate of transfer of individuals (out of) minus (into) the compartment k.

Thus

$$F = \left[\partial F_k(x_0)/\partial x_j \right] = \begin{bmatrix} 0 & s_0\alpha_1 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & s_0\alpha_2 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

$$V = \left[\partial V_k(x_0)/\partial x_j \right] = \begin{bmatrix} \mu+\varepsilon_1 & 0 & 0 & 0 \\ -\varepsilon_1 & \mu+r_1 & 0 & 0 \\ 0 & 0 & \mu+\varepsilon_2 & 0 \\ 0 & 0 & \varepsilon_2 & \mu+r_1 \end{bmatrix}. \tag{3.1}$$

The dominant eigenvalues of FV^{-1} are given by

$$R_1 = \frac{s_0\alpha_1\varepsilon_1}{(\mu+r_1)(\mu+\varepsilon_1)},$$

$$R_2 = \frac{s_0\alpha_2\varepsilon_2}{(\mu+r_2)(\mu+\varepsilon_2)}, \tag{3.2}$$

where R_1 and R_2 are reproduction numbers for strain one and strain two, respectively. It implies that the spectral radius of the matrix FV^{-1} is

$$R_0 = \rho\left(FV^{-1}\right) = \max\{R_1, R_2\}. \tag{3.3}$$

The two terms in (3.2) determine whether the infection of first and second disease will invade and they are called the basic reproductive numbers associated with first and second disease, respectively. The case $R_0 = 1$ gives a threshold condition. We show that both infections cannot invade, if $R_0 < 1$ and the infections can invade a population if $R_0 > 1$.

3.2 Steady-State Solutions and the Jacobian Matrix

The first object to investigate when analyzing dynamical systems is the existence of an equilibrium solution (stationary point). For this, we write the joint SEIR model as the system

$$\frac{dz}{dt} = f(z), \tag{3.4}$$

where

$$z(t) = \left(s(t), e_1(t), i_1(t), e_2(t), i_2(t)\right) \in R_+^5,$$

$$f(z) = \left(f_1(z), f_2(z), f_3(z), f_4(z), f_5(z)\right)^T,$$

$$f(z) = \begin{pmatrix} \mu(1-s(t)) - \alpha_1 i_1(t) s(t) - \alpha_2 i_2(t) s(t) \\ \alpha_1 i_1(t) s(t) - (\varepsilon_1 + \mu) e_1(t) \\ \varepsilon_1 e_1(t) - (r_1 + \mu) i_1(t) \\ \alpha_2 i_2(t) s(t) - (\varepsilon_2 + \mu) e_2(t) \\ \varepsilon_2 e_2(t) - (r_2 + \mu) i_2(t) \end{pmatrix}, \tag{3.5}$$

and T denotes the transpose. The equilibrium can then be obtained by equating $f(z) = 0$, therefore revealing three equilibrium solutions.

The first, which is the trivial solution, is given by

$$E_1 = \left(s^{*(1)}, e_1^{*(1)}, i_1^{*(1)}, e_2^{*(1)}, i_2^{*(1)} \right) = (1,0,0,0,0) \in \partial F, \tag{3.6}$$

This is called the diseases-free equilibrium and is trivial because, at this state, the entire population is susceptible to infection of both diseases. Hence, all individual are healthy and clearly stay healthy at all time. It is noted that

$z^* = \left(s^*, 0, 0, 0, 0 \right): s^* \neq 1$ is not steady-state; for then we have $\dfrac{ds}{dt} = \mu(1-s)$ which means that s grows

until it equals 1. This corresponds to the fact that recovered individuals from both diseases leave the population when they die, while newborn infants fall into the susceptible compartment.

