MODELLING DISEASE IN THE CHEMOSTAT

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Contents

1 Introduction

Extensive research in chemostat modelling has been conducted, as has research in epidemiological modelling. However, studies combining the two types of modelling are few and far between (see [1], [11], or [24] for example). In this thesis we have endeavoured to apply some simple epidemiological principles to a typical chemostat model. This has some interesting implications and applications, which will be discussed. We begin by introducing some simple ideas from each area separately, then we will discuss the possibilities and motivations for combining them.

1.1 The Chemostat

The first question to address is: What is a chemostat? In short, it is a device that was created to study bacterial growth in a controlled environment. More specifically, the chemostat is a vessel that contains a homogeneously mixed solution of bacteria, nutrient (that the bacteria consume) and liquid medium. The growth-limiting nutrient is pumped into the vessel at a constant rate, while the volume in the vessel is kept constant by allowing an outflow of the same rate as the inflow. See Figure 1 for a sketch of a generic chemostat apparatus.

Since its invention, the chemostat has been used to study lake ecology (e.g.

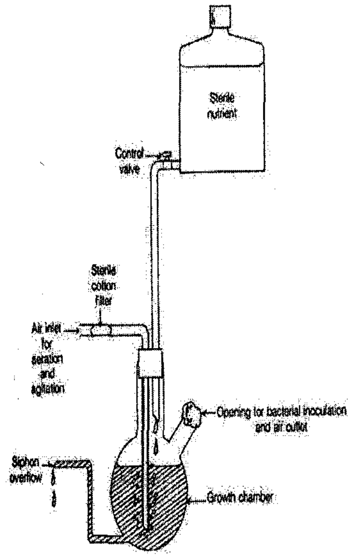

Figure 1: The chemostat

[12], [14], or [33]), wastewater treatment (e.g. [20], [26], or [29]) and population dynamics (e.g. [3] or [4]), to name a few. The chemostat is particularly useful for studying ecological systems because it allows for control of many of the variables involved (i.e. nutrient concentration, inflow/outflow rate) and so the resulting dynamics are better understood and explained. As Martin Boraas said in his study of rotifer dynamics, "The chemostat system facilitated unambiguous determinations of rotifer growth and fecundity, since food was supplied and wastes were removed at continuous, controlled rates" [4]. To learn more about the chemostat, its uses, and the mathematics behind it, see [25] and [31].

A basic model of the chemostat is:

$$\begin{aligned}\frac{dS}{dt} &= (S^0 - S(t))D - \sum_{i=1}^{n} \frac{x_i(t)p_i(S(t))}{\eta_i} \\ \frac{dx_i}{dt} &= x_i(t)(-D_i + p_i(S(t))), \qquad i = 1, 2, \ldots, n.\end{aligned}$$

In these equations, t denotes time, $x_i(t)$ represents the concentration of the ith population of microorganisms in the growth chamber at time t; $S(t)$ denotes the concentration of the growth-limiting nutrient at time t; $p_i(S(t))$ is a general function representing the conversion of food to biomass for the bacteria; η_i is a growth yield constant for population i; S^0 is the concentration of the growth limiting nutrient under investigation in the nutrient reservoir; D is the rate of ouflow from the main growth chamber; and $D_i = D + \epsilon_i$, where ϵ_i is the species specific death rate. All constants and concentrations have positive values, $S(0) \geq 0$, and $x_i(0) > 0$, $i = 1, 2, \ldots, n$. The dynamics of this system have been studied extensively (see [9], [17], [22], [39], or [40]). It is particularly interesting to note that in chemostat research it is proved that for a very general class of response functions ($p_i(S(t))$), for the model above, *at most* one competitor can survive. In other words, starting with n species, coexistence is *not* possible in the general case. This prompts part of our investigation: is there coexistence in nature and could it be modelled mathematically?

1.2 Modelling Epidemics

To address modelling epidemics we will explain two epidemic models that will be referred to. The most basic epidemic model is called the SI model. In this model, the population in consideration is divided into two classes: susceptible (S) and infected/infective (I). In general, an SI model of an epidemic is:

$$\begin{aligned}\frac{dS}{dt} &= -\beta S(t)I(t)\\ \frac{dI}{dt} &= \beta S(t)I(t)\end{aligned}$$

where β is the infectious contact rate of the disease. Adding one level of complexity gives the SIS model, which allows for recovery from the disease, with the recovered individuals immediately becoming susceptible again (as opposed to being "removed", which would be an SIR model.) The SIS model is:

$$\begin{aligned}\frac{dS}{dt} &= -\beta S(t)I(t) + \gamma I(t)\\ \frac{dI}{dt} &= \beta S(t)I(t) - \gamma I(t)\end{aligned}$$

where again β is the infectious contact rate and γ is the rate of recovery from the disease. This is the type of epidemic model we will incorporate into our chemostat model. For an introductory reference for these models and other epidemic models, see [6].

1.3 Modelling Epidemics in the Chemostat

The next logical step is to combine the two model types: epidemic and chemostat. There are two main motivations for this: a mathematical one and one driven by potential applications.

The first is that, as mentioned, in a straightforward "typical" chemostat model with n competitors, at most one will survive. This prompts the question: Could the incorporation of epidemic effects into the model change this, and moreover, could it induce the stable coexistence of bacterial competitors? Additionally, does this process happen in nature? This idea was brought on by the results achieved in [36], where an SI epidemic model was combined with a Lotka-Volterra competition model. In the study, it was shown that previously-absent oscillations were induced in the competing populations with the introduction of an epidemic.

The second motivation involves addressing the question above of whether this model has a meaningful application in nature, beginning with studying some bacterial-viral ecology. Induced coexistence of more than one bacterial population could have some interesting interpretations: bacterial diversity in a lake/marine ecosystem, controlling phytoplankton blooms, treatment of human bacterial infections, or the use of multiple bacteria in wastewater treatment, for example.

Mathematically, our model combines an SIS epidemic model with a model of exploitative competition in a chemostat. We chose an SIS model because an SI epidemic model in the chemostat had already been analysed in another context [13], which will be discussed later. The consumption functions will be assumed to be mass action. The exploitative competition involves two species, the stronger of which is affected by the disease. The virus population will not be modelled explicitly in our model, in agreement with most epidemic models. We will assume that the survival of the virus population is not solely dependent on the bacterial population we are modelling. We will now expand on our motivations and on some necessary background knowledge.

It is known that bacteria are present in abundance in marine and lake environments, but it was only recently discovered that viruses are also present, and in even greater abundance than bacteria [5]. Indeed, viruses have been found to have significant impacts on aquatic bacterial populations such as controlling phytoplankton blooms in the ocean. In a letter to Nature, authors Bergh et al. [2] state that "...virus infection may be an important factor in the ecological control of planktonic micro-organisms...". They feel that the significance of the role of viruses in any aquatic environment should not be neglected. Other research reinforces the idea that viruses and bacteriophages play a significant role in aquatic bacterial ecology: [2], [7], [21], [28], and [34] are a sample of this work. Bergh et al. also suggest that by enhancing bacterial diversity, a phage can act as a "controller". Phages reduce the effect of phytoplankton and phytobacterial blooms in the ocean by severely inhibiting the competitive capacity of the blooming microorganism, which allows "lesser" competitors to step in ([5], [7], [34]). Phages usually have a specificity with regards to their prey, and so they often end up attacking only the strongest competitor.

Now, to provide some microbiology background, it is necessary to answer two basic questions. First, what kind of viruses attack bacteria? These special (but not rare) viruses are called bacteriophages, or phages, for short. Phages potentially play a significant role in many bacterial ecological systems, for example it was by C. P. D. Brussard [7] that they "... can have a major impact on phytoplankton population dynamics." Secondly, how do viruses attack bacteria? This virus-bacterium interaction could affect how the model is created. Andre Lwoff's paper titled "Lysogeny" [23] provides a comprehensive look at phages, particularly lysogenic phages (as the title suggests), and at how they function. The following information on phages is attributed to [23]. Phages can be divided into two categories: virulent and temperate. Virulent phages reproduce by infecting a bacterium, replicating inside it, and bursting the cell (lysis), while temperate phages infect a bacterium in the same way, but do not lyse it afterwards. In the second case, the bacterium is now termed "lysogenic", which by definition, is "the hereditary power to produce bacteriophage" [23]. Eventually, lysogenic bacteria could produce new bacteriophages, but *most will not*. Also, after becoming lysogenic, some bacteria lose their lysogenic power, in other words becoming newly susceptible. These last properties of lysogenic bacteria/viruses are most relevant here because they support some choices in our model. We have allowed for "recovery" in our model, which could be a way of modelling lysogeny, since most lysogenic bacteria do not eventually lyse and produce phages and could be seen as recovering from their infection. Although they are not mentioned as often, there are examples of the widespread nature of lysogenic bacteria (also called temperate phages), as can be found in [35], where the proliferation of temperate viruses in Lake Superior was studied. Campbell [11] and Lwoff [23] also report on the widespread nature and significance of lysogenic (temperate) phages.

Some other potential applications deserve mention here. There is some renewed interest in studying the use of lysogenic phages in the treatment of bacterial infections in humans [37], due to the increase in antibiotic-resistant bacteria. Also, enhanced bacterial diversity in wastewater treatment methods might prove advantageous.

2 The model

Our model consists of two populations, competing exploitatively for a single growth-limiting nutrient, $S(t)$. One population, species x, is susceptible to a disease, and this population is divided into two subpopulations of susceptible ($x_s(t)$) and infective ($x_I(t)$). It is possible for the infective subpopulation to recover from the disease, at rate γ. The second population, species y, is not susceptible to the disease. We will analyse this system with a particular interest in determining under what conditions the coexistence of all three populations $x_s(t)$, $x_I(t)$, and $y(t)$ is possible. More specifically, we consider the following model:

$$\begin{aligned}
S'(t) &= (S^0 - S(t))D - \frac{\alpha_s x_s(t)S(t)}{\eta_s} - \frac{\alpha_I x_I(t)S(t)}{\eta_I} - \frac{\alpha_y y(t)S(t)}{\eta_y} \\
x_s'(t) &= x_s(t)(-D_s + \alpha_s S(t)) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\
x_I'(t) &= x_I(t)(-D_I + \alpha_I S(t)) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\
y'(t) &= y(t)(-D_y + \alpha_y S(t)) \\
&\quad \text{with} \quad S(0) \geq 0, x_s(0) \geq 0, x_I(0) \geq 0, \quad \text{and} \quad y(0) \geq 0.
\end{aligned} \tag{1}$$

In the model $S(t)$ denotes the concentration of the growth-limiting nutrient at time t; $x_s(t)$ represents the concentration of the "susceptible" population of microorganisms at time t; $x_I(t)$ represents the concentration of the "infective" population of microorganisms at time t; and $y(t)$ represents the concentration of the second population of microorganisms at time t. As for the parameters, S^0 is the concentration of nutrient in the nutrient reservoir; D is the rate of inflow from the nutrient reservoir and is also the rate of outflow from the main vessel (hence the volume is kept constant in a chemostat); D_s, D_I, and D_y

denote the sum of the species-specific death rate and the rate of ouflow of $x_s(t)$, $x_I(t)$, and $y(t)$ respectively; α_s, α_I, and α_y are the growth coefficients for $x_s(t)$, $x_I(t)$, and $y(t)$ respectively; η_s, η_I, and η_y are growth yield constants (i.e. representing the conversion of nutrient to biomass) for $x_s(t)$, $x_I(t)$, and $y(t)$ respectively; δ is the infectious contact rate of the disease (analogous to β in the SI model described earlier), and γ is the rate of recovery from the disease.

It is natural to assume that being infected is detrimental to the x_I population (as suggested in [11]), and so this will determine the relative values of the parameters. It will be assumed that $x_I(t)$ has a higher death rate than $x_s(t)$, so that $D_I > D_s$. By the same argument it will be assumed that $\alpha_s \geq \alpha_I$. Hence $\frac{D_s}{\alpha_s} < \frac{D_I}{\alpha_I}$. It will also be assumed that the infected population is less efficient in the nutrient conversion process, i.e. that $\eta_s \geq \eta_I$.

As for $y(t)$, we will show that for all species to coexist, it is necessary to assume that $y(t)$ is a weaker competitor than $x_s(t)$, i.e. $\frac{D_y}{\alpha_y} > \frac{D_s}{\alpha_s}$.

3 Preliminary results

3.1 Well-posedness

Lemma 3.1 (Solution Positivity) *Provided that $x_I(0) > 0$ and $y(0) > 0$, all solutions $S(t)$, $x_s(t)$, $x_I(t)$, and $y(t)$ of system (1) remain positive for all $t > 0$. If $x_s(0) > 0$ then $x_s(t)$ remains positive for all $t > 0$. Also if $x_I(0) = 0$, then $x_I(t) \equiv 0$, and similarly if $y(0) = 0$, then $y(t) \equiv 0$. If $x_I(0) = 0$ and $x_s(0) = 0$, then $x_s(t) \equiv 0$.*

Proof.

Assume $x_I(0) = 0$.

Since the right-hand side of (1) is differentiable, it follows by existence and uniqueness theory for initial value problems that if $x_I(t) \equiv 0$, the remaining subsystem has a unique solution. If $x_I(0) = 0$, $x_I(t) \equiv 0$ also satisfies the x_I equation of (1), and so appending $x_I(t) \equiv 0$ to the unique solution of the subsystem gives the unique solution of (1). If $y(0) = 0$, a similar argument yields $y(t) \equiv 0$.

Since system (1) is autonomous, it now follows from the above result that if $y(0) > 0$, then $y(t) > 0$ for all $t > 0$, since the face where $y(t) = 0$ is invariant. Hence, by uniqueness of solutions, $y(t) = 0$ cannot be reached in finite time by any trajectory originating in the interior of $\mathbb{R}^4_+$. Similarly, if $x_I(0) > 0$ then $x_I(t) > 0$ for all $t > 0$.

Suppose that $x_s(0) \geq 0$ and $x_I(0) > 0$. Then $x_s(t) > 0$ for sufficiently small positive t. If there exists a $t_1 > 0$ such that $x_s(t_1) = 0$ where $x_s(t) > 0$ for all $t \in (0, t_1)$, we have that $x_s'(t_1) \leq 0$. But this is a contradiction, since by (1), $x_s'(t_1) = \gamma x_I(t_1) > 0$.

If $x_I(0) = 0$ but $x_s(0) > 0$, it follows that $x_s(t) > 0$ for all $t > 0$ using existence and uniqueness theory. Similarly if $x_I(0) = 0$ and $x_s(0) = 0$ then $x_s(t) \equiv 0$.

Lastly, suppose that there exists a $t_2 > 0$ such that $S(t_2) = 0$, and $S(t) > 0$ for all $t \in (0, t_2)$. Again this would imply that $S'(t_2) \leq 0$ and draws a contradiction, since by (1), $S'(t_2) = S^0 D > 0$. ■

Lemma 3.2 (Boundedness of Solutions) *All solutions $S(t)$, $x_s(t)$, $x_I(t)$ and $y(t)$ of system (1) are bounded for all $t > 0$.*

Proof. Let A be the minimum of $(\frac{\alpha_s}{\eta_s}, \frac{\alpha_I}{\eta_I}, \frac{\alpha_y}{\eta_y})$, and let α be the maximum of $(\alpha_s, \alpha_I, \alpha_y)$. By definition, $D = \min(D, D_s, D_I, D_y)$. Now, notice that:

$$\begin{aligned}
S'(t) &\leq (S^0 - S(t))D - Ax_s(t)S(t) - Ax_I(t)S(t) - Ay(t)S(t) \\
x_s'(t) &\leq x_s(t)(-D + \alpha S(t)) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\
x_I'(t) &\leq x_I(t)(-D + \alpha S(t)) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\
y'(t) &\leq y(t)(-D + \alpha S(t)).
\end{aligned}$$

This means that

$$\begin{aligned}
\left(S(t) + \frac{A}{\alpha}x_s(t) + \frac{A}{\alpha}x_I(t) + \frac{A}{\alpha}y(t)\right)' &\leq (S^0 - S(t))D - \frac{AD}{\alpha}x_s(t) \\
&\quad -\frac{AD}{\alpha}x_I(t) - \frac{AD}{\alpha}y(t) \\
&= D(S^0 - S(t) - \frac{A}{\alpha}x_s(t) \\
&\quad -\frac{A}{\alpha}x_I(t) - \frac{A}{\alpha}y(t))
\end{aligned}$$

Now, let $z(t) = S(t) + \frac{A}{\alpha}x_s(t) + \frac{A}{\alpha}x_I(t) + \frac{A}{\alpha}y(t)$. Then using the previous calculation it follows that $z'(t) \leq D(S^0 - z(t))$. Solving this differential inequality we get

$$z(t) \leq S^0 - (S^0 - z(0))e^{-Dt}.$$

Therefore, given any $\epsilon > 0$, $z(t) \leq S^0 + \epsilon$ for all sufficiently large t. Since all solutions are nonnegative by Lemma 3.1, then all solutions are bounded, for all $t > 0$. ■

Corollary 3.1 *The set*

$$S = \{(S, x_s, x_I, y) : S, x_s, x_I, y \geq 0; 0 \leq S + \frac{A}{\alpha}(x_s + x_I + y) \leq S^0\}$$

is a global attractor for (1).

Proposition 3.1 *Consider system (1). If there exists a* $t_0 \geq 0$ *such that* $S(t_0) \leq S^0$ *then* $S(t) \leq S^0$ *for all* $t \geq t_0$.

Proof.

Suppose that there exists a first $t_1 \geq t_0$ such that $S(t_1) = S^0$. Then either $S(t_1) = S^0$, $x_s(t_1) = x_I(t_1) = y(t_1) = 0$, and we are at equilibrium and remain there forever, or at least one of $x_s(t_1)$, $x_I(t_1)$, or $y(t_1)$ is positive.

But from (1) we have

$$\begin{aligned} S'(t_1) &= (S^0 - S(t_1))D - \frac{\alpha_s x_s(t_1)S(t_1)}{\eta_s} - \frac{\alpha_I x_I(t_1)S(t_1)}{\eta_I} - \frac{\alpha_y y(t_1)S(t_1)}{\eta_y} \\ &= -\frac{\alpha_s x_s(t_1)S^0}{\eta_s} - \frac{\alpha_I x_I(t_1)S^0}{\eta_I} - \frac{\alpha_y y(t_1)S^0}{\eta_y} \\ &< 0 \end{aligned}$$

by Lemma 3.1, and hence the result follows. ■

3.2 Subsystems

There are two subsystems of (1) that are of interest.

Subsystem: Disease-free system, $x_I(0) = 0$

$$\begin{aligned} S'(t) &= (S^0 - S(t))D - \frac{\alpha_s x_s(t)S(t)}{\eta_s} - \frac{\alpha_y y(t)S(t)}{\eta_y} \\ x_s'(t) &= x_s(t)(-D_s + \alpha_s S(t)) \\ y'(t) &= y(t)(-D_y + \alpha_y S(t)) \\ &\quad \text{with} \quad S(0) \geq 0, \quad x_s(0) \geq 0, \quad \text{and} \quad y(0) \geq 0. \end{aligned}$$

If $x_I(0) = 0$ then $x_I(t) \equiv 0$, and the system is equivalent to a two-species chemostat model with no disease present, where the two populations are competing exploitatively for the nutrient. This model represents a special case of the model analysed in [39], where it is proved that, at most, one species can survive. More specifically, if $\frac{D_s}{\alpha_s} \geq S^0$ then $x_s(t) \to 0$ as $t \to \infty$, or if $\frac{D_y}{\alpha_y} \geq S^0$ then $y(t) \to 0$ as $t \to \infty$. On the other hand if $\frac{D_s}{\alpha_s} < \min\left(S^0, \frac{D_y}{\alpha_y}\right)$ then $x_s(t)$ is the sole survivor, whereas if $\frac{D_y}{\alpha_y} < \min\left(S^0, \frac{D_s}{\alpha_s}\right)$ then $y(t)$ is the sole survivor.

Subsystem: $y(0) = 0$

$$\begin{aligned} S'(t) &= (S^0 - S(t))D - \frac{\alpha_s x_s(t)S(t)}{\eta_s} - \frac{\alpha_I x_I(t)S(t)}{\eta_I} \\ x_s'(t) &= x_s(t)(-D_s + \alpha_s S(t)) - \delta x_s(t)x_I(t) + \gamma x_I(t) \qquad (2) \\ x_I'(t) &= x_I(t)(-D_I + \alpha_I S(t)) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\ &\quad \text{with} \quad S(0) \geq 0, x_s(0) \geq 0, \quad \text{and} \quad x_I(0) \geq 0. \qquad (3) \end{aligned}$$

When $y(0) = 0$, it follows immediately that $y(t) \equiv 0$. This system has not yet been analysed. Its local and global analysis will be included in this thesis.

In fact, much of the analysis of (1) is based on the analysis of this particular subsystem.

Notice that if $x_I(0) > 0$, a subsystem of (1) with $x_s(t) \equiv 0$ is not possible. The reason for this is that if $x_s(0) = 0$ but $x_I(0) > 0$, then $x_s'(0) = \gamma x_I(t) > 0$. Of course if $S(0) = 0$ there is also no subsystem possible without S, since the $S^0 D$ term in S' keeps $S(t) > 0$. Note that when $\gamma = 0$ the system (1) becomes an SI model in the chemostat. This model has been analysed with a different interpretation in [13] and [38].