The next two but non-trivial solutions are given as follows:

$$E_2 = \left(s^{*(2)}, e_1^{*(2)}, i_1^{*(2)}, e_2^{*(2)}, i_2^{*(2)} \right) \in \overset{o}{F}$$

where

$$s^{*(2)} = \frac{(\mu + r_1)(\mu + \varepsilon_1)}{\alpha_1 \varepsilon_1} = \frac{1}{R_1}, \quad e_1^{*(2)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_1)\varepsilon_1 + r_1(\mu + \varepsilon_1) \right)}{\alpha_1 \varepsilon_1 (\mu + \varepsilon_1)} = \frac{\mu}{(\mu + \varepsilon_1)} \left(1 - \frac{1}{R_1} \right), \quad e_2^{*(2)} = 0,$$

$$i_1^{*(2)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_1)\varepsilon_1 + r_1(\mu + \varepsilon_1) \right)}{(\mu + r_1)\alpha_1 (\mu + \varepsilon_1)} = \frac{\mu}{\alpha_1}(R_1 - 1), \quad i_2^{*(2)} = 0, \tag{3.7}$$

and

$$E_3 = \left(s^{*(2)}, e_1^{*(2)}, i_1^{*(2)}, e_2^{*(2)}, i_2^{*(2)} \right) \in \overset{o}{F},$$

where

$$s^{*(3)} = \frac{(\mu + r_2)(\mu + \varepsilon_2)}{\alpha_2 \varepsilon_2} = \frac{1}{R_2}, \quad e_1^{*(3)} = 0, \quad e_2^{*(3)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_2)\varepsilon_2 + r_2(\mu + \varepsilon_2) \right)}{\alpha_2 \varepsilon_2 (\mu + \varepsilon_2)} = \frac{\mu}{(\mu + \varepsilon_2)} \left(1 - \frac{1}{R_2} \right),$$

$$i_1^{*(3)} = 0, \quad i_2^{*(3)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_2)\varepsilon_2 + r_2(\mu + \varepsilon_2) \right)}{(\mu + r_2)\alpha_2 (\mu + \varepsilon_2)} = \frac{\mu}{\alpha_2}(R_2 - 1). \tag{3.8}$$

These are called the endemic equilibrium solutions. In these situations, the entire population is no more fully susceptible for both diseases. That is, both equilibria E_2 and E_3 are exclusive in a sense that only one disease is present in the population, while the second eventually dies out.

Having obtained the equilibrium solutions of system (2.4), we need to investigate their stabilities in order to better understand the dynamics of the model. Let $\bar{z}$ be an equilibrium (stationary) solution of (3.4). Then, $\bar{z}$ is a hyperbolic equilibrium solution if none of the eigenvalues of the Jacobian, $J_f(\bar{z})$ has zero real part. Otherwise, $\bar{z}$ is called a non-hyperbolic equilibrium (stationary) solution. The following theorem (see [20], p.8) gives the standard first approximation method for determining stability of equilibrium (stationary) solutions.

Theorem 3.1. *Let* $\overline{z} \in R_+^5$ *be an hyperbolic equilibrium (stationary) solution of* $dz/dt = f(z)$. *Then,* $\overline{z}$ *is asymptotically stable if* $\mathrm{Re}(\lambda) < 0$ *for all eigenvalues,* λ *of the Jacobian,* $J_f(\overline{z})$ *and it is unstable if* $\mathrm{Re}(\lambda) > 0$ *for at least one eigenvalue of* $J_f(\overline{z})$.

Typically, one can achieve this by using the Routh-Hurwitz criterion; however, this approach was intractable due to the complexity of the Huritz determinants. Therefore, in determining local stability of equilibrium solutions the theory of nonsingular M-matrices described in Schuette [21] was employed.

First, from equation, (3.5) we obtained the Jacobian matrix $J_f(\overline{z})$ of the system (2.4) as

$$J_f(z) = \begin{pmatrix} \partial f_1/\partial s & \cdot & \cdot & \partial f_1/\partial i_2 \\ \partial f_2/\partial s & \cdot & \cdot & \partial f_2/\partial i_2 \\ \cdot & \cdot & \cdot & \cdot \\ \partial f_5/\partial s & \cdot & \cdot & \partial f_5/\partial i_2 \end{pmatrix} = \begin{pmatrix} -\mu - i_1\alpha_1 - i_2\alpha_2 & 0 & -s\alpha_1 & 0 & -s\alpha_2 \\ i_1\alpha_1 & -\mu - \varepsilon_1 & s\alpha_1 & 0 & 0 \\ 0 & \varepsilon_1 & -\mu - r_1 & 0 & 0 \\ i_2\alpha_2 & 0 & 0 & -\mu - \varepsilon_2 & s\alpha_2 \\ 0 & 0 & 0 & \varepsilon_2 & -\mu - r_2 \end{pmatrix}. \quad (3.9)$$

We now proceed to analyze the of the joint-disease model.

3.3   Stability analysis of the disease-free equilibrium

In this section, we investigate whether the disease-free equilibrium is locally asymptotically stable. The local stability is linked to a threshold parameter called the basic reproduction number R_0. Therefore, using equation (3.9) the Jacobian evaluated at E_1 is given by

$$J = J_f(E_1) = \begin{pmatrix} -\mu & 0 & -\alpha_1 & 0 & -\alpha_2 \\ 0 & -\mu - \varepsilon_1 & \alpha_1 & 0 & 0 \\ 0 & \varepsilon_1 & -\mu - r_1 & 0 & 0 \\ 0 & 0 & 0 & -\mu - \varepsilon_2 & \alpha_2 \\ 0 & 0 & 0 & \varepsilon_2 & -\mu - r_2 \end{pmatrix}. \quad (3.10)$$

Let π_k be the sequence $\{1, 2, ..., k\}$ for $1 \le k \le 5$. By simple computation, the leading principal minors of $-J$ are

$$\begin{aligned}
-J_{\pi_1}^{\pi_1} &= \mu, \\
-J_{\pi_2}^{\pi_2} &= \mu(\mu + \varepsilon_1), \\
-J_{\pi_3}^{\pi_3} &= \mu(\mu(\mu + r_1) + (\mu + r_1 - \alpha_1)\varepsilon_1) = \mu(\mu + r_1)(\mu + \varepsilon_1)(1 - R_1), \\
-J_{\pi_4}^{\pi_4} &= \mu(\mu(\mu + r_1) + (\mu + r_1 - \alpha_1)\varepsilon_1)(\mu + \varepsilon_2) = \mu(\mu + r_1)(\mu + \varepsilon_1)(1 - R_1)(\mu + \varepsilon_2), \\
-J_{\pi_5}^{\pi_5} &= \mu(\mu(\mu + r_1) + (\mu + r_1 - \alpha_1)\varepsilon_1)(\mu(\mu + r_2) + (\mu + r_2 - \alpha_2)\varepsilon_2), \\
&= \mu\{(\mu + r_1)(\mu + \varepsilon_1)(1 - R_1)\}\{(\mu + r_2)(\mu + \varepsilon_2)(1 - R_2)\}.
\end{aligned} \quad (3.11)$$

From (3.11), the first two leading principal minors are clearly positive and the remaining leading principal minors would be positive if the following conditions holds:

$$R_1 < 1 \text{ and } R_2 < 1. \tag{3.12}$$

This implies that E_1, is locally asymptotically stable if and only if $R_1 < 1$ and $R_2 < 1$. Hence, we can summarise these findings in the following theorem.

Theorem 3.2. *The disease-free equilibrium E_1 of (2.4) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

The epidemiological implication of Theorem 3.2 is that if the initial populations of the various epidemiological classes are in the neighbourhood of the equilibrium solution and if basic reproduction numbers for both infections are less than 1 then both diseases die out.

Mathematically, we can show that the expression $R_0 > 1$ for the two strains of diseases is a sharp threshold parameter for the joint-disease model; if $R_0 \leq 1$ both viruses die out, if $R_0 > 1$ one of the two viruses remains endemic in the population. In order to show this, we use the direct method of Liapunov [22] to the stronger results that E_1 is globally asymptotically stable in the region F whenever $R_0 \leq 1$. Since we want to show that both viruses i disappear from the population when $R_0 \leq 1$ given any starting point in F. However, this leads to the construction of Liapunov function (3.13) for system (2.4) as

$$V(e_1, i_1, e_2, i_2) = \varepsilon_1 e_1 + (\mu + \varepsilon_1) i_1 + \varepsilon_2 e_2 + (\mu + \varepsilon_2) i_2. \tag{3.13}$$