4 Equilibria and Local Analysis

4.1 Equilibria

Equilibria of the following form are possible for (1):

$$\begin{aligned}
E_0 &= (S^0, 0, 0, 0) \\
E_{1x} &= (\bar{S}, \bar{x}_s, 0, 0) \\
E_{1y} &= (\breve{S}, 0, 0, \breve{y}) \\
E_2 &= (S^*, x_s^*, x_I^*, 0) \\
E_3 &= (\hat{S}, \hat{x}_s, \hat{x}_I, \hat{y})
\end{aligned}$$

where

$$\bar{S} = \frac{D_s}{\alpha_s}, \qquad \bar{x}_s = \left(\frac{D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right), \qquad \breve{S} = \frac{D_y}{\alpha_y},$$

$$\breve{y} = \left(\frac{D\eta_y}{D_y}\right)\left(S^0 - \frac{D_y}{\alpha_y}\right), \qquad x_s^* = \frac{D_I - \alpha_I S^* + \gamma}{\delta},$$

$$x_I^* = \frac{x_s^*(-D_s + \alpha_s S^*)}{(\delta x_s^* - \gamma)},$$

S^* satisfies $(S^0 - S^*)D - \dfrac{\alpha_s x_s^* S^*}{\eta_s} - \dfrac{\alpha_I x_I^* S^*}{\eta_I} = 0$ with $\dfrac{D_s}{\alpha_s} < S^* < \dfrac{D_I}{\alpha_I}$ [1],

$$\hat{S} = \frac{D_y}{\alpha_y}, \qquad \hat{x}_s = \left[D_I + \gamma - \alpha_I\left(\frac{D_y}{\alpha_y}\right)\right]\left(\frac{1}{\delta}\right), \qquad \hat{x}_I = \frac{\hat{x}_s(-D_s + \alpha_s \hat{S})}{(\delta \hat{x}_s - \gamma)},$$

$$\text{and} \qquad \hat{y} = \left[(S^0 - \hat{S})D - \frac{\alpha_s \hat{x}_s \hat{S}}{\eta_s} - \frac{\alpha_I \hat{x}_I \hat{S}}{\eta_I}\right]\left(\frac{\eta_y}{\alpha_y \hat{S}}\right).$$

[1] Please see §4.2.4 for justification.

4.2 Local analysis for subsystem (2)

Equilibria of the following form are possible for (2):

$$\begin{aligned} E_{0^*} &= (S^0, 0, 0) \\ E_{1^*} &= (\bar{S}, \bar{x}_s, 0) \\ E_{2^*} &= (S^*, x_s^*, x_I^*) \end{aligned}$$

where the components are as given in §4.1.

4.2.1 Jacobian for (2)

In order to determine the local stability of the equilibria we compute the following Jacobian matrix:

$$J = \begin{bmatrix} -D - \frac{\alpha_s}{\eta_s} x_s(t) - \frac{\alpha_I}{\eta_I} x_I(t) & -\frac{\alpha_s}{\eta_s} S(t) & -\frac{\alpha_I}{\eta_I} S(t) \\ \alpha_s x_s(t) & -D_s + \alpha_s S(t) - \delta x_I(t) & -\delta x_s(t) + \gamma \\ \alpha_I x_I(t) & \delta x_I(t) & -D_I + \alpha_I S(t) + \delta x_s(t) - \gamma \end{bmatrix}. \tag{4}$$

4.2.2 E_{0^*} local stability

Recall that $E_{0^*} = (S^0, 0, 0)$. E_{0^*} always exists. Evaluating the Jacobian (4) at E_{0^*}, we obtain:

$$J_{E_{0^*}} = \begin{bmatrix} -D & -\frac{\alpha_s}{\eta_s} S^0 & -\frac{\alpha_I}{\eta_I} S^0 \\ 0 & -D_s + \alpha_s S^0 & \gamma \\ 0 & 0 & -D_I + \alpha_I S^0 - \gamma \end{bmatrix}.$$

Since $J_{E_{0*}}$ is upper triangular, the eigenvalues can be read directly from the diagonal of the matrix:

$$\begin{aligned}\lambda_1 &= -D \\ \lambda_2 &= -D_s + \alpha_s S^0 \\ \lambda_3 &= -D_I + \alpha_I S^0 - \gamma\end{aligned}$$

Inspecting these eigenvalues, we can see that $\lambda_1 < 0$ always, $\lambda_2 < 0$ when $S^0 < \frac{D_s}{\alpha_s}$ and $\lambda_3 < 0$ when $S^0 < \frac{\gamma + D_I}{\alpha_I}$. However, by our assumptions on the growth and death rates, $\frac{D_s}{\alpha_s} < \frac{\gamma+D_I}{\alpha_I}$, and so E_{0*} is locally asymptotically stable if $S^0 < \frac{D_s}{\alpha_s}$ and is unstable if $S^0 > \frac{D_s}{\alpha_s}$.

4.2.3 E_{1*} local stability

Recall that $E_{1*} = (\bar{S}, \bar{x}_s, 0)$, where $\bar{S} = \frac{D_s}{\alpha_s}$ and $\bar{x}_s = \left(\frac{D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right)$. E_{1*} exists when its first two components are positive. The first component is always positive, and the second is positive when $S^0 > \frac{D_s}{\alpha_s}$. Hence E_{1*} exists when $S^0 > \frac{D_s}{\alpha_s}$.

Now, evaluating (4) at E_{1*} we obtain the following matrix:

$$J_{E_{1*}} = \begin{bmatrix} -D - \frac{\alpha_s}{\eta_s}\bar{x}_s & -\frac{\alpha_s}{\eta_s}\bar{S} & -\frac{\alpha_I}{\eta_I}\bar{S} \\ \alpha_s\bar{x}_s & -D_s + \alpha_s\bar{S} & -\delta\bar{x}_s + \gamma \\ \alpha_I\bar{x}_I & \delta\bar{x}_I & -D_I + \alpha_I\bar{S} + \delta\bar{x}_s - \gamma \end{bmatrix}.$$

Substituting in our specific values for E_{1*} gives:

$$\begin{bmatrix} -D - \left(\frac{\alpha_s D}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) & -\frac{\alpha_s}{\eta_s}\left(\frac{D_s}{\alpha_s}\right) & -\frac{\alpha_I}{\eta_I}\left(\frac{D_s}{\alpha_s}\right) \\ \left(\frac{\alpha_s D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) & -D_s + \alpha_s\left(\frac{D_s}{\alpha_s}\right) & -\left(\frac{\delta D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) + \gamma \\ 0 & 0 & -D_I + \alpha_I\left(\frac{D_s}{\alpha_s}\right) + \left(\frac{\delta D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) - \gamma \end{bmatrix},$$

which reduces to

$$\begin{bmatrix} -\frac{\alpha_s S^0 D}{D_s} & -\frac{D_s}{\eta_s} & -\frac{\alpha_I D_s}{\eta_I \alpha_s} \\ \left(\frac{\alpha_s D \eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) & 0 & -\left(\frac{\delta D \eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) + \gamma \\ 0 & 0 & -D_I + \alpha_I\left(\frac{D_s}{\alpha_s}\right) + \left(\frac{\delta D \eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right) - \gamma \end{bmatrix}.$$

The characteristic equation is:

$$(\lambda + D_I - \alpha_I \bar{S} - \delta \bar{x}_s + \gamma)\left(\lambda^2 + \left(\frac{\alpha_s S^0 D}{D_s}\right)\lambda + \alpha_s D\left(S^0 - \frac{D_s}{\alpha_s}\right)\right) = 0.$$

One eigenvalue comes directly out of the linear factor of this equation, yielding the first condition for stability of E_{1*}:

$$\lambda_1 = -D_I + \alpha_I \bar{S} + \delta \bar{x}_s - \gamma < 0.$$

This leaves a quadratic in λ:

$$\lambda^2 + \left(\frac{\alpha_s S^0 D}{D_s}\right)\lambda + \alpha_s D\left(S^0 - \frac{D_s}{\alpha_s}\right) = 0,$$

which can be analysed using the Routh-Hurwitz Criterion for two dimensions. That is, for a second order polynomial, the roots have negative real part if and only if the coefficients of the characteristic equation are positive [15] [18] [30]. The coefficient of the linear term is always positive. The constant term is positive whenever E_{1*} exists.

Hence, when it exists, E_{1*} is locally asymptotically stable when $-D_I + \alpha_I \bar{S} + \delta \bar{x}_s - \gamma < 0$. Substituting for $\bar{S}$ and $\bar{x}_s$, this condition can be rewritten as $S^0 < \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D \delta \eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$. Combining the existence and stability requirements it follows that E_{1*} exists and is locally asymptotically stable when $\frac{D_s}{\alpha_s} < S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$, and is unstable when the right inequality is reversed.

4.2.4 E_{2^*} local stability

Recall that $E_{2^*} = (S^*, x_s^*, x_I^*)$, where $x_s^* = \frac{D_I - \alpha_I S^* + \gamma}{\delta}$, $x_I^* = \frac{x_s^*(-D_s + \alpha_s S^*)}{(\delta x_s^* - \gamma)}$, and S^* satisfies $(S^0 - S^*)D - \frac{\alpha_s x_s^* S^*}{\eta_s} - \frac{\alpha_I x_I^* S^*}{\eta_I} = 0$. So that $x_s^* > 0$ and $x_I^* > 0$, it follows that $\frac{D_s}{\alpha_s} < S^* < \frac{D_I}{\alpha_I}$ †.

† Proof: $x_s^* > 0 \Longleftrightarrow S^* < \frac{D_I + \gamma}{\alpha_I}$, and $x_I^* > 0$ if and only if both its numerator and denominator have the same sign. If $S^* < \frac{D_s}{\alpha_s}$ then the denominator is positive but the numerator is negative. If $S^* > \frac{D_I}{\alpha_I}$ then the numerator is positive and the denominator is negative. However, they are both positive if $\frac{D_s}{\alpha_s} < S^* < \frac{D_I}{\alpha_I}$.■

Now, let us examine the conditions for existence of this equilibrium.

Lemma 4.1 (Existence and Uniqueness of E_{2^*} (when $\eta_s \geq \eta_I$)) *E_{2^*} exists and is unique if $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$.*

See Proofs (§8) for a proof of the above lemma.

We now return to finding conditions for the local stability of E_{2^*}. Evaluating the Jacobian (4) at E_{2^*} we obtain:

$$J_{E_{2^*}} = \begin{bmatrix} -D - \frac{\alpha_s}{\eta_s}x_s^* - \frac{\alpha_I}{\eta_I}x_I^* & -\frac{\alpha_s}{\eta_s}S^* & -\frac{\alpha_I}{\eta_I}S^* \\ \alpha_s x_s^* & -D_s + \alpha_s S^* - \delta x_I^* & -\delta x_s^* + \gamma \\ \alpha_I x_I^* & \delta x_I^* & -D_I + \alpha_I S^* + \delta x_s^* - \gamma \end{bmatrix},$$

which simplifies to

$$\begin{bmatrix} -\frac{S^0 D}{S^*} & -\frac{\alpha_s}{\eta_s}S^* & -\frac{\alpha_I}{\eta_I}S^* \\ \alpha_s x_s^* & -\frac{\gamma x_I^*}{x_s^*} & -\delta x_s^* + \gamma \\ \alpha_I x_I^* & \delta x_I^* & 0 \end{bmatrix}.$$

The characteristic equation is of the form $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where

$$\begin{aligned}
a_1 &= \frac{S^0 D}{S^*} + \frac{\gamma x_I^*}{x_s^*}, \\
a_2 &= \frac{\gamma S^0 D x_I^*}{x_s^* S^*} + \frac{\alpha_s^2 x_s^* S^*}{\eta_s} + \delta x_I^*(\delta x_s^* - \gamma) + \frac{\alpha_I^2 x_I^* S^*}{\eta_I}, \qquad \text{and} \\
a_3 &= \frac{\delta S^0 D x_I^*}{S^*}(\delta x_s^* - \gamma) + \alpha_s \alpha_I \delta S^* x_s^* x_I^* \left(\frac{1}{\eta_I} - \frac{1}{\eta_s}\right) \\
&\quad + \frac{\alpha_s \alpha_I \gamma S^* x_I^*}{\eta_s} + \frac{\alpha_I^2 \gamma S^* (x_I^*)^2}{\eta_I x_s^*}.
\end{aligned}$$

By the Routh-Hurwitz Criterion for third order polynomials , all roots of the characteristic equation have negative real part if and only if $a_1 > 0$, $a_3 > 0$, and $a_1 a_2 > a_3$ [15] [18] [30]. Given the positivity of parameters, $a_1 > 0$. The coefficient a_3 is positive when E_{2^*} exists, i.e. when $x_s^* > \frac{\gamma}{\delta}$.

Finally, we investigate the final condition, $a_1 a_2 > a_3$:

$$\begin{aligned}
a_1 a_2 - a_3 &= \frac{(S^0 D)^2 \gamma x_I^*}{x_s^* (S^*)^2} + \frac{S^0 D (\alpha_s)^2 x_s^*}{\eta_s} + \frac{S^0 D (\alpha_I)^2 x_I^*}{\eta_I} + \frac{\gamma^2 S^0 D (x_I^*)^2}{S^* (x_s^*)^2} \\
&\quad + \frac{(\alpha_s)^2 \gamma x_I^* S^*}{\eta_s} + \gamma \delta^2 (x_I^*)^2 - \frac{\gamma^2 \delta (x_I^*)^2}{x_s^*} \\
&\quad - \frac{\alpha_s \alpha_I \delta S^* x_s^* x_I^*}{\eta_I} + \frac{\alpha_s \alpha_I \delta S^* x_s^* x_I^*}{\eta_s} - \frac{\alpha_s \alpha_I \gamma x_I^* S^*}{\eta_s}
\end{aligned}$$

Since $S'(t) = 0$ at equilibrium, it follows from (2) that

$$S^0 = \frac{1}{D}\left(S^* D + \frac{\alpha_s x_s^* S^*}{\eta_s} + \frac{\alpha_I x_I^* S^*}{\eta_I}\right).$$

Therefore,

$$
\begin{aligned}
a_1a_2 - a_3 \;=\;& \frac{\left(S^*D + \frac{\alpha_s x_s^* S^*}{\eta_s} + \frac{\alpha_I x_I^* S^*}{\eta_I}\right)^2 \gamma x_I^*}{x_s^*(S^*)^2} \\
&+ \frac{\left(S^*D + \frac{\alpha_s x_s^* S^*}{\eta_s} + \frac{\alpha_I x_I^* S^*}{\eta_I}\right)(\alpha_s)^2 x_s^*}{\eta_s} \\
&+ \frac{\left(S^*D + \frac{\alpha_s x_s^* S^*}{\eta_s} + \frac{\alpha_I x_I^* S^*}{\eta_I}\right)(\alpha_I)^2 x_I^*}{\eta_I} \\
&+ \frac{\gamma^2\left(S^*D + \frac{\alpha_s x_s^* S^*}{\eta_s} + \frac{\alpha_I x_I^* S^*}{\eta_I}\right)(x_I^*)^2}{S^*(x_s^*)^2} \\
&+ \frac{(\alpha_s)^2\gamma x_I^* S^*}{\eta_s} + \gamma\delta^2(x_I^*)^2 - \frac{\gamma^2\delta(x_I^*)^2}{x_s^*} - \frac{\alpha_s\alpha_I\delta S^* x_s^* x_I^*}{\eta_I} \\
&+ \frac{\alpha_s\alpha_I\delta S^* x_s^* x_I^*}{\eta_s} - \frac{\alpha_s\alpha_I\gamma x_I^* S^*}{\eta_s} \\
=\;& \frac{(\gamma)^2(x_I^*)^2 D}{(x_s^*)^2} + \frac{(\gamma)^2\alpha_s(x_I^*)^2}{x_s^*\eta_s} + \frac{(\gamma)^2\alpha_I(x_I^*)^3}{(x_s^*)^2\eta_I} + \frac{D^2\gamma x_I^*}{x_s^*} \\
&+ \frac{2\alpha_s\gamma x_I^* D}{\eta_s} + \frac{2\alpha_I\gamma(x_I^*)^2 D}{x_s^*\eta_I} + \frac{(\alpha_s)^2\gamma x_I^* x_s^*}{(\eta_s)^2} + \frac{2\alpha_s\alpha_I\gamma(x_I^*)^2}{\eta_s\eta_I} \\
&+ \frac{\gamma(x_I^*)^3(\alpha_I)^2}{x_s^*(\eta_I)^2} + \frac{(\alpha_s)^2 x_s^* S^* D}{\eta_s} + \frac{(\alpha_s)^3(x_s^*)^2 S^*}{(\eta_s)^2} + \frac{(\alpha_s)^2\alpha_I x_s^* x_I^* S^*}{\eta_s\eta_I} \\
&+ \frac{(\alpha_I)^2 x_I^* S^* D}{\eta_I} + \frac{(\alpha_I)^2\alpha_s x_s^* x_I^* S^*}{\eta_s\eta_I} + \frac{(\alpha_I)^3(x_I^*)^2 S^*}{(\eta_I)^2} + \frac{(\alpha_s)^2\gamma x_I^* S^*}{\eta_s} \\
&+ \gamma\delta(x_I^*)^2\left(\delta - \frac{\gamma}{x_s^*}\right) + \frac{\alpha_s\alpha_I S^* x_I^*}{\eta_s}(\delta x_s^* - \gamma) - \frac{\alpha_s\alpha_I\delta S^* x_s^* x_I^*}{\eta_I}.
\end{aligned}
$$

Factoring out a common denominator we have:

$$\begin{aligned} a_1a_2 - a_3 \quad = \quad & \frac{1}{\eta_s^2\eta_I^2(x_s^*)^2}(\eta_s^2\eta_I^2(\gamma)^2(x_I^*)^2D + \eta_s\eta_I^2(\gamma)^2\alpha_s x_s^*(x_I^*)^2 + \eta_s^2\eta_I(\gamma)^2\alpha_I(x_I^*)^3 \\ & +D^2\eta_s^2\eta_I^2\gamma x_s^* x_I^* + 2\eta_s\eta_I^2\gamma\alpha_s(x_s^*)^2x_I^*D + 2\eta_s^2\eta_I\gamma\alpha_I x_s^*(x_I^*)^2D \\ & +\eta_I^2\gamma(\alpha_s)^2(x_s^*)^3x_I^* + 2\eta_s\eta_I\gamma\alpha_s\alpha_I(x_s^*)^2(x_I^*)^2 + \eta_s^2\gamma(\alpha_I)^2x_s^*(x_I^*)^3 \\ & +\eta_s\eta_I^2(\alpha_s)^2(x_s^*)^3S^*D + \eta_I^2(\alpha_s)^3(x_s^*)^4S^* + \eta_s^2\eta_I(\alpha_I)^2(x_s^*)^2x_I^*S^*D \\ & +\eta_s\eta_I\alpha_s\alpha_I(x_s^*)^3x_I^*(\alpha_s + \alpha_I - \eta_s\delta + \eta_I\delta) + \eta_s^2(\alpha_I)^3(x_s^*)^2(x_I^*)^2S^* \\ & +\eta_s^2\eta_I^2\gamma\delta x_s^*(x_I^*)^2(\delta x_s^* - \gamma) + \eta_s\eta_I^2\gamma(x_s^*)^2x_I^*(\alpha_s - \alpha_I)). \end{aligned} \tag{5}$$

Now, recall that if $a_1a_2 - a_3 > 0$, we have local asymptotic stability. Since we are assuming that $\alpha_s \geq \alpha_I$ and $x_s^* > \frac{\gamma}{\delta}$ holds in order for E_{2^*} to exist, a sufficient condition for $a_1a_2 - a_3 > 0$ and hence for E_{2^*} to be locally asymptotically stable is that $\frac{\alpha_I+\alpha_s}{\delta} \geq \eta_s - \eta_I$. Although the number of positive terms seems to far outweigh the number of negative terms in $a_1a_2 - a_3$, E_{2^*} can lose stability through a Hopf bifurcation, as we will show later.

We have just proven existence, uniqueness, and local asymptotic stability of E_{2^*} when $\eta_s \geq \eta_I$. For the case when $\eta_I > \eta_s$, we can similarly obtain a condition for existence, uniqueness, and local asymptotic stability of E_{2^*}, as summarized in the following results. In this case it is also possible for there to be multiple E_{2^*} equilibria, which will be illustrated with an example.

Lemma 4.2 (Existence and Uniqueness of E_{2^*} when $\eta_I > \eta_s$) *E_{2^*} exists and is unique when $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$ and when either of the following criteria hold:*

(a) $D_I < \gamma$, or

(b) $\eta_I \leq \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$.

See Proofs (§8) for a proof of the above lemma.

Lemma 4.3 (Local asymptotic stability of E_{2^*} when $\eta_I > \eta_s$) *E_{2^*} is locally asymptotically stable when $\eta_I \leq \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$ (this is criterion (b) for existence in the previous lemma).*

See Proofs (§8) for a proof of the above lemma.

Remark: In the case where $\eta_I > \eta_s$ and where criterion (b) from Lemma 4.2 is *not* satisfied, it is possible for more than one E_{2^*} to exist. See below for a detailed example of this case. Also in this case, it is interesting to note that $a_1a_2 - a_3$ is always positive (see equation (5)), and so loss of stability is never via a Hopf bifurcation. However $a_3 < 0$ is possible.

Example of nonunique E_{2^*}

As mentioned above, it is possible for more than one E_{2^*} equilibrium to arise. Recall that even though we have no explicit expression for E_{2^*}, we can examine it by examining the function $f(S)$, whose roots give possible values for the S component of E_{2^*}. $f(S)$ is defined explicitly in the proof of Lemma 4.1, in §8. We are only interested in roots which give an E_{2^*} with all components positive. Hence we only consider roots that fall in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$. It is possible to have three valid roots when the criterion (b) of Lemma 4.2 fails, i.e. when $\eta_I > \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$. We give a specific example of this case below, along with a graph of $f(S)$ under those circumstances. Note that two of the three equilibria of the form E_{2^*} arise out of a saddle-node bifurcation, which will be described in more detail in §6.