Therefore, the Liapunov derivative is given by

$$
\begin{aligned}
V' &= \varepsilon_1 e_1' + (\mu + \varepsilon_1) i_1' + \varepsilon_2 e_2' + (\mu + \varepsilon_2) i_2' \\
&= \varepsilon_1 \left(\alpha_1 i_1 s - (\mu + \varepsilon_1) e_1 \right) + (\mu + \varepsilon_1) \left(\varepsilon_1 e_1 - (\mu + r_1) i_1 \right) + \varepsilon_2 \left(\alpha_2 i_2 s - (\mu + \varepsilon_2) e_2 \right) \\
&\quad + (\mu + \varepsilon_2) \left(\varepsilon_2 e_2 - (\mu + r_2) i_2 \right) \\
&= \alpha_1 \varepsilon_1 i_1 s - (\mu + \varepsilon_1) \varepsilon_1 e_1 + (\mu + \varepsilon_1) \varepsilon_1 e_1 - (\mu + \varepsilon_1)(\mu + r_1) i_1 + \alpha_2 \varepsilon_2 i_2 s - (\mu + \varepsilon_2) \varepsilon_2 e_2 \\
&\quad + (\mu + \varepsilon_2) \varepsilon_2 e_2 - (\mu + \varepsilon_2)(\mu + r_2) i_2 \\
&= \left[\alpha_1 \varepsilon_1 s - (\mu + \varepsilon_1)(\mu + r_1) \right] i_1 + \left[\alpha_2 \varepsilon_2 s - (\mu + \varepsilon_2)(\mu + r_2) \right] i_2 \\
&= (\mu + \varepsilon_1)(\mu + r_1)[R_1 - 1] i_1 + (\mu + \varepsilon_2)(\mu + r_2)[R_2 - 1] i_2 \\
&\leq (\mu + \varepsilon_1)(\mu + r_1)[R_0 - 1] i_1 + (\mu + \varepsilon_2)(\mu + r_2)[R_0 - 1] i_2,
\end{aligned}
\tag{3.14}
$$

where $R_1 \leq R_0, R_2 \leq R_0$.

It is obvious that $V' = 0$ if and only if $i_1 = i_2 = 0$. Thus, the largest compact invariant set in the $\{(s, e_1, i_1, e_2, i_2) \in F \mid V' \leq 0\}$, when $R_0 \leq 1$, is the singleton $\{E_1\}$. LaSalle's Invariance Principle then implies that E_1 is globally stable in F. Hence, we can summarise these findings in the following theorem.

Theorem 3.3. *The disease-free equilibrium E_1 of (2.4) is globally asymptotically stable in F if $R_0 \leq 1$ and unstable if $R_0 > 1$.*

The epidemiological implication of Theorem 3.3 is that the infected fraction e_1, i_1, e_2 and i_2 of the population goes to zero in time so that both infections die out.

3.4 Stability of the Endemic Equilibrium

Herein, we study the endemic equilibria of the system (2.4). From Section 3.2, we found the non-zero steady state can be present if there is only one strain $i, \forall i = 1, 2$. Since the system (2.4) is symmetric with respect to

strain $i, \forall\, i = 1, 2$, therefore, we shall investigate the case when strain 1 is present in the population (strain 2 yields similar results).   In this case, there is no co-infected individual.

The endemic equilibrium in (3.7) can be shown to exist if $R_1 > 1$ as follows. From (3.7), we have

$$s^{*(2)} = \frac{(\mu + r_1)(\mu + \varepsilon_1)}{\alpha_1 \varepsilon_1} = \frac{1}{R_1},$$

$$e_1^{*(2)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_1)\varepsilon_1 + r_1(\mu + \varepsilon_1)\right)}{\alpha_1 \varepsilon_1 (\mu + \varepsilon_1)} = \frac{\mu}{(\mu + \varepsilon_1)}\left(1 - \frac{1}{R_1}\right), \qquad (3.15)$$

$$i_1^{*(2)} = \frac{-\mu\left(\mu^2 + (\mu - \alpha_1)\varepsilon_1 + r_1(\mu + \varepsilon_1)\right)}{(\mu + r_1)\alpha_1(\mu + \varepsilon_1)} = \frac{\mu}{\alpha_1}(R_1 - 1).$$

From (3.15), it can be seen that $e_1^{*(2)}$ and $i_1^{*(2)}$ are positive if the following condition holds:

$$R_1 > 1 \qquad\qquad (3.16)$$

Therefore, using equation (3.9) the Jacobian evaluated at E_2 is given by

$$J = J_f\left(E_2\right) = \begin{pmatrix} -\dfrac{\mu\alpha_1\varepsilon_1}{(\mu+r_1)(\mu+\varepsilon_1)} & 0 & -\dfrac{(\mu+r_1)(\mu+\varepsilon_1)}{\varepsilon_1} & 0 & -\dfrac{(\mu+r_1)\alpha_2(\mu+\varepsilon_1)}{\alpha_1\varepsilon_1} \\[2mm] -\dfrac{\mu\left(\mu(\mu+r_1)+(\mu+r_1-\alpha_1)\varepsilon_1\right)}{(\mu+r_1)(\mu+\varepsilon_1)} & -\mu-\varepsilon_1 & \dfrac{(\mu+r_1)(\mu+\varepsilon_1)}{\varepsilon_1} & 0 & 0 \\[2mm] 0 & \varepsilon_1 & -\mu+r_1 & 0 & 0 \\[2mm] 0 & 0 & 0 & -\mu-\varepsilon_2 & \dfrac{(\mu+r_1)\alpha_2(\mu+\varepsilon_1)}{\alpha_1\varepsilon_1} \\[2mm] 0 & 0 & 0 & \varepsilon_2 & -\mu-r_2 \end{pmatrix}.$$

$$(3.17)$$

Let π_k be the sequence $\{1, 2, \ldots, k\}$ for $1 \le k \le 5$. By simple computation, the leading principal minors of $-J$ are

$$-J^{\pi_1}_{\pi_1} = \frac{\mu\alpha_1\varepsilon_1}{(\mu+r_1)(\mu+\varepsilon_1)} = \mu R_1,$$

$$-J^{\pi_2}_{\pi_2} = \frac{\mu\alpha_1\varepsilon_1}{\mu+r_1} = \mu(\mu+\varepsilon_1)R_1,$$

$$-J^{\pi_3}_{\pi_3} = -\mu\left(\mu(\mu+r_1)+(\mu+r_1-\alpha_1)\varepsilon_1\right) = \mu(\mu+r_1)(\mu+\varepsilon_1)(R_1-1),$$

$$-J^{\pi_4}_{\pi_4} = -\mu\left(\mu(\mu+r_1)+(\mu+r_1-\alpha_1)\varepsilon_1\right)(\mu+\varepsilon_2) = \mu(\mu+r_1)(\mu+\varepsilon_1)(R_1-1)(\mu+\varepsilon_2), \qquad (3.18)$$

$$-J^{\pi_5}_{\pi_5} = -\frac{\mu\left(\mu(\mu+r_1)+(\mu+r_1-\alpha_1)\varepsilon_1\right)\left(-(\mu+r_1)\alpha_2\varepsilon_2(\mu+\varepsilon_1)+(\mu+r_2)\alpha_1\varepsilon_1(\mu+\varepsilon_2)\right)}{\alpha_1\varepsilon_1},$$

$$= \left\{\mu\left(1 - \frac{1}{R_1}\right)\right\}\left\{(\mu+r_2)(\mu+\varepsilon_2)(\mu+r_1)(\mu+\varepsilon_1)(R_1-R_2)\right\}.$$

From (3.18), the first two leading principal minors are clearly positive and the remaining leading principal minors would be positive if the following conditions holds:

$$R_1 > 1 \quad \text{and} \quad R_1 > R_2. \qquad\qquad (3.19)$$

This implies that E_2, is locally asymptotically stable if and only if $R_1 > 1$ and $R_1 > R_2$. Hence, we can summaries these findings in the following theorem.

Theorem 3.4. *The endemic equilibrium E_2 of (2.4) is locally asymptotically stable if $R_1 > 1$ and $R_1 > R_2$ and*

unstable if otherwise.

Similar results about the existence and stability can be deduce for another endemic equilibrium in (3.8). Hence, we can summaries these findings in the following theorem.