Take the following parameter values:

$$S^0 = 110, \quad D = 0.19, \quad D_s = 0.2, \quad D_I = 1, \quad \delta = 1,$$

$$\alpha_s = 0.5, \quad \alpha_I = 0.4, \quad \eta_s = 0.01, \quad \eta_I = 1, \quad \text{and} \quad \gamma = 0.02.$$

Note that the feasible region for S^* where we get positive equilibria is, in this case, in $S^* \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right) = (0.4, 2.5)$. Note also that the criterion $\eta_I \leq \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$ fails in this case, i.e. that $\eta_I = 1 > \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s \approx 0.01024$. These parameter values give the function

$$f(S) = -0.0792S^3 + 0.4024S^2 - 0.594684S + 0.209.$$

Solving $f(S) = 0$, we have three distinct equilibria E_{2^*}, with S^* component equal to: 0.5094696702, 2.074468768, and 2.496869643. Note that all three fall in the valid region (where the components of E_{2^*} are positive) of $S^* \in (0.4, 2.5)$. See Figure 2 for an illustration of $f(S)$ and its three valid roots.

This completes the local stability analysis of subsystem (2).

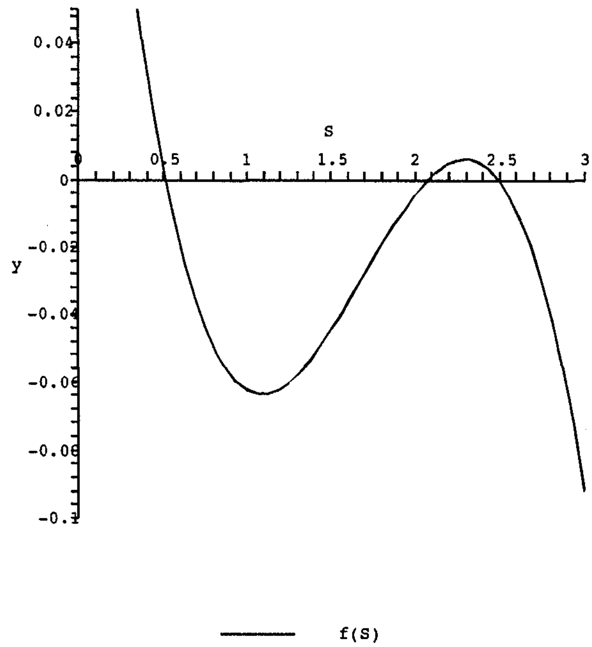

Figure 2: $f(S)$ vs. $S(t)$ when $\eta_I > \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$; parameters are $D = 0.19$, $D_s = 0.2$, $D_I = 1$, $\alpha_s = 0.5$, $\alpha_I = 0.4$, $\eta_s = 0.01$, $\eta_I = 1$, $\delta = 1$, and $\gamma = 0.02$; modelled in MAPLE. Note this cubic has three roots in the interval $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right) = (0.4, 2.5)$: 0.5094696702, 2.074468768, and 2.496869643, and hence E_{2^*} is not unique in this example.

4.3 Local analysis for the full system

4.3.1 Jacobian for (1)

Taking the partial derivatives of $S'(t)$, $x_s'(t)$, $x_I'(t)$, and $y(t)$ from (1), we compute the following Jacobian matrix:

$$J = \begin{bmatrix} -D - \frac{\alpha_s}{\eta_s} x_s(t) - \frac{\alpha_I}{\eta_I} x_I(t) - \frac{\alpha_y}{\eta_y} y(t) & -\frac{\alpha_s}{\eta_s} S(t) & -\frac{\alpha_I}{\eta_I} S(t) & -\frac{\alpha_y}{\eta_y} S(t) \\ \alpha_s x_s(t) & -D_s + \alpha_s S(t) - \delta x_I(t) & -\delta x_s(t) + \gamma & 0 \\ \alpha_I x_I(t) & \delta x_I(t) & -D_I + \alpha_I S(t) + \delta x_s(t) - \gamma & 0 \\ \alpha_y y(t) & 0 & 0 & -D_y + \alpha_y S(t) \end{bmatrix} \tag{6}$$

4.3.2 E_0 local stability

Recall that $E_0 = (S^0, 0, 0, 0)$. E_0 always exists. Substituting E_0 into the Jacobian (6), we obtain:

$$J_{E_0} = \begin{bmatrix} -D & -\frac{\alpha_s}{\eta_s}S^0 & -\frac{\alpha_I}{\eta_I}S^0 & \frac{\alpha_y}{\eta_y}S^0 \\ 0 & -D_s + \alpha_s S^0 & \gamma & 0 \\ 0 & 0 & -D_I + \alpha_I S^0 - \gamma & 0 \\ 0 & 0 & 0 & -D_y + \alpha_y S^0 \end{bmatrix}.$$

Notice that the above matrix contains the Jacobian matrix for E_{0*} as a submatrix, and so its characteristic equation is based on the characteristic equation from $J_{E_{0*}}$. Hence $S^0 < \frac{D_s}{\alpha_s}$ (which arose from the analysis of $J_{E_{0*}}$) is a necessary condition for the local asymptotic stability of E_0.

The fourth (new) eigenvalue $\lambda = -D_y + \alpha_y S^0$ is negative when $S^0 < \frac{D_y}{\alpha_y}$. Therefore E_0 is locally asymptotically stable when $S^0 < \min\left(\frac{D_s}{\alpha_s}, \frac{D_y}{\alpha_y}\right)$, and unstable if $S^0 > \frac{D_y}{\alpha_y}$ or $S^0 > \frac{D_s}{\alpha_s}$.

4.3.3 E_{1x} local stability

Recall that $E_{1x} = (\bar{S}, \bar{x}_s, 0, 0)$, where $\bar{S} = \frac{D_s}{\alpha_s}$ and $\bar{x}_s = \left(\frac{D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right)$. As with E_{1*}, E_{1x} exists when $\frac{D_s}{\alpha_s} < S^0$.

The Jacobian (6) at E_{1x} is:

$$J_{E_{1x}} = \begin{bmatrix} -\frac{\alpha_s S^0 D}{D_s} & -\frac{D_s}{\eta_s} & -\frac{\alpha_I D_s}{\eta_I \alpha_s} & -\frac{\alpha_y D_s}{\eta_y \alpha_s} \\ \alpha_s \quad \frac{\eta_s S^0 D}{D_s} - \frac{D\eta_s}{\alpha_s} & 0 & -\delta \quad \frac{\eta_s S^0 D}{D_s} - \frac{D\eta_s}{\alpha_s} \quad + \gamma & 0 \\ 0 & 0 & -D_I + \alpha_I \quad \frac{D_s}{\alpha_s} \quad + \delta \quad \frac{\eta_s S^0 D}{D_s} - \frac{D\eta_s}{\alpha_s} \quad - \gamma & 0 \\ 0 & 0 & 0 & -D_y + \alpha_y \quad \frac{D_s}{\alpha_s} \end{bmatrix}.$$

Again, notice that the above matrix contains the Jacobian matrix for E_{1*} as a 3×3 submatrix, and so its characteristic equation is based on the characteristic equation from $J_{E_{1*}}$. Its eigenvalues have negative real part provided $S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$.

The fourth and "new" eigenvalue that arises in system (1) is $\lambda = -D_y + \alpha_y\left(\frac{D_s}{\alpha_s}\right)$. This eigenvalue is negative under the assumption $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$, and so E_{1x} exists and is asymptotically stable when $\frac{D_s}{\alpha_s} < S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$ and $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$.

4.3.4 E_{1y} local stability

Recall that $E_{1y} = (\breve{S}, 0, 0, \breve{y})$, with $\breve{S} = \frac{D_y}{\alpha_y}$ and $\breve{y} = \left(\frac{D\eta_y}{D_y}\right)\left(S^0 - \frac{D_y}{\alpha_y}\right)$. E_{1y} exists when $S^0 > \frac{D_y}{\alpha_y}$. We will show that it is locally asymptotically stable when it exists and when $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$.

The Jacobian (6) at E_{1y} is:

$$J_{E_{1y}} = \begin{bmatrix} -\frac{\alpha_y S^0 D}{D_y} & -\frac{\alpha_s D_y}{\eta_s \alpha_y} & -\frac{\alpha_I D_y}{\eta_I \alpha_y} & -\frac{D_y}{\eta_y} \\ 0 & -D_s + \frac{\alpha_s D_y}{\alpha_y} & \gamma & 0 \\ 0 & 0 & -D_I + \alpha_I\left(\frac{D_y}{\alpha_y}\right) - \gamma & 0 \\ \left(\frac{\alpha_y D\eta_y}{D_y}\right)\left(S^0 - \frac{D_y}{\alpha_y}\right) & 0 & 0 & 0 \end{bmatrix}.$$

The characteristic equation is:

$$\left(-D_I + \frac{\alpha_I D_y}{\alpha_y} - \gamma - \lambda\right)\left(-D_s + \frac{\alpha_s D_y}{\alpha_y} - \lambda\right) \cdot \left[\lambda^2 + \frac{\alpha_y S^0 D}{D_y}\lambda + (\alpha_y D)\left(S^0 - \frac{D_y}{\alpha_y}\right)\right] = 0.$$

Two eigenvalues are immediately clear:

$$\lambda_1 = \alpha_I\left(\frac{D_y}{\alpha_y} - \frac{D_I + \gamma}{\alpha_I}\right)$$

$$\lambda_2 = \alpha_s \left(\frac{D_y}{\alpha_y} - \frac{D_s}{\alpha_s} \right)$$

Both λ_1 and λ_2 are negative when $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$.

We can use the Routh-Hurwitz Criterion for the remaining quadratic in λ, which requires that the coefficients of the quadratic be positive [15] [30] [18]. The first coefficient, $\frac{\alpha_y D S^0}{D_y}$, is always positive; the second coefficient, $\alpha_y D \left(S^0 - \frac{D_y}{\alpha_y} \right)$, is positive when E_{1y} exists.

Hence, E_{1y} is locally asymptotically stable when it exists and when $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$, but is unstable if $\frac{D_y}{\alpha_y} > \frac{D_s}{\alpha_s}$.

4.3.5 E_2 local stability

Recall that $E_2 = (S^*, x_s^*, x_I^*, 0)$, with the following conditions: $x_s^* = \frac{D_I - \alpha_I S^* + \gamma}{\delta}$, $x_I^* = \frac{x_s^*(-D_s + \alpha_s S^*)}{(\delta x_s^* - \gamma)}$, and S^* satisfies $(S^0 - S^*)D - \frac{\alpha_s x_s^* S^*}{\eta_s} - \frac{\alpha_I x_I^* S^*}{\eta_I} = 0$. So that $x_s^* > 0$ and $x_I^* > 0$, it follows that $\frac{D_s}{\alpha_s} < S^* < \frac{D_I}{\alpha_I}$. This criterion is proved in §4.2.4.

Lemma 4.4 (Existence and Uniqueness of E_2 (when $\eta_s \geq \eta_I$)) *E_2 exists and*

is unique when $S^0 > \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$.

Proof. For the proof of existence, refer to the proof of Lemma 4.1 in §8.

We now determine conditions for local asymptotic stability of E_2. Evaluating the Jacobian (6) about E_2 we obtain:

$$\begin{bmatrix} -\frac{S^0 D}{S^*} & -\frac{\alpha_s}{\eta_s} S^* & -\frac{\alpha_I}{\eta_I} S^* & -\frac{\alpha_y}{\eta_y} S^* \\ \alpha_s x_s^* & -\frac{\gamma x_I^*}{x_s^*} & -\delta x_s^* + \gamma & 0 \\ \alpha_I x_I^* & \delta x_I^* & 0 & 0 \\ 0 & 0 & 0 & -D_y + \alpha_y S^* \end{bmatrix}.$$

The characteristic equation is $(\lambda + D_y - \alpha_y S^*)(\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3) = 0$. In the cubic, a_1, a_2, and a_3 are defined identically to those defined for E_{2^*}. Hence the same analysis applies, and so when it exists and is unique, a sufficient condition for E_2 to be locally asymptotically stable is that $\frac{\alpha_s+\alpha_I}{\eta_s} \geq \delta$ and $S^* < \frac{D_y}{\alpha_y}$. See §4.2.4 for more details.

4.3.6 E_3 local stability

Recall that $E_3 = (\hat{S}, \hat{x}_s, \hat{x}_I, \hat{y})$, where

$$\begin{aligned}
\hat{S} &= \frac{D_y}{\alpha_y}, \\
\hat{x}_s &= \left[D_I + \gamma - \alpha_I\left(\frac{D_y}{\alpha_y}\right)\right]\left(\frac{1}{\delta}\right), \\
\hat{x}_I &= \frac{\hat{x}_s(-D_s + \alpha_s\hat{S})}{(\delta\hat{x}_s - \gamma)}, \text{ and} \\
\hat{y} &= \left[(S^0 - \hat{S})D - \frac{\alpha_s\hat{x}_s\hat{S}}{\eta_s} - \frac{\alpha_I\hat{x}_I\hat{S}}{\eta_I}\right]\left(\frac{\eta_y}{\alpha_y\hat{S}}\right).
\end{aligned}$$

E_3 exists when each of its components is positive: $\hat{S}$ is always positive; $\hat{x}_s$ is positive when $\frac{D_y}{\alpha_y} < \frac{D_I+\gamma}{\alpha_I}$; $\hat{x}_I$ is positive when $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$ and $\frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$; and $\hat{y}$ is positive when $S^0 > \frac{D_y}{\alpha_y}\left[\frac{\alpha_s(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})}{\delta\eta_s} + \frac{\alpha_I(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})(-D_s+\frac{\alpha_s D_y}{\alpha_y})}{\delta\eta_I(D_I-\frac{\alpha_I D_y}{\alpha_y})} + D\right]$. Now, since $\frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$ is stronger than $\frac{D_y}{\alpha_y} < \frac{D_I+\gamma}{\alpha_I}$, we can discard the latter condition. Hence E_3 exists when $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$, and when $S^0 > \frac{D_y}{\alpha_y}\left[\frac{\alpha_s(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})}{\delta\eta_s} + \frac{\alpha_I(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})(-D_s+\frac{\alpha_s D_y}{\alpha_y})}{\delta\eta_I(D_I-\frac{\alpha_I D_y}{\alpha_y})} + D\right]$.

Proposition 4.1 *If an equilibrium of the form E_3 exists, then E_{1x}, E_{1y}, and at least one equilibrium of the form E_2 exist.*

See Proofs (§8) for a proof of the above proposition.

It is interesting to note that it can be shown that $\hat{S} < S^*$ is also necessary for the existence of E_3. This result is included as a lemma below:

Lemma 4.5 *If E_3 exists, then $S^* > \hat{S} = \frac{D_y}{\alpha_y}$.*

See Proofs (§8) for a proof of the above lemma.

We consider the local stability of E_3 in the special case: $\eta_s = \eta_I = \eta$ and $D = D_s = D_I = D_y$. (See Appendix A.1 for the analysis without this restriction on the parameters.) Restricting the parameters in this way simplifies the analysis since it allows us to consider a limiting three dimensional system.

Let

$$z(t) = S^0 - S(t) - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta} - \frac{y(t)}{\eta_y}.$$

Then

$$\begin{aligned}
z'(t) &= -S'(t) - \frac{x_s'(t)}{\eta} - \frac{x_I'(t)}{\eta} - \frac{y'(t)}{\eta_y} \\
\Rightarrow z'(t) &= -S^0 D + S(t)D + \frac{x_s(t)D}{\eta} + \frac{x_I(t)D}{\eta} + \frac{y(t)D}{\eta_y} \\
&= D\left(-S^0 + S(t) + \frac{x_s(t)}{\eta} + \frac{x_I(t)}{\eta} + \frac{y(t)}{\eta_y}\right) \\
&= -Dz(t) \\
\Rightarrow z(t) &= z(0)e^{-Dt}
\end{aligned}$$

As $t \rightarrow \infty$, $z(t) \rightarrow 0$, which implies that as $t \rightarrow \infty$, $S(t) + \frac{x_s(t)}{\eta} + \frac{x_I(t)}{\eta} + \frac{y(t)}{\eta_y} \rightarrow S^0$.

Therefore we can consider the three dimensional limiting system obtained from (1) by replacing $S(t)$ by $S(t) = S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta} - \frac{y(t)}{\eta_y}$:

$$\begin{aligned} x_s'(t) &= x_s(t)\left(-D + \alpha_s\left(S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta} - \frac{y(t)}{\eta_y}\right)\right) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\ x_I'(t) &= x_I(t)\left(-D + \alpha_I\left(S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta} - \frac{y(t)}{\eta_y}\right)\right) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\ y'(t) &= y(t)\left(-D + \alpha_y\left(S^0 - S(t) - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta} - \frac{y(t)}{\eta_y}\right)\right) \end{aligned} \tag{7}$$

This system has the corresponding interior equilibrium $E_{int} = (\hat{x}_s, \hat{x}_I, \hat{y})$. The three eigenvalues of this system will have the same sign as three eigenvalues of the full four dimensional system; the fourth eigenvalue is negative. The Jacobian matrix for (7) reduces to:

$$\begin{bmatrix} -\frac{\alpha_s\hat{x}_s}{\eta} - \frac{\gamma\hat{x}_I}{\hat{x}_s} & -\frac{\alpha_s\hat{x}_s}{\eta} - \delta\hat{x}_s + \gamma & -\frac{\alpha_s\hat{x}_s}{\eta_y} \\ \frac{\alpha_I\hat{x}_I}{\eta} + \delta\hat{x}_I & -\frac{\alpha_I\hat{x}_I}{\eta} & -\frac{\alpha_I\hat{x}_I}{\eta_y} \\ -\frac{\alpha_y\hat{y}}{\eta} & -\frac{\alpha_y\hat{y}}{\eta} & -\frac{\alpha_y\hat{y}}{\eta_y} \end{bmatrix}.$$

The characteristic equation is of the form $\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$, where

$$\begin{aligned} a_1 &= \frac{\alpha_s\hat{x}_s}{\eta} + \frac{\gamma\hat{x}_I}{\hat{x}_s} + \frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}, \\ a_2 &= \frac{\gamma\hat{x}_I}{\hat{x}_s}\left(\frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}\right) + \frac{\delta\hat{x}_s\hat{x}_I}{\eta}(\alpha_s - \alpha_I) + \delta\hat{x}_I(\delta\hat{x}_s - \gamma) + \frac{\gamma\alpha_I\hat{x}_I}{\eta}, \quad \text{and} \\ a_3 &= \frac{\delta\alpha_y\hat{x}_I\hat{y}}{\eta_y}(\delta\hat{x}_s - \gamma). \end{aligned}$$

By the Routh-Hurwitz criterion [15] [30] [18], local stability of E_{int} is guaranteed when $a_1 > 0$, $a_3 > 0$, and $a_1a_2 > a_3$. It is clear that $a_1 > 0$. Under our assumption that $\alpha_s \geq \alpha_I$ and that E_{int} exists, i.e. that $\hat{x}_s > \frac{\gamma}{\delta}$, it is clear that $a_3 > 0$. As for $a_1a_2 > a_3$:

$$
\begin{aligned}
a_1a_2 - a_3 &= \left(\frac{\alpha_s\hat{x}_s}{\eta} + \frac{\gamma\hat{x}_I}{\hat{x}_s} + \frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}\right)\left[\frac{\gamma\hat{x}_I}{\hat{x}_s}\left(\frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}\right)\right.\\
&\quad \left. + \frac{\delta\hat{x}_s\hat{x}_I}{\eta}(\alpha_s - \alpha_I) + \delta\hat{x}_I(\delta\hat{x}_s - \gamma) + \frac{\gamma\alpha_I\hat{x}_I}{\eta}\right]\\
&\quad - \frac{\delta\alpha_y\hat{x}_I\hat{y}}{\eta_y}(\delta\hat{x}_s - \gamma)\\
&= \left(\frac{\alpha_s\hat{x}_s}{\eta} + \frac{\gamma\hat{x}_I}{\hat{x}_s} + \frac{\alpha_I\hat{x}_I}{\eta}\right)\left[\frac{\gamma\hat{x}_I}{\hat{x}_s}\left(\frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}\right)\right.\\
&\quad \left. + \frac{\delta\hat{x}_s\hat{x}_I}{\eta}(\alpha_s - \alpha_I) + \delta\hat{x}_I(\delta\hat{x}_s - \gamma) + \frac{\gamma\alpha_I\hat{x}_I}{\eta}\right]\\
&\quad + \frac{\alpha_y\hat{y}}{\eta_y}\left[\frac{\gamma\hat{x}_I}{\hat{x}_s}\left(\frac{\alpha_I\hat{x}_I}{\eta} + \frac{\alpha_y\hat{y}}{\eta_y}\right) + \frac{\delta\hat{x}_s\hat{x}_I}{\eta}(\alpha_s - \alpha_I) + \frac{\gamma\alpha_I\hat{x}_I}{\eta}\right].
\end{aligned}
$$

Under our assumptions that $\alpha_s \geq \alpha_I$ and that E_{int} exists, i.e. that $\hat{x}_s > \frac{\gamma}{\delta}$, it is clear that $a_1a_2 - a_3 > 0$. Hence E_{int} is locally asymptotically stable when it exists. However, our parameters are still limited by our initial assumptions that $\eta_s = \eta_I = \eta$ and $D = D_s = D_I = D_y$. Hence we have shown that under these restrictions on the parameters, E_3 is locally asymptotically stable when it exists. If we relax these assumptions it is possible for E_3 to lose stability through a Hopf bifurcation as will be shown later.