Theorem 3.5. *The endemic equilibrium E_3 of (2.4) is locally asymptotically stable if $R_2 > 1$ and $R_2 > R_1$ and unstable if otherwise.*

4. Numerical Simulations

In this section, we explore the theoretical results contained in this paper using simulations. We use the parameter values listed in Table 1.

Table 1: Description and estimation of parameters.

Parameter	Description	Estimated Value
α_1	Transmission coefficient of strain 1	Variable
α_2	Transmission coefficient of strain 2	Variable
ε_1	Per-capita latent rate for strain 1	$0.003 \, \text{year}^{-1}$
ε_2	Per-capita latent rate for strain 2	$0.002 \, \text{year}^{-1}$
r_1	Per-capita recovery rate for strain 1	$0.05 \, \text{year}^{-1}$
r_2	Per-capita recovery rate for strain 2	$0.04 \, \text{year}^{-1}$
μ	Natural death rate	$0.0000391 \, \text{year}^{-1}$

The following figures depict the numerical results obtained for system (2.4). Firstly, we show some numerical results for the system (2.4) for $\alpha_1 = \alpha_2 = 0.03$, so that $R_1 = 0.5918 < 1$, $R_2 = 0.73349 < 1$ with $R_1 < R_2$. Figure 1 presents the trajectories and plane figure.
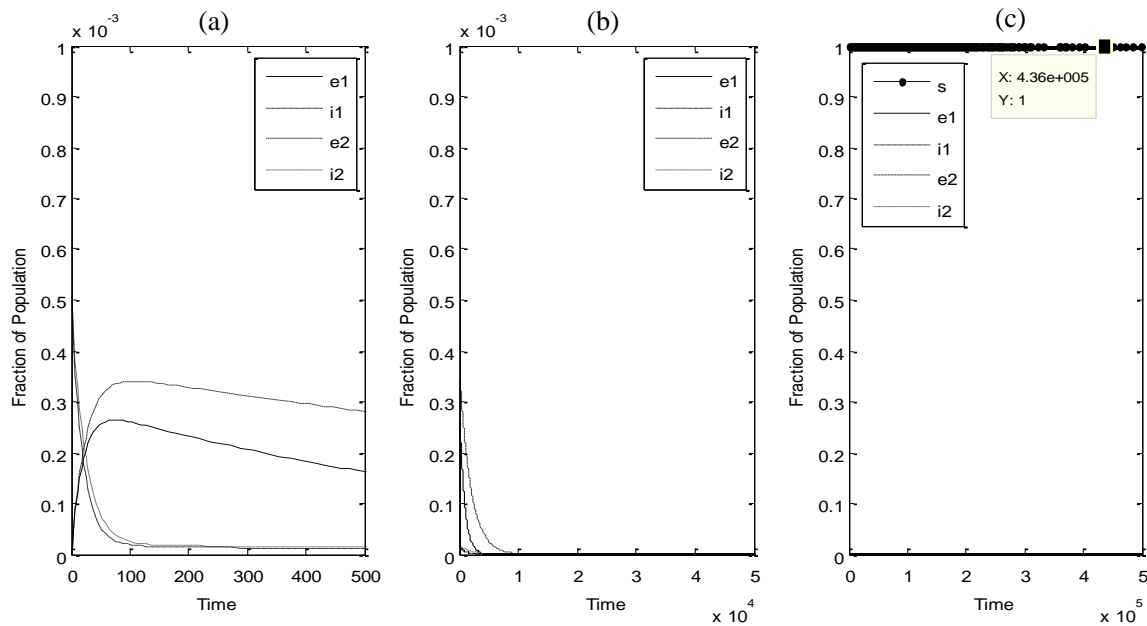
Figure 1: Trajectories of system (2.4) when $\alpha_1 = \alpha_2 = 0.03$, so that $R_1 = 0.5918 < 1$, $R_2 = 0.73349 < 1$ with $R_1 < R_2$ It shows that the disease-free equilibrium E_1 is stable.

From Figure 1, we can see that the trajectories of system (2.4) converge to the disease-free equilibrium that is in agreement with Theorem 3.3.
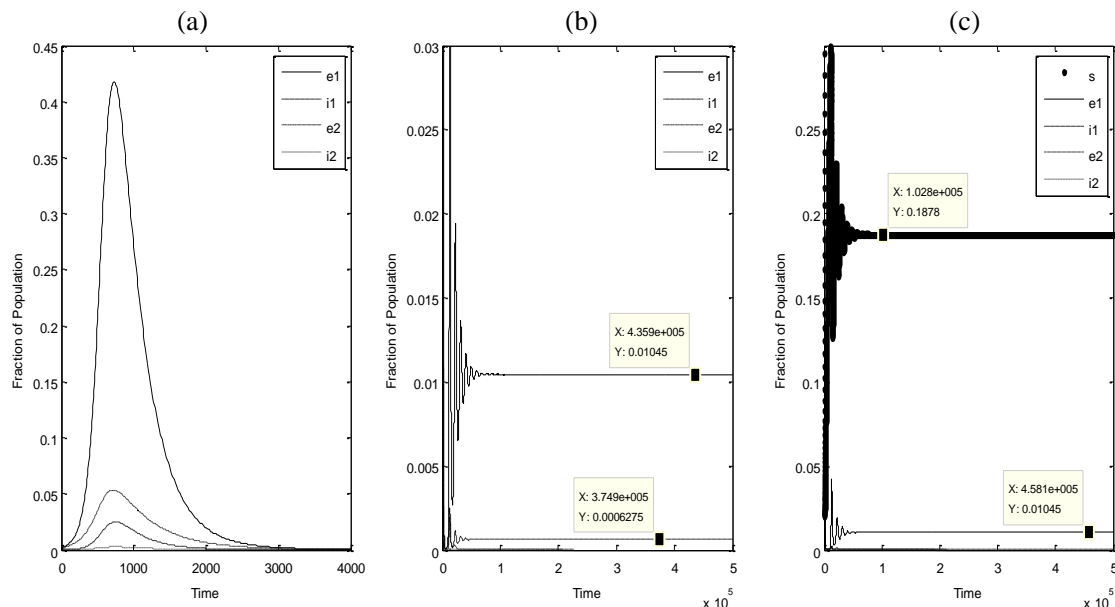
Figure 2: Trajectories of system (2.4) when $\alpha_1 = 0.27$, $\alpha_2 = 0.2$, so that $R_1 = 5.3263 > 1$, $R_2 = 4.8993 > 1$ with $R_2 < R_1$. It shows that the endemic equilibrium E_2 is stable.

Figure 2, depicts the trajectories plot and plane figure for the system (2.4) when $\alpha_1 = 0.27$, $\alpha_2 = 0.2$, so that $R_1 = 5.3263 > 1$, $R_2 = 4.8993 > 1$ with $R_2 < R_1$. It shows what happens after the exposed and infective fractions decreased to a low level, the slow processes of deaths of recovered individuals and the births of new susceptibles

gradually increases the susceptible fractions enough that another small epidemic occurs. This process of alternating rapid epidemics and the slow regeneration of susceptible continues as the trajectories approach the endemic state, which is in agreement with Theorem 3.4.

5. Discussion and Conclusion

In this paper, we have presented a basic mathematical model within a deterministic framework for describing the epidemiology of two – strains or infections that govern complete cross protection. By using, the Hurwitz criterion, Lyapunou stability theory and Lasalles's invariant set theorem, both the local and global stability of the equilibria of the proposed model are proven. Three types of equilibria solutions for the system (2.4) are found: when both strains of diseases are absent, when only strain 1 is present or only strain 2 is present. The basic reproduction number R_1 and R_2 provide the threshold conditions that determine the competitive outcome of the two strains of diseases. The local and global stability of the disease-free equilibrium E_1 has been proved for $R_1 < 1$, $R_2 < 1$ and the disease will die out. When $R_1 > 1$, $R_2 < R_1$, a endemic equilibrium E_2 exist and it is locally stable. While when $R_2 > 1$, $R_1 < R_2$, there exists an endemic equilibrium E_3 and is also locally stable. A good agreement is obtained between the analytical and numerical results.

As it was noted in Section 2, the model considered in this paper is a basic model with vital dynamics, in which we aimed to capture main features in the dynamic of the spread of two infectious diseases in a population. This model or its generalization can be useful studying various scenarios on how two strains or infections interact.