Note that since eigenvalues of a matrix are continuously dependent on the parameters, it follows that local stability of E_3 still holds at least under small perturbation of the parameters. See for example Figure 3, where we obtain coexistence of all three populations even though the difference between the D's as well as between the η's is relatively large.

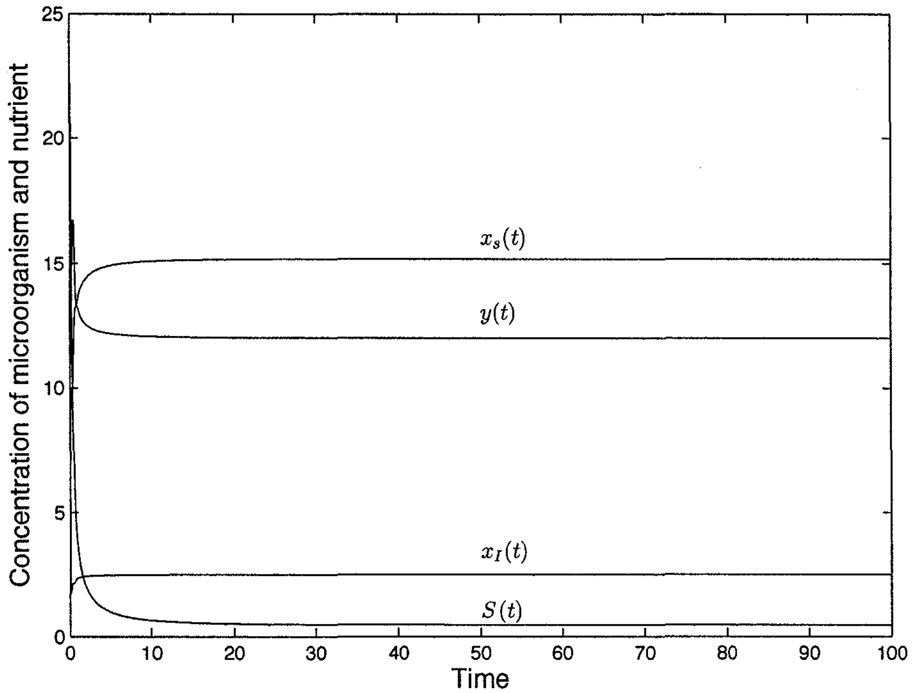

Figure 3: Timeseries illustrating coexistence of all three species in system (1). Simulated using MATLAB [19] and XPPAUT [16] software with parameter values: $S^0 = 10$, $D = 8$, $D_s = 10$, $D_I = 20$, $D_y = 15$, $\alpha_s = 7$, $\alpha_I = 5$, $\alpha_y = 6$, $\eta_s = 10$, $\eta_I = 5$, $\eta_y = 7$, $\delta = 0.7$, and $\gamma = 0.2$. Initial conditions were: $(S(0), x_s(0), x_I(0), y(0)) = (10, 2, 3, 5)$.

Recall for the next two tables that our assumptions are: $D_s < D_I$, $\alpha_s \geq \alpha_I$, $\frac{D_s}{\alpha_s} < \frac{D_I}{\alpha_I}$, and $\eta_s \geq \eta_I$.

4.3.7 Table 1: local stability of subsystem (2) summarized

Table 1: Equilibria - Existence and Stability

	Existence†	Local Asymptotic Stability (assuming the equilibrium exists)
E_{0^*}	always	$S^0 < \frac{D_s}{\alpha_s}$
E_{1^*}	$S^0 > \frac{D_s}{\alpha_s}$	$S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$
E_{2^*}	$S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$	$\frac{\alpha_s+\alpha_I}{\eta_s} \geq \delta^\ddagger$

4.3.8 Table 2: local stability of the full system (1) summarized

Table 2: Equilibria - Existence and Stability

	Existence†	Local Asymptotic Stability (assuming the equilibrium exists)
E_0	always	$S^0 < \min\left(\frac{D_s}{\alpha_s}, \frac{D_y}{\alpha_y}\right)$
E_{1x}	$S^0 > \frac{D_s}{\alpha_s}$	*
E_{1y}	$S^0 > \frac{D_y}{\alpha_y}$	$\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$
E_2	$S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$	$\frac{\alpha_s+\alpha_I}{\eta_s} \geq \delta^\ddagger$ and $S^* < \frac{D_y}{\alpha_y}$
E_3	$\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$ and **	when it exists***

† An equilibrium is assumed to exist if, and only if, all of its components are nonnegative.

‡ This condition is only sufficient. See §4.1 for more details.

* $S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$ and $\frac{D_y}{\alpha_y} > \frac{D_s}{\alpha_s}$

** $S^0 > \frac{D_y}{\alpha_y}\left[\frac{\alpha_s(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})}{\delta\eta_s} + \frac{\alpha_I(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})(-D_s+\frac{\alpha_s D_y}{\alpha_y})}{\delta\eta_I(D_I-\frac{\alpha_I D_y}{\alpha_y})} + D\right]$

*** This is only proven under the assumption that $\eta_s = \eta_I = \eta$ and

$D = D_s = D_I = D_y$.

5 Global Analysis

Since they will be used several times, it is useful to see the following theorems, with consideration of the following system:

$$x'(t) = f(x(t)), \tag{8}$$

where $f : \Omega^* \subset \mathbb{R}^n \to \mathbb{R}$ is a continuously differentiable function. The next two results are as written in [39] although the first was originally proved in Lyapunov's 1892 doctoral thesis (according to [27]).

Definition:

We call V a Lyapunov function on $\Omega \subseteq \Omega^*$ for (8) if

(i) V is continuous on Ω,

(ii) V is not continuous at $\bar{x} \in \bar{\Omega}$ (the closure of Ω) implies that

$$\lim_{x \to \bar{x}, x \in \Omega} V(x) = +\infty$$

(iii) $\dot{V} = \nabla V \cdot f \leq 0$ on Ω.

Theorem 5.1 (LaSalle's Extension Theorem) *Assume that V is a Lyapunov function for (8) on Ω. Define $\Omega = \{x \in \bar{\Omega} \cap \Omega^* : \dot{V}(x) = 0\}$. Let $\mathcal{M}$ denote the largest invariant set in Ω. Then every bounded (for $t \geq 0$) trajectory of (8) that remains in Ω (for $t \geq 0$) approaches the set $\mathcal{M}$ as $t \to \infty$.*

5.1 Global stability of steady states of subsystem (2)

5.1.1 E_{0^*} global stability

Recall that $E_{0^*} = (S^0, 0, 0)$. Using a Lyapunov argument, we will show that E_{0^*} is globally asymptotically stable when it is locally asymptotically stable (i.e. $S^0 < \frac{D_s}{\alpha_s}$) and when $S^0 \leq \frac{D_I}{\alpha_I}(\frac{\eta_I}{\eta_s})$, or, in other words, when $S^0 \leq \min\{\frac{D_I \eta_I}{\alpha_I \eta_s}, \frac{D_s}{\alpha_s}\}$.

Consider the following Lyapunov function:

$$V(S, x_s, x_I) = S - S^0 - S^0(\ln(S) - \ln(S^0)) + k_1 x_s + k_2 x_I$$

with k_1, k_2 positive non-zero constants to be determined.

At the equilibrium E_{0^*}, $V(E_{0^*}) = V(S^0, 0, 0) = 0$. It should also be shown that $V(S, x_s, x_I) > 0$ for $(S, x_s, x_I) \neq E_{0^*}$. The last two terms are always positive. Looking at the remaining terms which form a single-variable function in S it can be shown that this function has a negative derivative for $S < S^0$ and positive derivative for $S > S^0$. Hence it is decreasing to E_{0^*} and then increasing after it, or, in other words, V has a minimum at E_{0^*} and is positive elsewhere. Hence $V(S, x_s, x_I) > 0$ for $(S, x_s, x_I) \neq E_{0^*}$.

We want to show $\dot{V} \leq 0$ under the conditions stated above.

$$\begin{aligned}
\dot{V} &= \dot{S} - S^0 \left(\frac{\dot{S}}{S}\right) + k_1 \dot{x}_s + k_2 \dot{x}_I \\
&= (S^0 - S)D - \frac{\alpha_s x_s S}{\eta_s} - \frac{\alpha_I x_I S}{\eta_I} \\
&\quad - \frac{S^0}{S}\left[(S^0 - S)D - \frac{\alpha_s x_s S}{\eta_s} - \frac{\alpha_I x_I S}{\eta_I}\right] \\
&\quad + k_1[x_s(-D_s + \alpha_s S) - \delta x_s x_I + \gamma x_I]
\end{aligned}$$

$$
\begin{aligned}
& +k_2[x_I(-D_I+\alpha_I S)+\delta x_s x_I-\gamma x_I] \\
= \ & (S^0-S)D\left(\frac{S-S^0}{S}\right)-x_s\left[\frac{\alpha_s}{\eta_s}(S-S^0)-k_1(-D_s+\alpha_s S)\right] \\
& -x_I\left[\frac{\alpha_I}{\eta_I}(S-S^0)-k_1\gamma+k_2\gamma-k_2(-D_I+\alpha_I S)\right] \\
& -x_s x_I\delta[k_1-k_2]
\end{aligned}
$$

Let $k=k_1=k_2$. Then we have

$$
\begin{aligned}
\dot{V} &= -\left(\frac{D(S-S^0)^2}{S}\right)-x_s\left[\frac{\alpha_s}{\eta_s}(S-S^0)-k(-D_s+\alpha_s S)\right] \\
& \quad -x_I\left[\frac{\alpha_I}{\eta_I}(S-S^0)-k(-D_I+\alpha_I S)\right] \\
&= -\left(\frac{D(S-S^0)^2}{S}\right)-x_s\left[\alpha_s S\left(\frac{1}{\eta_s}-k\right)-\frac{\alpha_s}{\eta_s}S^0+kD_s\right] \\
& \quad -x_I\left[\alpha_I S\left(\frac{1}{\eta_I}-k\right)-\frac{\alpha_I}{\eta_I}S^0+kD_I\right] \\
&= T1+T2+T3
\end{aligned}
$$

Clearly $T1=-\left(\frac{D(S-S^0)^2}{S}\right)$ is nonpositive. Taking $k=\frac{1}{\eta_s}$, both $T2=-x_s\left[\alpha_s S\left(\frac{1}{\eta_s}-k\right)-\frac{\alpha_s}{\eta_s}S^0+kD_s\right]$ and $T3=-x_I\left[\alpha_I S\left(\frac{1}{\eta_I}-k\right)-\frac{\alpha_I}{\eta_I}S^0+kD_I\right]$ are nonpositive when E_{0^*} is locally asymptotically stable ($S^0<\frac{D_s}{\alpha_s}$) and $S^0\leq\frac{D_I}{\alpha_I}(\frac{\eta_I}{\eta_s})$. This gives $\dot{V}\leq 0$.

Now, recall that $S\leq S^0$ (due to Proposition 3.1), and $S^0<\frac{D_s}{\alpha_s}$ when E_{0^*} is locally asymptotically stable. These inequalities will be used below. We will write $\dot{V}$ in the following way:

$$\dot{V}=-P_0-P_1-P_2$$

for $P_0,P_1,P_2\geq 0$. $\dot{V}=0$ if and only if $P_0=P_1=P_2=0$. First, $P_0=0\iff S=S^0$. This leaves $P_1=x_s[-\frac{1}{\eta_s}(-D_s+\alpha_s S^0)]=0$, which can only be solved by $x_s = 0$. The same is true for P_2, and so $x_I = 0$ also.

In other words, $\dot{V} = 0 \iff (S, x_s, x_I) = (S^0, 0, 0)$.

Then, by the LaSalle Extension Theorem, since all solutions are positive and bounded (by Lemmas 3.1 and 3.2), every solution of (2) for which $S(0) > 0$, $x_s(0) > 0$, $x_I(0) > 0$, approaches $\mathcal{M}$, where $\mathcal{M}$ is the largest invariant subset of

$$\Omega = \{(S, x_s, x_I) \in int\mathbb{R}^3_+ : \dot{V}(S, x_s, x_I) = 0\}.$$

Since the only option for Ω is $\Omega = \{(S, x_s, x_I)\} = \{(S^0, 0, 0)\}$, then $\mathcal{M} = \Omega = \{(S^0, 0, 0)\}$, and E_{0^*} is globally asymptotically stable when $S^0 \leq \min\{\frac{D_I \eta_I}{\alpha_I \eta_s}, \frac{D_s}{\alpha_s}\}$. Note that if $\eta_s = \eta_I$ (which is not unlikely), then E_{0^*} is globally asymptotically stable when it is locally asymptotically stable.

Remark: In the less likely case that $\eta_I > \eta_s$, instead take $k = \frac{1}{\eta_I}$. We then have that E_{0^*} is globally asymptotically stable when $S^0 \leq \frac{D_s}{\alpha_s}(\frac{\eta_s}{\eta_I})$.

5.1.2 E_{1^*} global stability

Recall that $E_{1^*} = (\bar{S}, \bar{x}_s, 0)$, with $\bar{S} = \frac{D_s}{\alpha_s}$ and $\bar{x}_s = \left(\frac{D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right)$. Using a Lyapunov argument, we will show that E_{1^*} is globally asymptotically stable when it is locally asymptotically stable (i.e. $S^0 < \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$) provided that the parameter D_I is sufficiently large.

Consider the following Lyapunov function:

$$V(S, x_s, x_I) = S - \bar{S} - \bar{S}(\ln(S) - \ln(\bar{S})) + k_1[x_s - \bar{x}_s - \bar{x}_s(\ln(x_s) - \ln(\bar{x}_s))] + k_2 x_I$$

with k_1, $k_2 > 0$ positive non-zero constants to be determined.

At the equilibrium E_{1^*}, $V(E_{1^*}) = V(\bar{S}, \bar{x}_s, 0) = 0$. Next, it must be shown that $V(S, x_s, x_I) > 0$ for $(S, x_s, x_I) \neq E_{1^*}$. To do this, we view V as a composition of 3 single-variable functions, the first two of which are the same, while the last is clearly always positive for $x_I \neq 0$. The two similar functions have negative derivative for $S < \bar{S}$ and $x_s < \bar{x}_s$ and positive derivative for $S > \bar{S}$ and $x_s > \bar{x}_s$. Hence V has a minimum at E_{1^*} and is positive elsewhere, or, in other words, $V(S, x_s, x_I) > 0$ for $(S, x_s, x_I) \neq E_{1^*}$.

We will now examine the time derivative of V:

$$
\begin{aligned}
\dot{V} &= \dot{S}\left(\frac{S-\bar{S}}{S}\right) + k_1\dot{x_s}\left(\frac{x_s-\bar{x}_s}{x_s}\right) + k_2\dot{x_I} \\
&= \left(\frac{S-\bar{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_s x_s S}{\eta_s} - \frac{\alpha_I x_I S}{\eta_I}\right] \\
&\quad + k_1\left(\frac{x_s-\bar{x}_s}{x_s}\right)[x_s(-D_s+\alpha_s S) - \delta x_s x_I] + k_1\gamma x_I\left(\frac{x_s-\bar{x}_s}{x_s}\right) \\
&\quad + k_2[x_I(-D_I+\alpha_I S) + \delta x_s x_I - \gamma x_I] \\
&= \left(\frac{S-\bar{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_s \bar{x}_s S}{\eta_s}\right] \\
&\quad + \left(\frac{S-\bar{S}}{S}\right)\left[\frac{\alpha_s \bar{x}_s S}{\eta_s} - \frac{\alpha_s x_s S}{\eta_s} - \frac{\alpha_I x_I S}{\eta_I}\right] \\
&\quad + k_1(x_s-\bar{x}_s)\alpha_s\left(-\frac{D_s}{\alpha_s} + S\right) \\
&\quad + k_2 x_I\left[-D_I + \alpha_I S + \delta x_s - \gamma + \frac{k_1}{k_2}\gamma\left(\frac{x_s-\bar{x}_s}{x_s}\right) - \frac{k_1}{k_2}\delta(x_s-\bar{x}_s)\right] \\
&= \left(\frac{S-\bar{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_s \bar{x}_s S}{\eta_s}\right] \\
&\quad + (S-\bar{S})\left[\frac{\alpha_s \bar{x}_s}{\eta_s} - \frac{\alpha_s x_s}{\eta_s}\right] + k_1(x_s-\bar{x}_s)\alpha_s(S-\bar{S}) \\
&\quad + k_2 x_I[-D_I + \alpha_I S + \delta x_s - \gamma + \frac{k_1}{k_2}\gamma\left(\frac{x_s-\bar{x}_s}{x_s}\right) \\
&\quad - \frac{k_1}{k_2}\delta(x_s-\bar{x}_s) - \frac{(S-\bar{S})\alpha_I}{k_2\eta_I}] \\
&= \left(\frac{S-\bar{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_s \bar{x}_s S}{\eta_s}\right] \\
&\quad - \alpha_s\left(\frac{1}{\eta_s}\right)(S-\bar{S})(x_s-\bar{x}_s) + k_1\alpha_s(x_s-\bar{x}_s)(S-\bar{S})
\end{aligned}
$$

$$
\begin{aligned}
&+k_2x_I[-D_I+\alpha_I S+\delta x_s-\gamma+\gamma\frac{k_1}{k_2}-\gamma\frac{k_1}{k_2}\left(\frac{\bar{x}_s}{x_s}\right)\\
&-\frac{k_1}{k_2}\delta x_s+\frac{k_1}{k_2}\delta\bar{x}_s-\frac{S\alpha_I}{k_2\eta_I}+\frac{\bar{S}\alpha_I}{k_2\eta_I}]\\
= \;& T1+\alpha_s(S-\bar{S})(x_s-\bar{x}_s)\left(k_1-\frac{1}{\eta_s}\right)\\
&+k_2x_I\left(-D_I+\frac{\alpha_I\bar{S}}{k_2\eta_I}+\frac{k_1}{k_2}\delta\bar{x}_s-\gamma+\gamma\frac{k_1}{k_2}\right)\\
&+k_2x_I\left[\alpha_I S\left(1-\frac{1}{k_2\eta_I}\right)+\delta x_s\left(1-\frac{k_1}{k_2}\right)-\gamma\frac{k_1}{k_2}\left(\frac{\bar{x}_s}{x_s}\right)\right]
\end{aligned}
$$

First, let $k_1=\frac{1}{\eta_s}$, to eliminate the second term. Then we have:

$$
\begin{aligned}
\dot{V} \;=\;& T1+k_2x_I\left(-D_I+\frac{\alpha_I\bar{S}}{k_2\eta_I}+\frac{\delta\bar{x}_s}{\eta_s k_2}-\gamma+\frac{\gamma}{\eta_s k_2}\right)\\
&+k_2x_I\left[\alpha_I S\left(1-\frac{1}{k_2\eta_I}\right)+\delta x_s\left(1-\frac{1}{\eta_s k_2}\right)-\frac{\gamma}{\eta_s k_2}\left(\frac{\bar{x}_s}{x_s}\right)\right]
\end{aligned}
$$

where $T1=\left(\frac{S-\bar{S}}{S}\right)\left[(S^0-S)D-\frac{\alpha_s\bar{x}_s S}{\eta_s}\right]\leq 0$ always: if $S\in(0,\bar{S}]$, then $\left(\frac{S-\bar{S}}{S}\right)\leq 0$ and $\left[(S^0-S)D-\frac{\alpha_s\bar{x}_s S}{\eta_s}\right]=S^0D\left(1-\frac{\alpha_s S}{D_s}\right)\geq 0$; and when $S>\bar{S}$ then the signs are switched, and it remains that $T1\leq 0$. Now, let $k_2=\frac{1}{\eta_s}$. We now have:

$$
\dot{V}=T1+\frac{1}{\eta_s}x_I\left(-D_I+\frac{\eta_s}{\eta_I}(\alpha_I\bar{S})+\delta\bar{x}_s\right)+\frac{1}{\eta_s}x_I\left[\alpha_I S\left(1-\frac{\eta_s}{\eta_I}\right)-\gamma\left(\frac{\bar{x}_s}{x_s}\right)\right]. \quad (9)
$$

Now, recall that E_{1*} is locally asymptotically stable when

$$
-D_I+\alpha_I\bar{S}+\delta\bar{x}_s-\gamma<0.
$$

Note the similarity between the above condition and the second term of (9). Now, since it is likely that the difference between η_s and η_I will be small, the $\frac{\eta_s}{\eta_I}(\alpha_I\bar{S})$ term will not be much bigger than $\alpha_I\bar{S}$. So if D_I is sufficiently large, then the second term is nonpositive. The third term is clearly nonpositive, and so with D_I sufficiently large, $\dot{V} \leq 0$.

It is worth noting that if $\eta_s = \eta_I = \eta$,

$$\dot{V} = T1 + \frac{1}{\eta} x_I \left[-D_I + \alpha_I \bar{S} + \delta \bar{x}_s - \gamma \left(\frac{\bar{x}_s}{x_s} \right) \right],$$

which is nonpositive for all t, except for when $\bar{x}_s < x_s$. However, in that exception, $\dot{V} \leq 0$ if D_I is sufficiently large.

Now, given that D_I is sufficiently large and recalling that E_{1^*} exists and is locally asymptotically stable when $\frac{D_s}{\alpha_s} < S^0 < \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$, we investigate the conditions for $\dot{V} = 0$.