Appendix (Proof of Theorem 2.1)

Under the given initial conditions, it is easy to prove that the solutions of system (2.4) are positive; if not, there exists a first time t_1 such that

$$s(t_1) = 0, \ s'(t_1) < 0, \ e_1(t_1) \geq 0, \ i_1(t_1) \geq 0, \ e_2(t_1) \geq 0, \ i_2(t_1) \geq 0, \ \text{for} \ 0 < t < t_1, \qquad (A.1)$$

there exists a t_2

$$e_1(t_2) = 0, \ e_1'(t_2) < 0, \ s(t_2) \geq 0, \ i_1(t_2) \geq 0, \ e_2(t_2) \geq 0, \ i_2(t_2) \geq 0, \ \text{for} \ 0 < t < t_2, \qquad (A.2)$$

there exists a t_3

$$i_1(t_3) = 0, \ i_1'(t_3) < 0, \ s(t_3) \geq 0, \ e_1(t_3) \geq 0, \ e_2(t_3) \geq 0, \ i_2(t_3) \geq 0, \ \text{for} \ 0 < t < t_3, \qquad (A.3)$$

there exists a t_4

$$e_2(t_4) = 0, \ e_2'(t_4) < 0, \ s(t_4) \geq 0, \ e_1(t_4) \geq 0, \ i_1(t_4) \geq 0, \ i_2(t_4) \geq 0, \ \text{for} \ 0 < t < t_4, \qquad (A.4)$$

there exists a t_5

$$i_2(t_5) = 0, \ i_2'(t_5) < 0, \ s(t_5) \geq 0, \ e_1(t_5) \geq 0, \ i_1(t_5) \geq 0, \ e_2(t_5) \geq 0, \ \text{for} \ 0 < t < t_5, \qquad (A.5)$$

In the first case, we have

$$s'(t_1) = \mu < 0, \qquad (A.6)$$

which is a contradiction since $\mu \geq 0$ and so $s(t) \geq 0, t \geq 0$. In the second case, we have

$$e_1'(t_2) = \alpha_1 i_1(t_2) s(t_2) < 0, \qquad (A.7)$$

which is in contradiction with $\alpha_1 > 0$ and thus $e_1(t) \geq 0, t \geq 0$. In the third case, we have

$$i_1'(t_3) = \varepsilon_1 e_1(t_3) < 0, \qquad (A.8)$$

which is in contradiction with $\varepsilon_1 > 0$ and thus $i_1(t) \geq 0, t \geq 0$. In the fourth case, we have

$$e_2'(t_4) = \alpha_2 i_2(t_4) s(t_4) < 0, \qquad (A.9)$$

which is in contradiction with $\alpha_2 > 0$ and thus $e_1(t) \geq 0, t \geq 0$. In the fifth case, we have

$$i_2'(t_5) = \varepsilon_2 e_2(t_5) \geq 0, \qquad (A.10)$$

which is in contradiction with $\varepsilon_2 > 0$ and thus $i_1(t) \geq 0, t \geq 0$.

Thus, in all cases, $s(t), \ e_1(t), \ i_1(t), \ e_2(t), \ i_2(t)$ remain positive for $t \geq 0$.

Let $(s(t), e_1(t), i_1(t), e_2(t), i_2(t)) \in R_+^5$ be any solution with nonnegative initial condition, adding equations in system (2.4) gives

$$n'(t) = \mu - \mu n(t) - r_1 i_1 - r_2 i_2,$$
$$\leq \mu - \mu n^*, \qquad (A.11)$$

where

$$\hat{n}(t) = \, (\,) + \, _1(\,)t + \, _1(i) \, t + \, _2(e) \, + (\,) \, = (\,)n \, (\,).$$ $$(A.12)$$

It follows that

$$0 \le \hat{n}(t) \le \frac{\mu}{\mu} + n(0)e^{-\mu t},$$ $$(A.13)$$

where $\hat{n}(0)$ represents initial values of the total population since $\hat{n}(0) = n(0) - r(0) = n(0)$. Thus

$$0 \le \hat{n}(t) \le 1 \ \text{ as } \ t \to \infty.$$

This completes the proof.

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