Rewriting 9, we obtain:

$$\dot{V} = T1 - \left(\frac{1}{\eta_s} \right) x_I (P_0)$$

where $P_0 = \left[D_I - \frac{\eta_s}{\eta_I}(\alpha_I \bar{S}) - \delta \bar{x}_s - \alpha_I S \left(1 - \frac{\eta_s}{\eta_I} \right) + \gamma \left(\frac{\bar{x}_s}{x_s} \right) \right]$. $P_0 > 0$ when D_I is sufficiently large. By expressing $\dot{V}$ in this way it can be seen that the only way to solve $\dot{V} = 0$ is when $T1 = 0$ and $x_I = 0$. It has already been shown above that whether $S < \bar{S}$ or $S > \bar{S}$, $T1 < 0$. Hence only $S = \bar{S}$ solves $T1 = 0$.

In other words, $\dot{V} = 0$ iff $S = \bar{S}$ and $x_I = 0$. Then by the LaSalle Extension Theorem, since all solutions are positive and bounded (by Lemmas 3.1 and 3.2), every solution of (2) for which $S(0) > 0$, $x_s(0) > 0$, $x_I(0) > 0$, approaches $\mathcal{M}$, where $\mathcal{M}$ is the largest invariant subset of

$$\Omega = \{(S, x_s, x_I) \in int\mathbb{R}^3_+ : \dot{V}(S, x_s, x_I) = 0\}.$$

But

$$\Omega = \{(S, x_s, x_I) \in int\mathbb{R}^3_+ : S = \bar{S}, x_I = 0, x_S > 0\}.$$

This implies that $S' = 0$ and $x_I' = 0$, although the latter will not be needed. Taking S' from (2), we get:

$$S' = (S^0 - S(t))D - \frac{\alpha_s x_s(t)S(t)}{\eta_s} - \frac{\alpha_I x_I(t)S(t)}{\eta_I} = 0.$$

Substituting in $S = \bar{S}$ and $x_I = 0$, we get:

$$(S^0 - \bar{S})D - \frac{\alpha_s x_s(t)\bar{S}}{\eta_s} = 0.$$

This can be solved explicitly for $x_s(t)$, yielding

$$x_s(t) = \frac{D\eta_s}{D_s}\left(S^0 - \frac{D_s}{\alpha_s}\right) = \bar{x}_s.$$

Hence the largest invariant subset of Ω is $\mathcal{M} = (\bar{S}, \bar{x}_s, 0) = E_{1^*}$, and so E_{1^*} is globally asymptotically stable when it is locally asymptotically stable provided that in addition, D_I is sufficiently large.

Remark: If $\eta_s < \eta_I$, then take $k_2 = \frac{1}{\eta_I}$.

$$\begin{aligned}\dot{V} &= T1 + \frac{1}{\eta_I}x_I\left(-D_I + \alpha_I\bar{S} + \frac{\eta_I}{\eta_s}(\delta\bar{x}_s) - \gamma\left(1 - \frac{\eta_I}{\eta_s}\right)\right) \\ &\quad + \frac{1}{\eta_I}x_I\left[\delta x_s\left(1 - \frac{\eta_I}{\eta_s}\right) - \frac{\eta_I\gamma}{\eta_s}\left(\frac{\bar{x}_s}{x_s}\right)\right]\end{aligned}$$

A similar argument to the previous one applies, resulting again in $\dot{V} \leq 0$ for D_I sufficiently large. Hence, in this case, E_{1^*} is globally asymptotically stable when it is locally asymptotically stable provided that in addition, D_I is sufficiently large.

5.1.3 E_{2^*} global stability

The following three theorems will be needed for our argument. The first is a consequence of the Poincaré-Bendixson Theorem, which is also called the Poincaré-Bendixson trichotomy [31]:

Theorem 5.2 (Poincaré-Bendixson trichotomy) *Let $\gamma^+(y_0)$ be a positive semi-orbit of (8) which remains in a closed and bounded subset K of $\mathbb{R}^2$, and suppose that K contains only a finite number of rest points. Then one of the following holds:*

(i) *$\omega(y_0)$ is a rest point;*

(ii) *$\omega(y_0)$ is a periodic orbit;*

(iii) *$\omega(y_0)$ contains a finite number of rest points and a set of trajectories γ_i whose alpha and omega limit sets consist of one of these rest points for each trajectory γ_i.*

Theorem 5.3 (Dulac criterion) *Suppose that (8) is two-dimensional. Let Γ be a simply connected region in $\mathbb{R}^2$ and let $\beta(x)$ be a continuously differentiable scalar function defined on Γ. If $\nabla(f(x)\beta(x))$ does not change sign and is not identically zero in the region Γ, then there are no nontrivial periodic orbits in Γ. [31]*

Next is a result from [31] regarding asymptotic systems. The result is as follows: [31]

Consider two systems of ordinary differential equations of the form

$$z' = Az, \qquad y' = f(z, y), \tag{10}$$

and

$$x' = f(0, x), \tag{11}$$

where

$$A \in \mathbb{R}^m \times \mathbb{R}^m, \qquad z \in \mathbb{R}^m, \qquad (z, y) \in \mathcal{S} \subset \mathbb{R}^m \times \mathbb{R}^n,$$

$$x \in \Omega = \{x : (0, x) \in \mathcal{S}\} \subset \mathbb{R}^n.$$

Some assumptions are necessary for the result: f is continuously differentiable, $\mathcal{S}$ is positively invariant for (10), and (10) is dissipative in the sense that there is a compact subset of $\mathcal{S}$ into which every solution eventually enters and remains.

The following theorem will require the following hypotheses:

(H1) All of the eigenvalues of A have negative real parts.

(H2) Equation (11) has a finite number of rest points in Ω, each of which is hyperbolic for (11). Denote these rest points by $X_1, X_2, \ldots, X_p$.

(H3) The dimension of the stable manifold of X_i is n for $1 \leq i \leq r$, and the dimension of the stable manifolds of X_j is less than n for $j = r+1, \ldots, p$. In symbols, $\dim(M^+(X_i)) = n$, $i = 1, \ldots, r$; $\dim(M^+(X_j)) < n$ for $j = r+1, \ldots, p$.

(H4) $\Omega = \bigcup_{i=1}^{p} M^{+}(X_i)$.

(H5) Equation (11) does not possess a cycle of rest points.

Theorem 5.4 *Let (H1)-(H5) hold and let $(z(t), y(t))$ be a solution of (10). Then, for some i,*

$$\lim_{t\to\infty} (z(t), y(t)) = (0, X_i).$$

In other words, $\mathcal{S} \subset \bigcup_{i=1}^{p} \Lambda^{+}(0, X_i)$. Furthermore, $\bigcup_{i=r+1}^{p} \Lambda^{+}(0, X_i)$ has Lebesgue measure zero.

The proof of this theorem can be found in [31].

We now consider the special case that $D = D_s = D_I$ and $\eta_s = \eta_I = \eta$. Subsystem (2) then becomes:

$$\begin{aligned}
S'(t) &= (S^0 - S(t))D - \frac{\alpha_s x_s(t)S(t)}{\eta} - \frac{\alpha_I x_I(t)S(t)}{\eta} \\
x_s'(t) &= x_s(t)(-D + \alpha_s S(t)) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\
x_I'(t) &= x_I(t)(-D + \alpha_I S(t)) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\
&\text{with} \quad S(0) \geq 0, \quad x_s(0) \geq 0, \quad \text{and} \quad x_I(0) \geq 0.
\end{aligned} \tag{12}$$

Making this assumption on the parameters will allow us to reduce (12) to a two-dimensional limiting system.

Let

$$z(t) = S^0 - S(t) - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}.$$

Then

$$z'(t) = -S'(t) - \frac{x_s'(t)}{\eta} - \frac{x_I'(t)}{\eta}$$

$$
\begin{aligned}
\Rightarrow z'(t) &= -S^0 D + S(t)D + \frac{x_s(t)D}{\eta} + \frac{x_I(t)D}{\eta} \\
&= D\left(-S^0 + S(t) + \frac{x_s(t)}{\eta} + \frac{x_I(t)}{\eta}\right) \\
&= -Dz(t) \\
\Rightarrow z(t) &= z(0)e^{-Dt}
\end{aligned}
$$

As $t \to \infty$, $z(t) \to 0$, which implies that as $t \to \infty$, $S(t) + \frac{x_s(t)}{\eta} + \frac{x_I(t)}{\eta} \to S^0$. Therefore, in the limiting system, $S(t) = S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}$. We will now use Theorem 5.4 to rewrite system (12) in the form of (10):

$$
\begin{aligned}
z'(t) &= -Dz \qquad (13) \\
x_s'(t) &= x_s(t)\left(-D + \alpha_s\left(S^0 - z(t) - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}\right)\right) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\
x_I'(t) &= x_I(t)\left(-D + \alpha_I\left(S^0 - z(t) - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}\right)\right) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\
&\text{with} \quad x_s(0) \geq 0, \quad x_I(0) \geq 0, \\
&\mathcal{S} = \{(z, x_s, x_I) : x_s > 0, x_I > 0, \frac{x_s}{\eta} + \frac{x_I}{\eta} + z \leq S^0\}, \\
&\text{and} \quad \text{where} \quad y(t) = (x_S(t), x_I(t))^T.
\end{aligned}
$$

As $t \to \infty$, $z(t) \to 0$ with exponential convergence. Therefore the asymptotic system in the form of (11) is given by:

$$
\begin{aligned}
x_s'(t) &= x_s(t)\left(-D + \alpha_s\left(S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}\right)\right) - \delta x_s(t)x_I(t) + \gamma x_I(t) \\
x_I'(t) &= x_I(t)\left(-D + \alpha_I\left(S^0 - \frac{x_s(t)}{\eta} - \frac{x_I(t)}{\eta}\right)\right) + \delta x_s(t)x_I(t) - \gamma x_I(t) \\
&\text{where} \quad \Omega = \{(x_s, x_I) : x_s > 0, x_I > 0, \frac{x_s}{\eta} + \frac{x_I}{\eta} \leq S^0\}. \qquad (14)
\end{aligned}
$$

System (14) has three equilibria, call them X_1, X_2, and X_3, where $X_3 = (0,0)$, $X_2 = (\frac{\eta}{\alpha_s}(-D + \alpha_s S^0), 0)$, and $X_1 = (x_s^*, x_I^*)$, with x_s^* and x_I^* as in §4.2. The reverse numbering is to accomodate the statement of Theorem 5.4. The local stability results of subsystem (2) apply to (14), and so we have that when $\frac{D}{\alpha_s} < S^* < \frac{D}{\alpha_I}$, $\frac{\gamma}{\delta} < x_s^* < \frac{D+\gamma}{\delta}$, and $\frac{\alpha_s}{\alpha_I} \geq 1$, X_3 is unstable, X_2 is a saddle point, and X_1 is locally asymptotically stable.

Globally, we have that all solutions are bounded above and below by Lemma 3.2, and we can describe the stable manifolds of each of these equilibria. First, X_3 has no stable manifold, since it is a repelling equilibrium. X_2 has the x_s-axis as its stable manifold, and finally X_1 has Ω as its stable manifold. Next, we conclude that there can be no cycles of rest points, since the only trajectory connecting equilibria goes from X_3 to X_2 to X_1, and it cannot leave X_1 since X_1 is locally asymptotically stable.

We now apply the Dulac criterion to show that there are no periodic orbits in (14). Take $\beta = \frac{1}{x_s x_I}$ on $\Gamma = \{(x_s, x_I) : x_s > 0, x_I > 0\}$. Then

$$\begin{aligned} \nabla \cdot \beta f &= \frac{\partial}{\partial x_s}\beta f_1 + \frac{\partial}{\partial x_I}\beta f_2 \\ &= -\frac{1}{x_I \eta} - \frac{\gamma}{x_s^2} - \frac{1}{x_s \eta} \\ &< 0. \end{aligned}$$

Since $\nabla \cdot \beta f$ is negative, by the Dulac criterion there are no periodic orbits in (14). Now, by the Poincaré-Bendixson trichotomy we can conclude that X_1 is a globally stable equilibrium point with respect to solutions with $x_s(0) > 0$, $X_I(0) > 0$, and $\frac{1}{\eta}(x_s(0) + x_I(0) < S^0$.

Next we use the above result with Theorem 5.4 to conclude that E_{2^*} is globally asymptotically stable.

Before applying Theorem 5.4 to our system, we will show that the five hypotheses (H1) - (H5) are satisfied. In our systems (14) and (14), $m = 1$ and $n = 2$. Also, $\mathcal{S}$ is positively invariant for (14), and (14) is dissipative (all trajectories are bounded for $t \geq 0$ as proven in Lemma 3.2).

Here, $A = [-D]$, a 1×1 matrix. Hence (H1) is satisfied since A has only one eigenvalue, which is always negative. From the work done above, it is clear that both (H2) and (H3) are satisfied, with $\dim(M^+(X_1)) = 2$, $\dim(M^+(X_2)) = 1$, and $\dim(M^+(X_3)) = 0$. (H4) follows, and lastly (H5) was verified above.

We now conclude that, by Theorem 5.4, for some i,

$$\lim_{t\to\infty}(z(t), y(t)) = (0, X_i).$$

In other words, every trajectory of (14) converges to an equilibrium point of (14). Lastly we conclude that this equilibrium point can only be X_1, due to the dynamics in the $x_s x_I$-plane. Hence, under the assumption that $D = D_s = D_I$ and $\eta_s = \eta_I = \eta$ and that E_{2*} exists (i.e. that $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$), E_{2*} is globally asymptotically stable.

5.2 Global stability of steady states of (1)

5.2.1 E_0 global stability

Recall that $E_0 = (S^0, 0, 0, 0)$. Using a Lyapunov argument, we will show that E_0 is globally asymptotically stable when it is locally asymptotically stable (i.e. $S^0 < \frac{D_s}{\alpha_s}$) and when $S^0 \leq \frac{D_I}{\alpha_I}(\frac{\eta_I}{\eta_s})$.

Consider the Lyapunov function

$$V(S, x_s, x_I, y) = S - S^0 - S^0(\ln(S) - \ln(S^0)) + k_1 x_s + k_2 x_I + k_3 y,$$

with $k_1 = k_2 = \frac{1}{\eta_s}$ and $k_3 = \frac{1}{\eta_y}$.

$$\begin{aligned}\dot{V} &= -\frac{(S-S^0)^2 D}{S} - \frac{x_s}{\eta_s}(D_s - S^0\alpha_s) - x_I\left(\frac{D_I}{\eta_s} - \frac{S^0\alpha_I}{\eta_I}\right) \\ &\quad -\frac{y}{\eta_y}(D_y - S^0\alpha_y) - \alpha_I S x_I\left(\frac{1}{\eta_I} - \frac{1}{\eta_s}\right),\end{aligned}$$

and hence global stability of E_0 can be proved with a similar proof to that for the global stability of E_{0^*}. Our assumption of $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$ is necessary to complete the proof. The same LaSalle Extension argument applies, with $\mathcal{M} = \Omega = (S^0, 0, 0, 0)$, showing E_0 is globally asymptotically stable when it is locally asymptotically stable and when $S^0 \leq \frac{D_I}{\alpha_I}(\frac{\eta_I}{\eta_s})$, under our assumption that $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$.

5.2.2 E_{1x} global stability

Recall that $E_{1x} = (\bar{S}, \bar{x}_s, 0, 0)$, with $\bar{S} = \frac{D_s}{\alpha_s}$ and $\bar{x}_s = \left(\frac{D\eta_s}{D_s}\right)\left(S^0 - \frac{D_s}{\alpha_s}\right)$. Using a Lyapunov argument, we will show that E_{1y} is globally asymptotically stable when it is locally asymptotically stable (i.e. $S^0 < \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$) provided that D_I is sufficiently large.

Consider the Lyapunov function

$$V(S, x_s, x_I, y) = S - \bar{S} - \bar{S}(\ln(S) - \ln(\bar{S})) + k_1[x_s - \bar{x}_s - \bar{x}_s(\ln(x_s) - \ln(\bar{x}_s))] + k_2 x_I + k_3 y$$

with $k_1 = k_2 = \frac{1}{\eta_s}$, and $k_3 = \frac{1}{\eta_y}$.

$$\begin{aligned}\dot{V} &= \left(\frac{S-\bar{S}}{S}\right)\left[(S^0 - S)D - \frac{\alpha_s \bar{x}_s S}{\eta_s}\right] + \frac{1}{\eta_s}x_I\left(-D_I + \frac{\eta_s}{\eta_I}(\alpha_I \bar{S}) + \delta\bar{x}_s\right) \\ &\quad + \frac{1}{\eta_s}x_I\left[\alpha_I S\left(1 - \frac{\eta_s}{\eta_I}\right) - \gamma\left(\frac{\bar{x}_s}{x_s}\right)\right] + \frac{y}{\eta_y}(-D_y + S^0\alpha_y),\end{aligned}$$

and hence global stability of E_{1x} can be proved with a similar proof to that for the global stability of E_{1*}. Our assumption of $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y}$ is again necessary to complete the proof. The same LaSalle Extension argument applies, with

$$\Omega = \{(S, x_s, x_I, y) \in int\mathbb{R}_+^4 : S = \bar{S}, x_I = 0, x_S > 0, y = 0\}$$

and $\mathcal{M} = (\bar{S}, \bar{x}_s, 0, 0) = E_{1x}$ as the largest invariant subset of Ω, hence proving global asymptotic stability for E_{1x} when it is locally asymptotically stable provided that D_I is sufficiently large.

5.2.3 E_{1y} global stability

Recall that $E_{1y} = (\breve{S}, 0, 0, \breve{y})$, with $\breve{S} = \frac{D_y}{\alpha_y}$ and $\breve{y} = \left(\frac{D\eta_y}{D_y}\right)\left(S^0 - \frac{D_y}{\alpha_y}\right)$. Using a Lyapunov argument, we will show that E_{1y} is globally asymptotically stable when it is locally asymptotically stable (i.e. $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$) and when $\frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}\frac{\eta_I}{\eta_s}$.

Consider the following Lyapunov function:

$$V(S, x_s, x_I, y) = S - \breve{S} - \breve{S}(\ln(S) - \ln(\breve{S})) + k_1 x_s + k_2 x_I + k_3[y - \breve{y} - \breve{y}(\ln(y) - \ln(\breve{y}))]$$

with k_1, k_2, k_3 positive non-zero constants to be determined.

$$\begin{aligned}
\dot{V} &= \dot{S}\left(\frac{S - \breve{S}}{S}\right) + k_1\dot{x}_s + k_2\dot{x}_I + k_3\dot{y}\left(\frac{y - \breve{y}}{y}\right) \\
&= \left(\frac{S - \breve{S}}{S}\right)\left[(S^0 - S)D - \frac{\alpha_s x_s S}{\eta_s} - \frac{\alpha_I x_I S}{\eta_I} - \frac{\alpha_y y S}{\eta_y}\right] \\
&\quad + k_1[x_s(-D_s + \alpha_s S) - \delta x_s x_I + \gamma x_I] \\
&\quad + k_2 x_I(-D_I + \alpha_I S + \delta x_s - \gamma) + k_3(y - \breve{y})(-D_y + \alpha_y S)
\end{aligned}$$

Let $k_1 = k_2 = k$ and $k_3 = \frac{1}{\eta_y}$. Then we have

$$\begin{aligned}
&= \left(\frac{S-\breve{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_y \breve{y} S}{\eta_y}\right] \\
&\quad + \left(\frac{S-\breve{S}}{S}\right)\left(\frac{\alpha_y S}{\eta_y}(\breve{y}-y)\right) + (S-\breve{S})\left(-\frac{\alpha_s x_s}{\eta_s} - \frac{\alpha_I x_I}{\eta_I}\right) \\
&\quad + kx_s(-D_s + \alpha_s S) + kx_I(-D_I + \alpha_I S) + \frac{1}{\eta_y}(y-\breve{y})(-D_y + \alpha_y S) \\
&= \left(\frac{S-\breve{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_y \breve{y} S}{\eta_y}\right] \\
&\quad + (S-\breve{S})\left(\frac{\alpha_y}{\eta_y}(\breve{y}-y)\right) + x_s\left[k(-D_s+\alpha_s S) - \frac{\alpha_s S}{\eta_s}\right] \\
&\quad + x_I\left[k(-D_I+\alpha_I S) - \frac{\alpha_I S}{\eta_I}\right] - \left(\frac{D_y}{\alpha_y}\right)\left(-\frac{\alpha_s x_s}{\eta_s} - \frac{\alpha_I x_I}{\eta_I}\right) \\
&\quad + \frac{\alpha_y}{\eta_y}(y-\breve{y})(S-\breve{S}) \\
&= \left(\frac{S-\breve{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_y \breve{y} S}{\eta_y}\right] \\
&\quad + x_s\left[k(-D_s+\alpha_s S) - \frac{\alpha_s S}{\eta_s} + \frac{D_y}{\alpha_y}\frac{\alpha_s}{\eta_s}\right] \\
&\quad + x_I\left[k(-D_I+\alpha_I S) - \frac{\alpha_I S}{\eta_I} + \frac{D_y}{\alpha_y}\frac{\alpha_I}{\eta_I}\right] \\
&= \left(\frac{S-\breve{S}}{S}\right)\left[(S^0-S)D - \frac{\alpha_y \breve{y} S}{\eta_y}\right] + \alpha_s x_s S\left(k - \frac{1}{\eta_s}\right) + \alpha_I x_I S\left(k - \frac{1}{\eta_I}\right) \\
&\quad + x_s\left(-kD_s + \frac{D_y \alpha_s}{\eta_s \alpha_y}\right) + x_I\left(-kD_I + \frac{D_y \alpha_I}{\eta_I \alpha_y}\right)
\end{aligned}$$

Since the first term can be rewritten as $-\frac{S^0 D \alpha_y}{S D_y}\left(S - \frac{D_y}{\alpha_y}\right)^2$, it is always nonpositive. Setting $k = \frac{1}{\eta_s}$ eliminates the second term and gives a negative fourth term when $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}$, i.e. when E_{1y} is locally asymptotically stable. The fifth term is nonpositive when $\frac{D_y}{\alpha_y} \leq \frac{D_I}{\alpha_I}\frac{\eta_I}{\eta_s}$. Hence $\dot{V} < 0$, and hence E_{1y} is globally asymptotically stable when it is locally asymptotically stable and when

$\frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}\frac{\eta_I}{\eta_s}$. ■

Remark: For the (not so likely) case when $\eta_I > \eta_s$, we have global asymptotic stability of E_{1y}, when it is locally asymptotically stable and when $\frac{D_y}{\alpha_y} < \frac{D_s}{\alpha_s}\frac{\eta_s}{\eta_I}$.

5.2.4 E_2 global stability

Lemma 5.1 *If $\frac{D_y}{\alpha_y} > \frac{D_I}{\alpha_I}$, then $y(t) \to 0$ as $t \to \infty$.*

Proof.

Recall our assumptions that $D_s \leq D_I$ and $\alpha_s \geq \alpha_I$.

First, taking the second and third equations from system (1), we obtain:

$$\begin{aligned} (x_s + x_I)'(t) &= x_s(t)(-D_s + \alpha_s S(t)) + x_I(t)(-D_I + \alpha_I S(t)) \\ &\geq (x_s + x_I)(t)(-D_I + \alpha_I S(t)). \end{aligned}$$

Integrating both sides of the above inequality with respect to t, we have

$$\begin{aligned} \int_0^t \frac{(x_s + x_I)'(t)}{(x_s + x_I)(t)} dt &\geq \int_0^t (-D_I + \alpha_I S(t)) dt \\ \Rightarrow \quad \ln((x_s + x_I)(t)) - \ln((x_s + x_I)(0)) &\geq -D_I t + \alpha_I \int_0^t S(t) dt \end{aligned}$$

$$\Rightarrow \quad \int_0^t S(t) dt \leq \frac{D_I t + \ln((x_s + x_I)(t)) - \ln((x_s + x_I)(0))}{\alpha_I}. \tag{15}$$

But, taking the last equation of system (1), we have

$$\int_0^t \frac{y'(t)}{y(t)} dt = \int_0^t (-D_y + \alpha_y S(t)) dt$$

$$
\begin{aligned}
\Rightarrow \quad \ln(y(t)) - \ln(y(0)) &= -D_y t + \alpha_y \int_0^t S(t)dt \\
\Rightarrow \quad \ln(y(t)) &= \ln(y(0)) - D_y t + \alpha_y \int_0^t S(t)dt. \qquad (16)
\end{aligned}
$$

Combining equations (15) and (16) we have

$$
\begin{aligned}
\ln(y(t)) &\leq \ln(y(0)) - D_y t \\
&\quad + \alpha_y \left[\frac{D_I t + \ln((x_s + x_I)(t)) - \ln((x_s + x_I)(0))}{\alpha_I} \right] \\
\Rightarrow \quad \ln(y(t)) &\leq \ln(y(0)) + \frac{\alpha_y}{\alpha_I} \ln\left(\frac{(x_s + x_I)(t)}{(x_s + x_I)(0)} \right) \\
&\quad + \alpha_y t \left(\frac{D_I}{\alpha_I} - \frac{D_y}{\alpha_y} \right). \qquad (17)
\end{aligned}
$$

Now, we know that $y(t) \geq 0$ for all $t \geq 0$ (Lemma 3.1) and so,

$$\liminf_{t \to \infty} y(t) \geq 0.$$

Also, since $x_s(t) \geq 0$ and $x_I(t) \geq 0$ for all $t \geq 0$ (Lemma 3.1) and both $x_s(t)$ and $x_I(t)$ are bounded above (Lemma 3.2),

$$\limsup_{t \to \infty} (x_s + x_I)(t) < \infty.$$

Therefore, if $\frac{D_y}{\alpha_y} > \frac{D_I}{\alpha_I}$, by equation (17),

$$\limsup_{t \to \infty} (\ln(y(t))) = -\infty,$$

and so $y(t) \to 0$ as $t \to \infty$.■

Theorem 5.5 *If $\frac{D_y}{\alpha_y} > \frac{D_I}{\alpha_I}$, E_2 is globally asymptotically stable for system (1) whenever E_{2^*} is globally asymptotically stable for subsystem (2).*

Proof.

We obtain this result by applying Theorem 5.4 to system (1) and subsystem (2).

Corollary 5.1 *If $x_s(t) \to 0$, $x_I(t) \to 0$, and $\frac{D_y}{\alpha_y} = \frac{D_I}{\alpha_I}$, then $y(t) \to 0$.*

6 Bifurcation Analysis

There are three possible types of bifurcations of equilibria in system (1): transcritical, saddle-node and Hopf. As well it is possible to have a saddle-node bifurcation of limit cycles and a homoclinic bifurcation. All bifurcation diagrams included below were created using MATLAB [19] and XPPAUT [16] software. In all bifurcation diagrams, a solid/dashed line represents a stable/unstable equilibrium, and a closed/open circle represents an stable/unstable periodic orbit.

6.1 Case 1: $\eta_s \geq \eta_I$

Transcritical Bifurcations

In the case where $\eta_s \geq \eta_I$, there is a successive transfer of stability from E_0 to E_{1x} to E_2 to E_3, each transfer via a transcritical bifurcation as the parameter S^0 is increased. Let $\Gamma = \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$, and let $\Psi = \frac{D_y}{\alpha_y} + \frac{D_y}{\alpha_y D\delta}\left(D_I + \gamma - \frac{\alpha_I D_y}{\alpha_y}\right)\left(\frac{\alpha_s}{\eta_s} + \frac{\alpha_I(-D_s + \frac{\alpha_s D_y}{\alpha_y})}{\eta_I(D_I - \frac{\alpha_I D_I}{\alpha_y})}\right)$. For S^0 in $\left(0, \frac{D_s}{\alpha_s}\right)$, E_0 is stable. E_0 coalesces with and transfers stability to E_{1x} when $S^0 = \frac{D_s}{\alpha_s}$. Similarly for E_{1x} to E_2 and E_2 to E_3, at $S^0 = \Gamma$ and at $S^0 = \Psi$, respectively.

See Figures 4 and 5 for graphs of the transcritical bifurcations in the parameter S^0. In this simulation, the parameters were chosen as follows: $D = 8$, $D_s = 10$, $D_I = 20$, $D_y = 15$, $\alpha_s = 7$, $\alpha_I = 5$, $\alpha_y = 6$, $\eta_s = 10$, $\eta_I = 5$, $\eta_y = 7$, $\delta = 0.7$, and $\gamma = 0.2$. From the diagrams it is clear that there are three transfers of stability, occurring at $\frac{D_s}{\alpha_s} \approx 1.43$, $\Gamma \approx 3.76$, and $\Psi \approx 8.34$. There are four graphs, each showing the progression in one of the four variables of system (1).

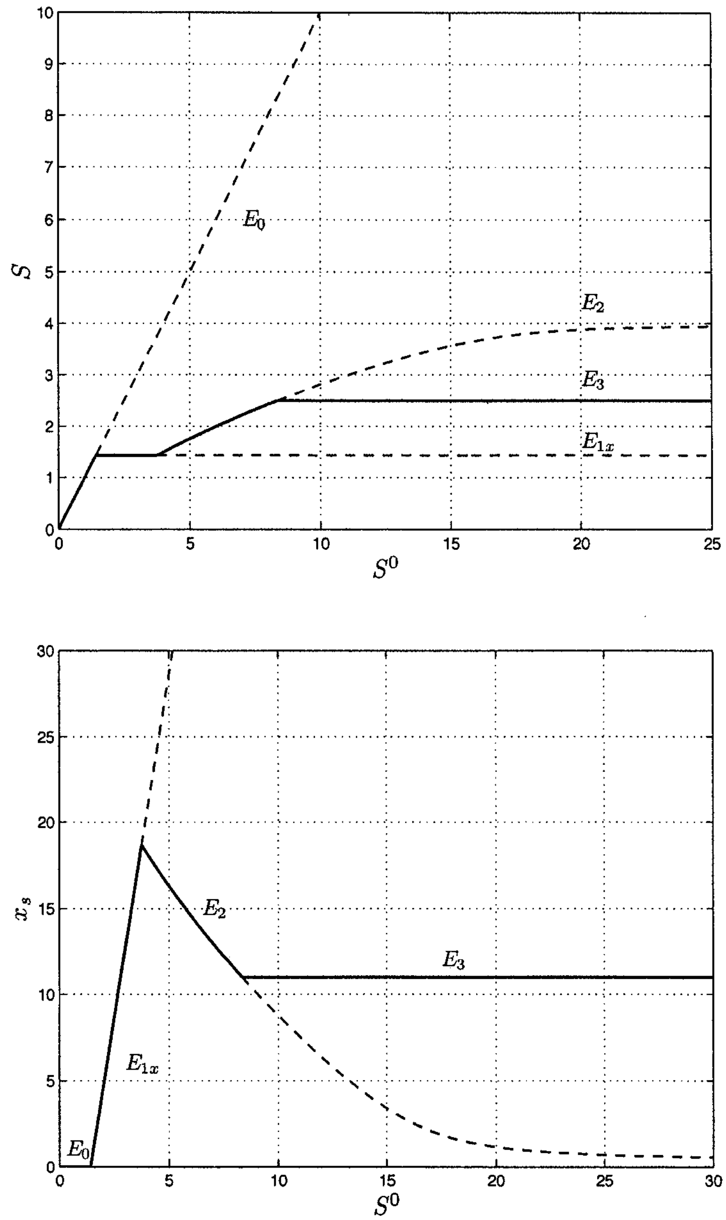

Figure 4: Bifurcation diagram for system (1). Both the upper and lower panels are in the case that $\eta_s \geq \eta_I$, with bifurcation parameter S^0, the upper and lower panels have S and x_s on the ordinate axis, respectively; both show the series of transcritical bifurcations that occur where stability is transferred successively from E_0 to E_{1x} to E_2 to E_3; parameters used in the simulation were $D = 8$, $D_s = 10$, $D_I = 20$, $D_y = 15$, $\alpha_s = 7$, $\alpha_I = 5$, $\alpha_y = 6$, $\eta_s = 10$, $\eta_I = 5$, $\eta_y = 7$, $\delta = 0.7$, and $\gamma = 0.2$.

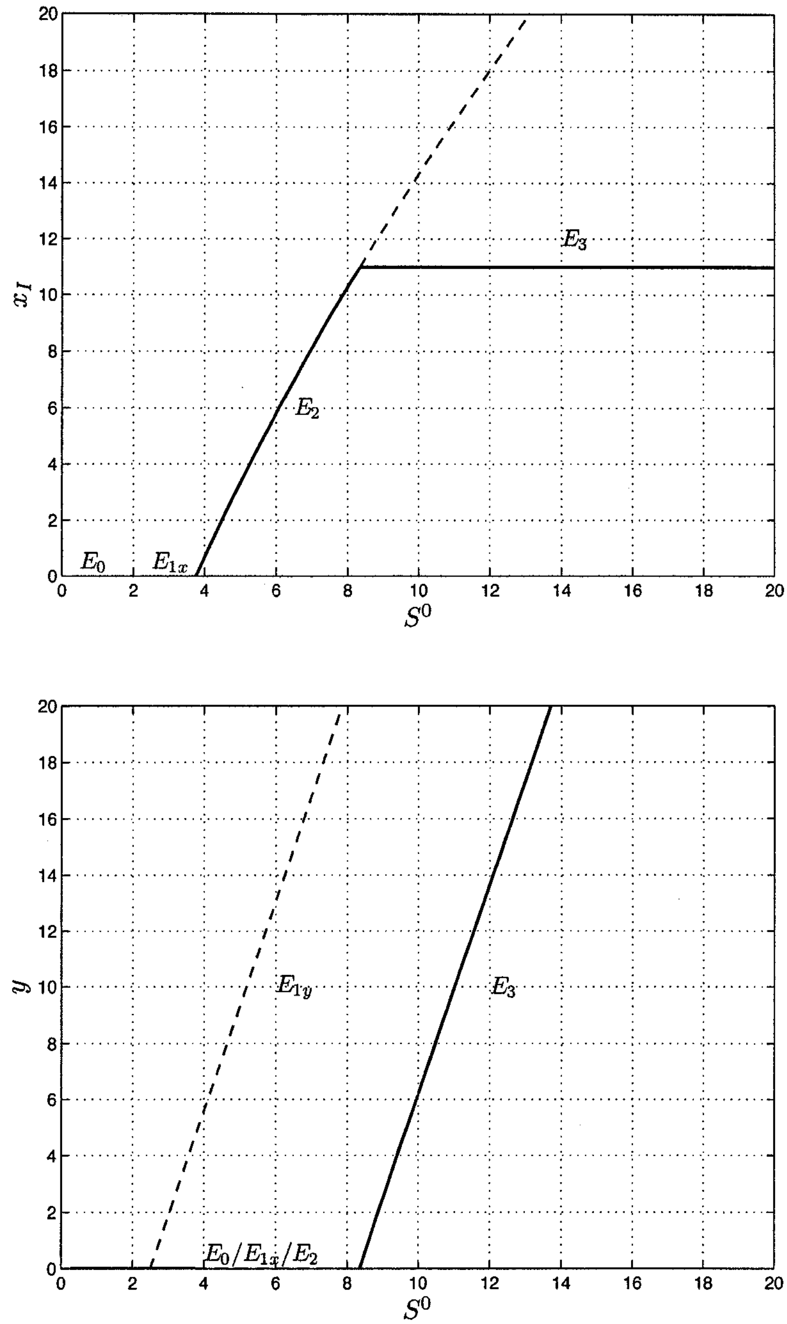

Figure 5: Bifurcation diagram for system (1). Both upper and lower panels are in the case that $\eta_s \geq \eta_I$, with bifurcation parameter S^0, the upper and lower panels have x_I and y on the ordinate axis, respectively; both panels show the transfer of stability from E_2 to E_3; parameters as in Figure 4.

Hopf Bifurcation

We showed that the conditions for local asymptotic stability of E_{2*} were merely sufficient (in §4.2.4), and that E_2 can lose stability via a transcritical bifurcation above. In fact, a Hopf bifurcation resulting in a periodic orbit is possible. As the parameter η_s is increased, we see the appearance of an unstable periodic orbit about E_{2*} (and equivalently E_2) via a Hopf bifurcation (see Figure 6). We provide bifurcation diagrams in $S(t)$, $x_s(t)$, and $x_I(t)$ for subsystem (2). Similar diagrams occur in the full system. Notice that there is also a saddle-node bifurcation of limit cycles and hence a parameter range in which at least two periodic orbits exist, one orbitally asymptotically stable, and the other unstable.

6.2 Case 2: $\eta_s < \eta_I$ (less likely case)

Transcritical Bifurcations

When $\eta_s < \eta_I < \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$, there are three transcritical bifurcations that occur, much the same as in the case of $\eta_s \geq \eta_I$, depicted in Figures 4 and 5. The condition above was derived in §4.2.4, in the "Example of nonunique E_{2*}". When this condition is violated, there is only one transcritical bifurcation in system (1).

Saddle-node Bifurcations

We have mentioned that it is possible for three E_2 equilibria to appear, one via a transcritical bifurcation with E_{1x} (see "Example of nonunique E_{2*}" following Lemma 4.3). When $\eta_s < \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s < \eta_I$, two more can appear via a saddle-node bifurcation, as S^0 is varied. In the subsystem (2), two stable and one unstable equilibrium appear. See Figures 7 and 8 for representative

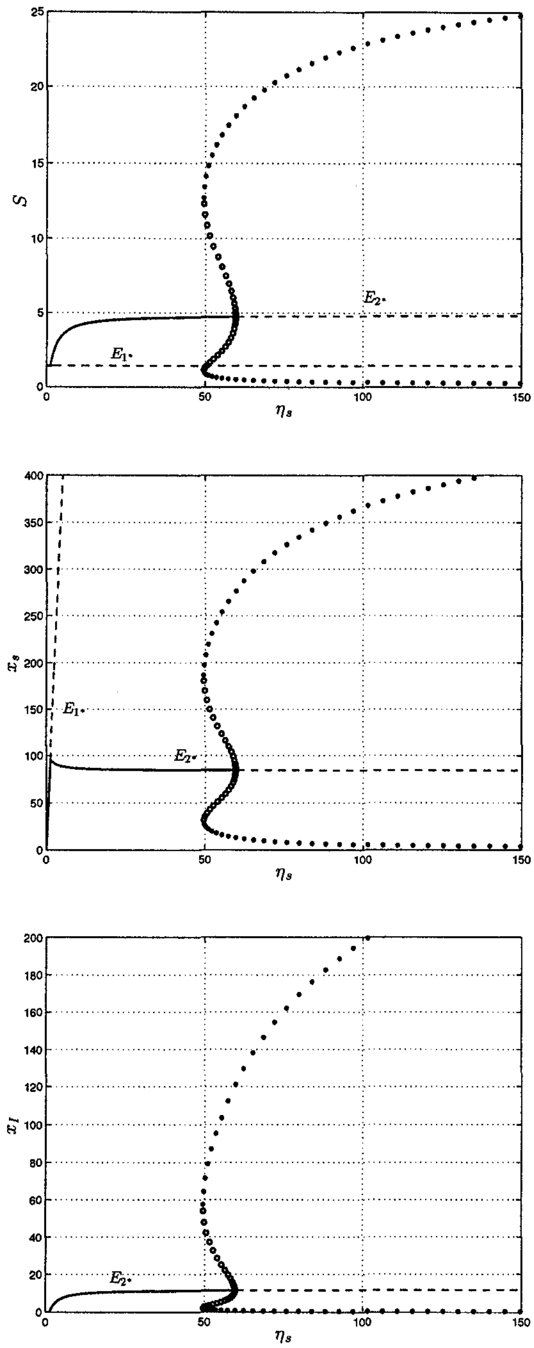

Figure 6: Hopf bifurcation of E_{2*} as η_s is varied for subsystem (2), the upper, middle and lower panels have S, x_s, and x_I on the ordinate axis, respectively; parameters are $S^0 = 100$, $D = 8$, $D_s = 10$, $D_I = 200$ $\alpha_s = 7$, $\alpha_I = 6.5$, $\eta_I = 0.5$, $\delta = 2$, and $\gamma = 0.01$. Recall that the Hopf bifurcation is not possible unless $\eta_s > \eta_I$.

bifurcation diagrams. In the full system (1), we have two unstable and one stable equilibria of the form E_2 appearing, as visible in Figures 9 a and b, 10, and 11 a.

Hopf Bifurcations and Homoclinic Orbits

When $\eta_I > \eta_s$ it is possible for a stable periodic orbit to appear around an unstable E_3. Figures 9 to 10 illustrate this Hopf bifurcation in all four variables of system (1). The periodic orbits increase in period as the parameter S^0 is decreased. In fact, it appears that as S^0 approaches a critical value (around $S^0 = 173.9$ in the bifurcation diagram in Figures 9 to 10) the period of the periodic orbits approaches infinity. It seems that the periodic orbits are originating from a homoclinic orbit that involves the E_2 equilibrium that is a saddle point. In other words, as S^0 is varied, there are two transcritical bifurcations from E_0 to E_1 and from E_1 to E_2, a saddle-node bifurcation of E_2 at around $S^0 = 173.9$ (in our bifurcation diagram), a homoclinic orbit appears that involves E_2 (which has value $(2.498, 0.0207, 30.02, 0)$ in our simulation), and then as S^0 continues to increase a large periodic orbit appears (which is stable), which then shrinks in period and amplitude until it disappears in a Hopf bifurcation of E_3. It is interesting to reflect on how these dynamics could be interpreted biologically. For instance, as S^0 increases past 900, the coexistence of x_s, x_I and y seems more likely. Taking a relatively smaller S^0 value, say, $S^0 = 180$, the oscillations of the x_s and x_I populations would be very large, with their low values getting dangerously close to 0, so that a stochastic event could easily wipe both populations out. This seems less likely to occur as S^0 becomes larger.

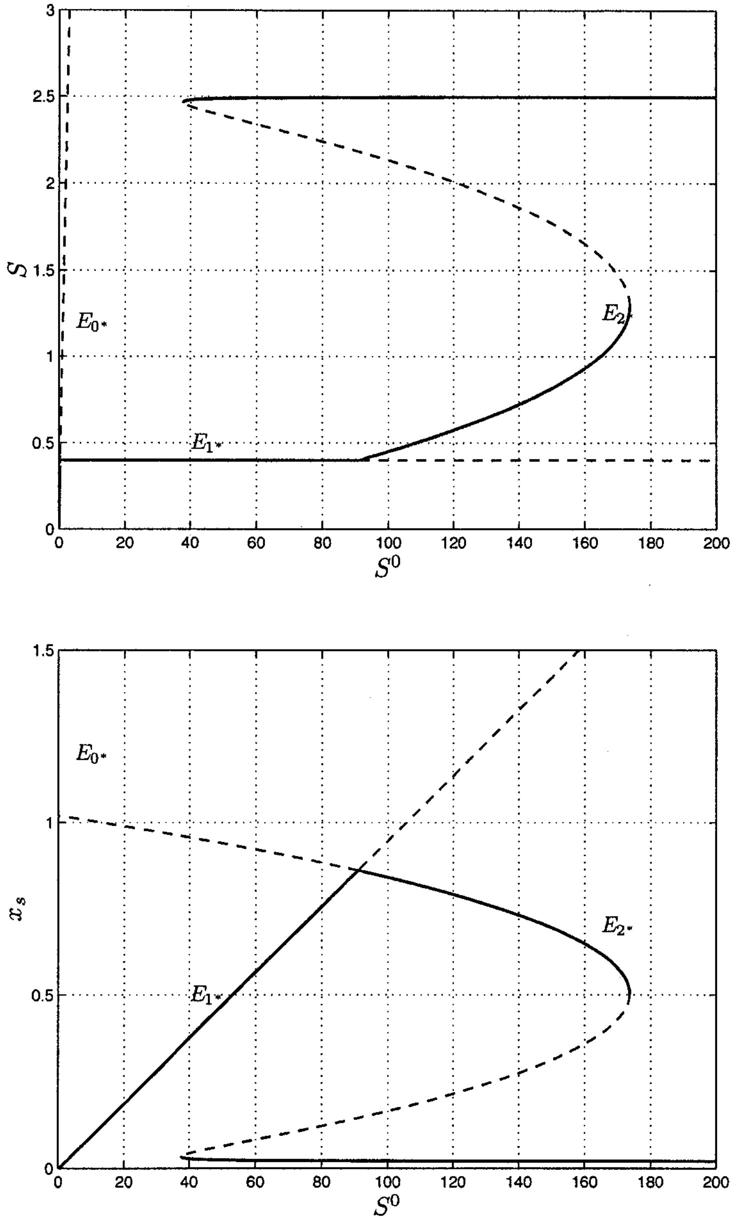

Figure 7: Bifurcation diagrams for (2). Both panels show a transcritical bifurcation involving E_{1*} and E_{2*} and the saddle-node bifurcation of E_{2*} when $\eta_I > \eta_s$ with bifurcation parameter S^0 for subsystem (2), the upper and lower panels have S and x_s on the ordinate axis, respectively; parameters are $D = 0.19$, $D_s = 0.2$, $D_I = 1$ $\alpha_s = 0.5$, $\alpha_I = 0.4$, $\eta_s = 0.01$, $\eta_I = 1$, $\delta = 1$, and $\gamma = 0.02$.

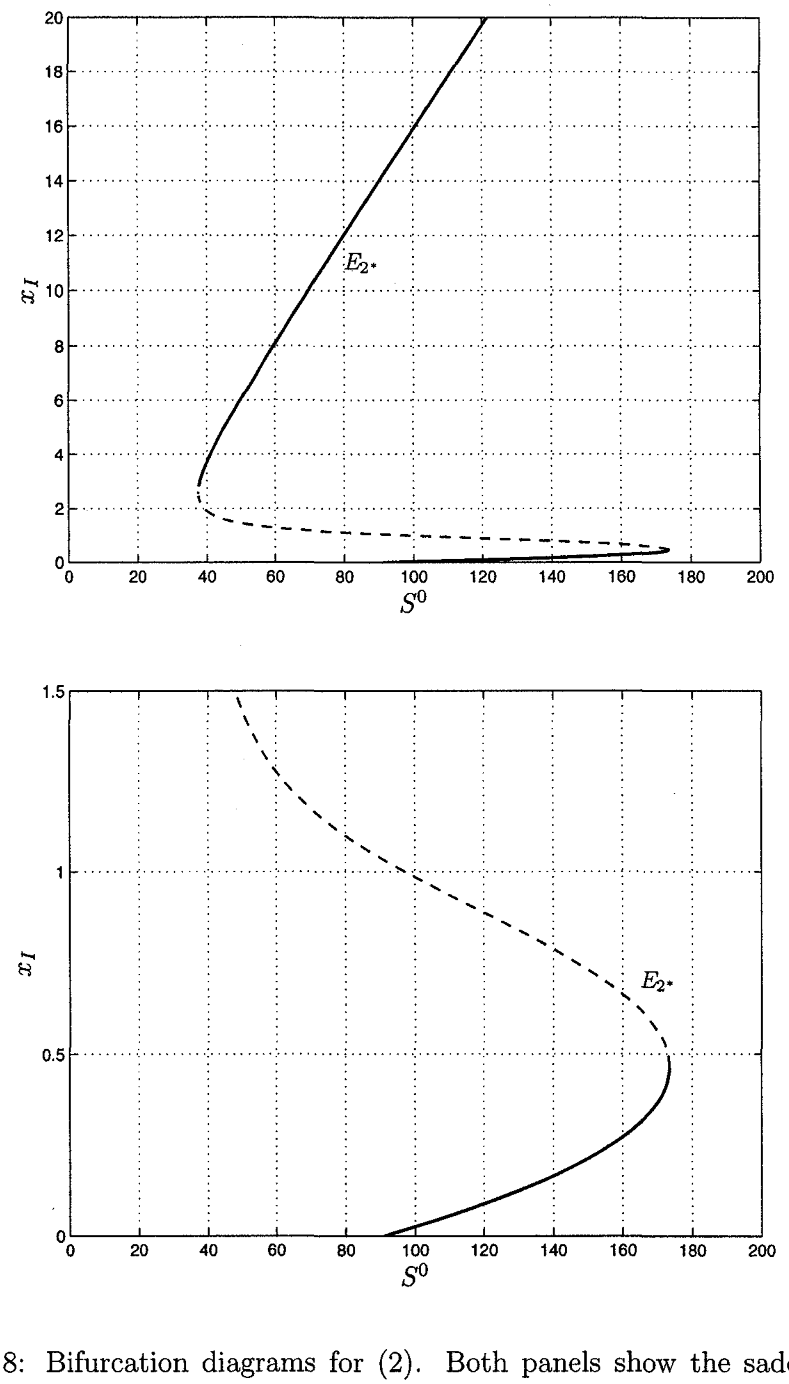

Figure 8: Bifurcation diagrams for (2). Both panels show the saddle-node bifurcation of E_{2*} when $\eta_I > \eta_s$, in subsystem (2), the upper and lower panels both have x_I on the ordinate axis; lower panel is a zoomed-in view of the upper panel; bifurcation parameter is S^0; parameters are as in Figure 7.

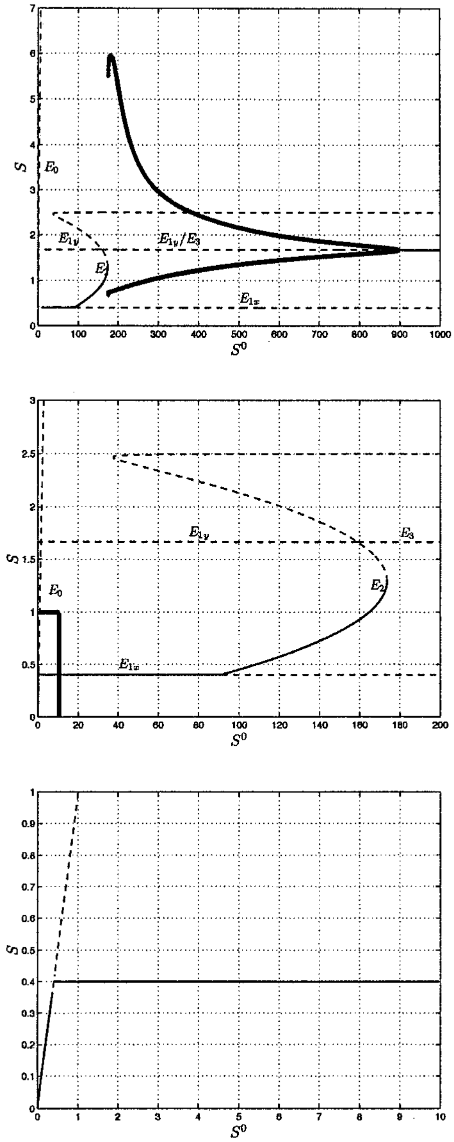

Figure 9: Bifurcation diagram for system (1). All panels are in the case that $\eta_I > \eta_s$ and with bifurcation parameter S^0, the upper, middle, and lower panels all have S on the ordinate axis; the upper panel shows the Hopf bifurcation of E_3 and the homoclinic bifurcation where a stable periodic orbit is born out of one of the unstable E_2 equilibria; the middle panel shows the saddle-node bifurcation of E_2; and the lower panel is a zoomed-in view of the bold box in the middle panel, showing the transcritical bifurcation from E_0 to E_1; parameters are $D = 0.19$, $D_s = 0.2$, $D_I = 1$, $D_y = 1$, $\alpha_s = 0.5$, $\alpha_I = 0.4$, $\alpha_y = 0.6$, $\eta_s = 0.01$, $\eta_I = 1$, $\eta_y = 1$, $\delta = 1$, and $\gamma = 0.02$.

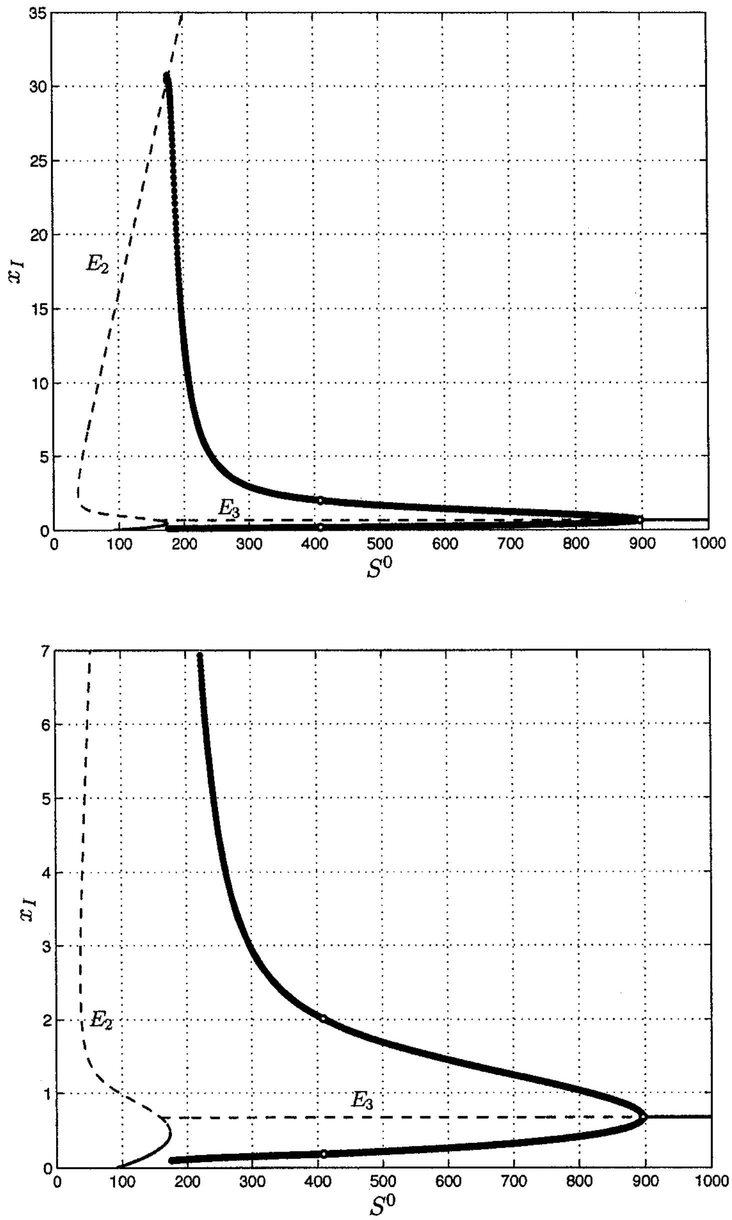

Figure 10: Bifurcation diagram for system (1), with $\eta_I > \eta_s$, the upper and lower panels both have x_I on the ordinate axis. Hopf, saddle-node, and homoclinic bifurcations are present in both panels. Upper panel illustrates where the periodic orbit coalesces with E_2. Lower panel is a close-up of the upper panel, showing the saddle-node and Hopf bifurcations in more detail. Bifurcation parameter is S^0; parameters are as in Figure 9.

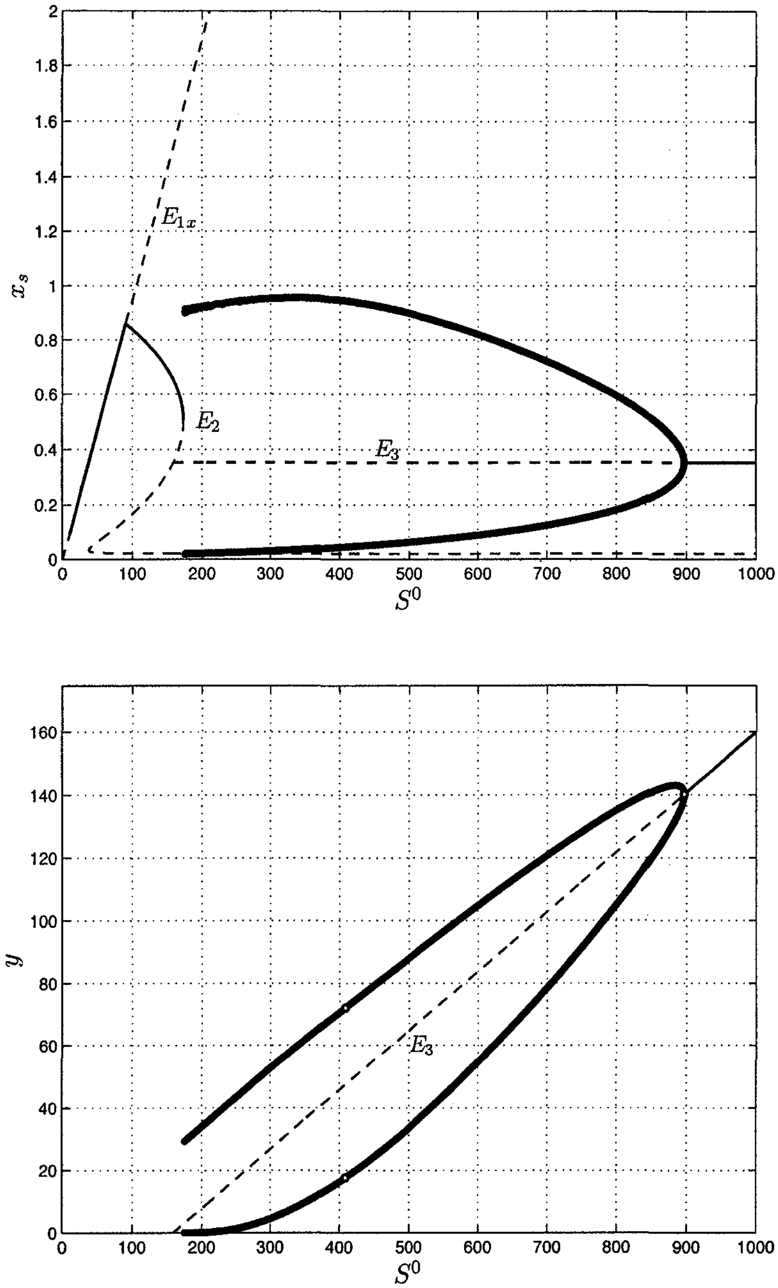

Figure 11: Bifurcation diagram for system (1), with $\eta_I > \eta_s$, the upper and lower panels have x_s and y on the ordinate axis, respectively. Hopf, saddle-node, and homoclinic bifurcations are visible. Bifurcation parameter is S^0; parameters are as in Figure 9.

7 Discussion

In this thesis a model for disease in the chemostat was analysed. It was found that global stability of equilibria E_0, E_{1x}, E_{1y}, and E_2 could be proven under certain conditions, and that a coexistent equilibrium E_3 could be locally asymptotically stable.

There are some possible ecological ramifications to our results. First, the local stability of the coexistence equilibrium supports the natural phenomenon observed in nature where the presence of viruses in the ocean provides enhanced bacterial diversity and coexistence. There are two sides to this idea, however. Although our results support the idea that the virus presence ensures diversity, there is the flip side that without the virus, diversity could be reduced. In an extreme case, an attempt to rid a bacterium species of a virus could end in creating a super-competitor, with the aided bacterium outcompeting all other species. Whereas before removal there was coexistence of multiple bacteria, after the virus is removed one bacterium species wins out. Another possible ramification of our results is in wastewater treatment. As mentioned in the introduction, chemostats are often used in modelling wastewater treatment methods. New methods could be developed that require the use of multiple bacteria, which could be enabled through the addition of a virus.

Mathematically, there are some results that could have interesting interpretations. For example, as seen in Figure 6, as the parameter η_s is increased, the populations experience larger and larger oscillations. This makes some sense, since the strength of η_s corresponds to the ability of the microorganism to convert nutrient to biomass, and the better the nutrient-converter, the larger the high point in the population size. However, the surprising result is that in addition to having a larger population at the high point in an oscillation, the low point dips closer and closer to zero. Although deterministically the population would not die out, a stochastic event like a cold spell or another type of disease could easily wipe out this strong species at one of its low points. Another result deserves interpretation: the dependence of outcomes of the populations on the initial conditions, which can be seen again in Figure 6, and also in Figures 7 and 8. This is the idea that depending on some seemingly simple parameters (such as S^0, the concentration of the nutrient in the nutrient reservoir), the final outcomes of the populations could be drastically different. First, referring to Figure 6, if η_s has a value around 55, depending on the initial conditions of the populations, the outcome could be either large oscillations or stable coexistence. These outcomes could be very different, since as mentioned, populations undergoing large oscillations are more susceptible to stochastic elimination. Similarly, in Figures 7 and 8, it can be seen that if S^0 were chosen above 180, the outcome would be a very high nutrient level, a very low (yet stable) population of x_s, and a huge infected population x_I. In this outcome, although it is deterministically stable, again, it seems likely that a stochastic event could wipe out x_s. However, if S^0 were lowered to a level around 120, there is the possible outcome of a higher x_s population combined with a low or high x_I population. Referring again to Figure 8, there is another interesting interpretation. If the x_I population had approached the low, stable value at the bottom of the upper panel figure, it would be very difficult to change the chemostat conditions to increase the population size. For instance, it would require lowering the S^0 level drastically, to below 35, before the x_I population could converge to the higher values of the upper stable equilibrium.

If S^0 isn't lowered enough, the x_I population could not escape the basin of attraction of the lower equilibrium.

As mentioned in the introduction, there was a similar study to ours done by van den Driessche and Zeeman [36]. They analysed a model of Lotka-Volterra competition where a disease was introduced to weaken the stronger competitor. They used an SI model for the disease, and our results were very similar to theirs: they found that depending on the parameters, both endemic coexistence and oscillatory endemic coexistence was possible between the two competing populations.

There have been other models created in a similar context to the one studied here. A brief summary of this work will be discussed, along with how our model is different from these other attempts.

Mestivier et al. [24] investigate virus-coerced coexistence and diversity in marine bacteria. Their model is based in a chemostat but, unlike our model, they model the virus explicitly. They provide a linear analysis and present a few simulations, and find that coexistence between two bacterial populations is induced by the addition of a virulent virus. It would be interesting to further develop this initial analysis, since the implications are the same as those of our model.

In the study of bacteria-bacteriophage ecology by Beretta et al. [1], the model is set not in a chemostat but in an "open environment", such as the thermoclinic layer of the sea. There is a thorough analysis of a model which also includes the virus as one of its populations. However, these authors were more concerned with phage-bacteria coexistence instead of coexistence between different species of bacteria. They also specify that they are choosing to neglect temperate phages and lysogenic strains [1]. We are more concerned with long-term survival and the possibility of coexistence of different bacterial populations.

It was mentioned earlier (in §3.2) that an SI epidemic/chemostat model had already been analysed with a different interpretation. Interestingly, the context/application had nothing to do with epidemiology; it was a model of a foodweb with a predator feeding on two trophic levels [13], [38]. Many models can be used for different applications other than their intended one. For instance, the model in [24] could be identically viewed as a model for predator-prey interactions in the chemostat. As such, our model could also describe various applications, and so we have included one possibility here. Although chemostats are typically used to study bacteria, our system could be seen as modelling a fish population in a lake, where fish are competing exploitatively for their food, and where one is affected by a disease. Within the lake/ocean context, there could be other similar scenarios that a lake or marine ecologist could use.

Throughout our analysis of the this model, some possible modifications became apparent. We will include these modifications as possible future directions for this research. For one, the model could be adjusted to fit a more general virus-bacteria interaction. For instance, although most lysogenic bacteria remain so indefinitely (i.e. do not lyse and produce new viruses), some do not. Those that do not will lyse and release a number of new viruses into the system, which could be accounted for in the model. This could be done by adding the virus population to the model, and by incorporating the number of viruses produced by lysis.

Also, the mode of infection and the mechanism by which the virus spreads could be incorporated into the model in a different way. Currently the spread of the virus is modelled using the principle of mass action, however, it is not clear that proximity between sick and healthy bacteria affects the rate of infection. Infection could be spreading via the virus-bacterium interactions only.

Another part of the model that could be modified is its inclusion of recovery. We have included this for reasons previously mentioned, such as the idea of lysogenic bacteria being seen as "recovered" when they do not eventually lyse. This said, perhaps the model might be more accurate without including recovery at all, or by more accurately representing the complex nature of lysogeny.

Much of the research on virus-induced bacterial diversity refers to virulent, as opposed to temperate, viruses (that is, when the type of virus is specified). One reason for this may be that the intracellular material released when an infected bacterium lyses (such as Nitrogen) provides food for other species of bacteria and hence improves diversity [5], [7]. However, it is possibly due to the mentioned focus on virulent viruses that the virus population is modelled explicitly in the papers discussed above ([1], [11], and [24]). Modelling the virus in this way (as opposed to modelling it implicitly as we have) could be a possible avenue to explore.

8 Proofs

Recall that we are assuming that $\alpha_s \geq \alpha_I$, $D < D_s < D_I$, and $\eta_s \geq \eta_I$, unless specified otherwise.

Proof of Lemma 4.1.

Recall that we would like to prove that E_{2*} exists and is unique if $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$.

We substitute $x_s^* = \frac{D_I - \alpha_I S^* + \gamma}{\delta}$ and $x_I^* = \frac{x_s^*(-D_s+\alpha_s S^*)}{(\delta x_s^* - \gamma)}$ into $S'(t)$ from system (2) (and multiply both sides of the resulting $S'(t) = 0$ equation by $\eta_s\eta_I\delta(D_I - \alpha_I S)$ to get a cubic in S (which will be zero at S^*). The resulting cubic, call it $f(S)$ (with $f(S^*) = 0$), is:

$$\begin{aligned}
f(S) &= D\eta_s\eta_I\delta(S^0 - S)(D_I - \alpha_I S) - \alpha_s\eta_I(D_I - \alpha_I S)(D_I - \alpha_I S + \gamma)S \\
&\quad -\alpha_I\eta_s(D_I - \alpha_I S + \gamma)(-D_s + \alpha_s S)S \\
&= D\eta_s\eta_I\delta S^0 D_I + S(-S^0 D\alpha_I\eta_s\eta_I\delta - D\eta_s\eta_I\delta D_I - \alpha_s\eta_I D_I\gamma - \alpha_s\eta_I D_I^2 \\
&\quad +\alpha_I\eta_s D_s\gamma + \alpha_I\eta_s D_s D_I) + S^2(\alpha_I D\eta_s\eta_I\delta + 2\alpha_s\alpha_I\eta_I D_I + \alpha_s\alpha_I\eta_I\gamma \\
&\quad -\alpha_I^2\eta_s D_s - \alpha_s\alpha_I\eta_s\gamma - \alpha_s\alpha_I\eta_s D_I) + S^3\alpha_s\alpha_I^2(\eta_s - \eta_I)
\end{aligned}$$

We will show that when $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$ there is only one positive root $S^* \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ of this function, and hence a unique E_{2*}. First we assume $\eta_s > \eta_I$, and so the coefficient of S^3 is positive. Hence as S goes to positive infinity, $f(S)$ goes to positive infinity. As S^* goes to negative infinity, $f(S)$ goes to negative infinity. (We will consider the case of $\eta_s = \eta_I$ shortly.)

At 0, $f(0) = D\eta_s\eta_I\delta S^0 D_I > 0$ and so there must be at least one negative root of $f(S)$. At $\frac{D_I}{\alpha_I}$, $f(\frac{D_I}{\alpha_I}) = -D_I\eta_s\gamma(-D_s + \alpha_s\frac{D_I}{\alpha_I}) < 0$. This means that there is additionally one positive root that is beyond $\frac{D_I}{\alpha_I}$. This leaves one root, and whether or not it falls in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ will depend on the sign of $f(S)$ at $\frac{D_s}{\alpha_s}$. We investigate this now:

$$\begin{aligned}
f\left(\frac{D_s}{\alpha_s}\right) &= D\eta_s\eta_I\delta\left(S^0 - \frac{D_s}{\alpha_s}\right)\left(D_I - \alpha_I\frac{D_s}{\alpha_s}\right) \\
&\quad -\alpha_s\eta_I\left(D_I - \alpha_I\frac{D_s}{\alpha_s}\right)\left(D_I - \alpha_I\frac{D_s}{\alpha_s} + \gamma\right)\frac{D_s}{\alpha_s} \\
&= D\eta_s\eta_I\delta\left(D_I - \alpha_I\frac{D_s}{\alpha_s}\right)\left[\left(S^0 - \frac{D_s}{\alpha_s}\right) - \frac{D_s}{D\eta_s\delta}\left(D_I - \alpha_I\frac{D_s}{\alpha_s} + \gamma\right)\right] \\
&= D\eta_s\eta_I\delta\left(D_I - \alpha_I\frac{D_s}{\alpha_s}\right)\left[S^0 - \frac{D_s}{D\eta_s\delta}\left(\frac{D\eta_s\delta}{\alpha_s} + D_I - \alpha_I\frac{D_s}{\alpha_s} + \gamma\right)\right]
\end{aligned}$$

From the equations above we can see that $f(\frac{D_s}{\alpha_s})$ is positive precisely when $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$. Now when $f(\frac{D_s}{\alpha_s})$ is positive, there is exactly one root in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$, and hence E_{2*} exists and is unique. Otherwise if $f\left(\frac{D_s}{\alpha_s}\right) < 0$ then no E_{2*} exists. Note that in this case E_{1*} is locally asymptotically stable.

Now when $\eta_s = \eta_I$, $f(S)$ becomes a quadratic; call it $\hat{f}(S)$. $\hat{f}(S)$ has some properties in common with $f(S)$:

$$\begin{aligned}
\hat{f}(0) &= D(\eta)^2\delta S^0 D_I > 0, \\
\hat{f}(\frac{D_I}{\alpha_I}) &= \frac{\eta D_I\gamma}{\alpha_I}(\alpha_I D_s - \alpha_s D_I) < 0, \quad \text{and} \\
\hat{f}(\frac{D_s}{\alpha_s}) &= \eta\left(D_I - \frac{\alpha_I D_s}{\alpha_s}\right)\left(D\eta\delta\left(S^0 - \frac{D_s}{\alpha_s}\right) - D_s\left(D_I - \frac{\alpha_I D_s}{\alpha_s} + \gamma\right)\right) \\
&> 0 \quad \text{when} \quad S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s}).
\end{aligned}$$

This shows that $\hat{f}(S)$ must have two positive roots, only one of which allows all components of E_{2*} to be positive, since it falls in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$. This particular root falls in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ if and only if $S^0 > \frac{D_s}{\delta D\eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$. ■

Proof of Lemma 4.2.

Here we will prove that, when $\eta_I > \eta_s$, at least one E_{2*} exists when $S^0 > \frac{D_s}{\delta D \eta_s}(\gamma + \frac{D\delta\eta_s}{\alpha_s} + D_I - \frac{\alpha_I D_s}{\alpha_s})$, and that E_{2*} is unique when either of the following criteria hold:

(a) $D_I < \gamma$, or

(b) $\eta_I \leq \frac{\alpha_s \gamma \eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$.

We will use two different configurations of the equation $S'(t) = 0$ from (1) to prove parts (a) and (b) of the lemma. To prove part (a), we use the following configuration.

Let

$$G(S, x_I) = (S^0 - S)D - \frac{\alpha_I x_I S}{\eta_I}$$

and

$$H(S, x_s) = \frac{\alpha_s x_s S}{\eta_s}.$$

where $S'(S^*, x_s^*, x_I^*) = G(S^*, x_I^*) - H(S^*, x_s^*) = 0$. We have strategically separated the cubic $S'(t) = 0$ into the two functions G and H, and their intersections represent solutions of the cubic and hence possible equilibria for E_{2*}. We will find criteria for G and H to have only one root for $S \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ when $\eta_I > \eta_s$, thus proving part of the lemma.

$$\begin{aligned}
\frac{dG}{dS} &= -D - \frac{\alpha_I \frac{dx_I}{dS} S}{\eta_I} - \frac{\alpha_I x_I}{\eta_I} \\
&= -D\left(\frac{\alpha_I S}{\eta_I}\right)\left(\frac{\gamma\alpha_I(-D_s + \alpha_s S) + \alpha_s(-\alpha_I S + D_I + \gamma)(D_I - \alpha_I S)}{\delta(D_I - \alpha_I S)^2}\right) \\
&< 0 \quad \text{for} \quad S \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right) \\
\frac{dH}{dS} &= \frac{\alpha_s \frac{dx_s}{dS} S}{\eta_s} + \frac{\alpha_s x_s}{\eta_s}
\end{aligned}$$

$$
\begin{aligned}
&= -\frac{\alpha_s \alpha_I S}{\delta \eta_s} + \frac{\alpha_s x_s}{\eta_s} \\
&= -\frac{\alpha_s \alpha_I S}{\delta \eta_s} + \frac{\alpha_s(-\alpha_I S + D_I + \gamma)}{\delta \eta_s} \\
&= \frac{-2\alpha_s \alpha_I S + \alpha_s D_I + \alpha_s \gamma}{\delta \eta_s} \\
&> 0 \quad \text{for} \quad S \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I} \right), \quad \text{when} \quad D_I < \gamma.
\end{aligned}
$$

The above results show that G is decreasing in the meaningful region of $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$, and H is increasing in the same region when $D_I < \gamma$. The last necessary piece of information to conclude that we have a unique equilibrium is that $G(\frac{D_s}{\alpha_s}) > H(\frac{D_s}{\alpha_s})$ and that $G(\frac{D_I}{\alpha_I}) < H(\frac{D_I}{\alpha_I})$: (here we rewrite G and H completely in terms of S)

$$
\begin{aligned}
& S^0 > \frac{D_s}{D\delta\eta_s}\left(D_I + \gamma - \frac{\alpha_I D_s}{\alpha_s} + \frac{\delta D \eta_s}{\alpha_s} \right) \\
\Leftrightarrow \quad & (S^0 - \frac{D_s}{\alpha_s})D - \frac{(D_I - \frac{\alpha_I D_s}{\alpha_s} + \gamma)D_s}{\delta \eta_s} > 0 \\
\Leftrightarrow \quad & (S^0 - \frac{D_s}{\alpha_s})D - \frac{(D_I - \alpha_I \frac{D_s}{\alpha_s} + \gamma)(-D_s + \alpha_s \frac{D_s}{\alpha_s})}{\delta(D_I - \alpha_I \frac{D_s}{\alpha_s})} \left(\frac{\alpha_I}{\eta_I} \frac{D_s}{\alpha_s} \right) \\
& > \frac{(D_I - \alpha_I \frac{D_s}{\alpha_s} + \gamma)\alpha_s \frac{D_s}{\alpha_s}}{\delta \eta_s} \\
\Leftrightarrow \quad & G(\frac{D_s}{\alpha_s}) > H(\frac{D_s}{\alpha_s}).
\end{aligned}
$$

And we know that $H(S)$ goes to positive infinity at $\frac{D_I}{\alpha_I}$, which ensures one and only one intersection of $G(S)$ and $H(S)$ in $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$.

To prove part (b), we use the following configuration.

Let

$$
g(S) = \frac{\delta D(S^0 - S)}{S}
$$

and

$$h(S) = \left[\frac{\alpha_s}{\eta_s} + \frac{\alpha_I(-D_s + \alpha_s S)}{\eta_I(D_I - \alpha_I S)}\right](D_I + \gamma - \alpha_I S),$$

where $S'(S^*) = g(S^*) - h(S^*) = 0$. Again, the intersections of $g(S)$ and $h(S)$ represent possible equilibria E_{2^*}. We will again find criteria for g and h to have only one intersection for $S \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ when $\eta_I > \eta_s$, and thus prove the rest of the lemma.

$$\begin{aligned} g'(S) &= -\frac{\delta D S^0}{S^2} \\ &< 0 \end{aligned}$$

Hence $g(S)$ is decreasing. We will now derive a condition so that $h(S)$ is increasing, so that there will be a unique intersection.

$$\begin{aligned} h'(S) &= -\alpha_I\left[\frac{\alpha_s}{\eta_s} + \frac{\alpha_I(-D_s + \alpha_s S)}{\eta_I(D_I - \alpha_I S)}\right] + (D_I + \gamma - \alpha_I S)\left[\frac{\alpha_I(\alpha_s D_I - \alpha_I D_s)}{\eta_s(D_I - \alpha_I S)^2}\right] \\ &= \frac{1}{\eta_s\eta_I(D_I - \alpha_I S)^2}[\alpha_I(-\alpha_s\eta_I(D_I - \alpha_I S)^2 \\ &\quad -\alpha_I\eta_s(-D_s + \alpha_s S)(D_I - \alpha_I S) + \eta_s(D_I + \gamma - \alpha_I S)(\alpha_s D_I - \alpha_I D_s))] \\ &= \frac{1}{\eta_s\eta_I(D_I - \alpha_I S)^2}[\alpha_I(-\alpha_s\eta_I(D_I - \alpha_I S)^2 \\ &\quad +\eta_s(-\alpha_s\alpha_I D_I S + \alpha_s\alpha_I^2 S^2 + \alpha_s D_I^2 + \gamma\alpha_s D_I - \gamma\alpha_I D_s - \alpha_s\alpha_I D_I S))] \\ &= \frac{\alpha_I}{\eta_s\eta_I(D_I - \alpha_I S)^2}[-\alpha_s\eta_I(D_I - \alpha_I S)^2 + \eta_s\alpha_s(D_I - \alpha_I S)^2 \\ &\quad +\eta_s\gamma(\alpha_s D_I - \alpha_I D_s)] \end{aligned}$$

Recall that we are looking only at solutions with $\frac{D_s}{\alpha_s} < S < \frac{D_I}{\alpha_I}$. The sign of the terms inside the square brackets in the above expression will determine the sign of $h'(S)$. We look at those terms only:

$$\begin{aligned}
& -\alpha_s\eta_I(D_I-\alpha_I S)^2+\eta_s\alpha_s(D_I-\alpha_I S)^2+\eta_s\gamma(\alpha_s D_I-\alpha_I D_s) \\
= \; & \eta_s\gamma(\alpha_s D_I-\alpha_I D_s)+\alpha_s(D_I-\alpha_I S)^2(\eta_s-\eta_I) \\
= \; & \eta_s\gamma(\alpha_s D_I-\alpha_I D_s)-\alpha_s(\eta_I-\eta_s)(D_I-\alpha_I\frac{D_I}{\alpha_I})^2 \\
> \; & 0 \quad \text{when} \quad \eta_I \le \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I-\alpha_I D_s}+\eta_s
\end{aligned}$$

We now have that $g(S)$ is decreasing and $h(S)$ is increasing (under the stated conditions). It remains to be shown that $g(\frac{D_s}{\alpha_s}) > h(\frac{D_s}{\alpha_s})$ and that $g(\frac{D_I}{\alpha_I}) < h(\frac{D_I}{\alpha_I})$.

$$\begin{aligned}
& S^0 > \frac{D_s}{D\delta\eta_s}\left(D_I+\gamma-\frac{\alpha_I D_s}{\alpha_s}+\frac{\delta D\eta_s}{\alpha_s}\right) \\
\Leftrightarrow \; & (S^0-\frac{D_s}{\alpha_s})\delta D > (D_I-\frac{\alpha_I D_s}{\alpha_s}+\gamma)\frac{D_s}{\eta_s} \\
\Leftrightarrow \; & \frac{(S^0-\frac{D_s}{\alpha_s})\delta D}{\frac{D_s}{\alpha_s}} > (D_I-\frac{\alpha_I D_s}{\alpha_s}+\gamma)\frac{\alpha_s}{\eta_s} \\
\Leftrightarrow \; & g(\frac{D_s}{\alpha_s}) > h(\frac{D_s}{\alpha_s}).
\end{aligned}$$

And we know that $h(S)$ goes to positive infinity at $\frac{D_I}{\alpha_I}$, which ensures one and only one intersection of $g(S)$ and $h(S)$ in $\left(\frac{D_s}{\alpha_s},\frac{D_I}{\alpha_I}\right)$ when $\eta_I \le \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I-\alpha_I D_s}+\eta_s$.

■

Proof of Lemma 4.3.

Here we will prove that, when $\eta_I > \eta_s$, E_{2*} is locally asymptotically stable if $\eta_I \le \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I-\alpha_I D_s}+\eta_s$.

When $\eta_I > \eta_s$ we have the same characteristic equation as when $\eta_s > \eta_I$. The same inequalities must hold concerning a_1, a_2, and a_3, i.e. that $a_1 > 0$,

$a_3 > 0$, and $a_1 a_2 > a_3$. To begin, a_1 is positive regardless of the relative values of η_s and η_I. The other two conditions remain to be shown.

Using a_3 as defined in §4.2.4, we have:

$$\begin{aligned} a_3 &= \frac{\delta S^0 D x_I^*}{S^*}(\delta x_s^* - \gamma) + \frac{\alpha_s \alpha_I \delta S^* x_s^* x_I^*}{\eta_I} \\ &\quad - \frac{\alpha_s \alpha_I \delta S^* x_s^* x_I^*}{\eta_s} + \frac{\alpha_s \alpha_I \gamma S^* x_I^*}{\eta_s} + \frac{\alpha_I^2 \gamma S^* (x_I^*)^2}{\eta_I x_s^*} \\ &> x_I^* S^* \alpha_I \left(\frac{\alpha_s \delta x_s^*}{\eta_I} - \frac{\alpha_s \delta x_s^*}{\eta_s} + \frac{\alpha_s \gamma}{\eta_s} + \frac{\alpha_I \gamma x_I^*}{\eta_I x_s^*} \right) \quad \text{since} \quad \delta x_s^* > \gamma. \end{aligned}$$

It suffices to show that the term inside the brackets is nonnegative. Replacing $x_I^* = \frac{x_s^*(-D_s + \alpha_s S^*)}{(\delta x_s^* - \gamma)}$ and finding a common denominator, it follows that the expression inside the brackets equals

$$\left[\frac{1}{\eta_s \eta_I (\delta x_s^* - \gamma)}\right] [\alpha_s \delta \eta_s x_s^* (\delta x_s^* - \gamma) - \alpha_s \delta \eta_I x_s^* (\delta x_s^* - \gamma) \\ + \alpha_s \gamma \eta_I (\delta x_s^* - \gamma) + \alpha_I \gamma \eta_s (-D_s + \alpha_s S^*)].$$

We can neglect the denominator, since it is always positive when E_{2^*} exists. There are four terms in the expression. The final term, $\alpha_I \gamma \eta_s (-D_s + \alpha_s S^*)$, is positive, since $S^* > \frac{D_s}{\alpha_s}$. This leaves three terms. We find a common factor of $(\delta x_s^* - \gamma)$ (which is positive when E_{2^*} exists), and are left with the following expression:

$$\alpha_s \delta \eta_s x_s^* - \alpha_s \delta \eta_I x_s^* + \alpha_s \gamma \eta_I.$$

Factoring $\delta \alpha_s x_s^*$ out of two terms and replacing x_s^* by $x_s^* = \frac{D_I - \alpha_I S^* + \gamma}{\delta}$ we arrive at:

$$\alpha_s \gamma \eta_I - \alpha_s (D_I - \alpha_I S^* + \gamma)(\eta_I - \eta_s).$$

Replacing S^* by its smallest possible value, $\frac{D_s}{\alpha_s}$, it follows that,

$$\begin{aligned}
& \alpha_s\gamma\eta_I - \alpha_s(D_I - \alpha_I S^* + \gamma)(\eta_I - \eta_s) \\
\geq\; & \alpha_s\gamma\eta_I - \alpha_s(D_I - \alpha_I \frac{D_s}{\alpha_s} + \gamma)(\eta_I - \eta_s) \\
=\; & \alpha_s\gamma\eta_I - (\alpha_s D_I - \alpha_I D_s + \alpha_s\gamma)(\eta_I - \eta_s) \\
=\; & \alpha_s\gamma\eta_s - (\alpha_s D_I - \alpha_I D_s)(\eta_I - \eta_s) \\
\geq\; & 0, \quad \text{when} \quad \eta_I \leq \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s
\end{aligned}$$

Hence $a_3 > 0$ when $\eta_I \leq \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$.

Now, it remains to be shown that $a_1a_2 > a_3$. First, recall that (5) (in §4.2.4) is an expression for $a_1a_2 - a_3$. Under our current assumption that $\eta_I > \eta_s$ in addition to our assumptions that $\alpha_s \geq \alpha_I$ and $\delta x_s^* > \gamma$, this expression is positive.

Hence, in the case of $\eta_I > \eta_s$, when it exists, E_{2^*} is locally asymptotically stable when $\eta_I \leq \frac{\alpha_s\gamma\eta_s}{\alpha_s D_I - \alpha_I D_s} + \eta_s$. ■

Proof of Proposition 4.1.

Here we prove that if an equilibrium of the form E_3 exists, then E_{1x}, E_{1y}, and at least one equilibrium of the form E_2 exist.

Any equilibrium of the form of E_2 or E_3 must have components satisfying $x_s(S) = \frac{-\alpha_I S + D_I + \gamma}{\delta}$ and $x_I(S) = \frac{x_S(-D_s + \alpha_s S)}{\delta x_s - \gamma}$. Also $y(\hat{S}) > 0$ for E_3, but $y(S^*) = 0$ for E_2.

Consider the following function

$$H(S) = (S^0 - S)D - \frac{\alpha_s S x_s(S)}{\eta_s} - \frac{\alpha_I S x_I(S)}{\eta_I}.$$

Then $H(\hat{S}) > 0$, since

$$(S^0 - \hat{S})D - \frac{\alpha_s \hat{S} x_s(\hat{S})}{\eta_s} - \frac{\alpha_I \hat{S} x_I(\hat{S})}{\eta_I} - \frac{\alpha_y \hat{S} y(\hat{S})}{\eta_y} = 0$$

and $y(\hat{S}) > 0$.

For $S \in (\hat{S}, \frac{D_I}{\alpha_I})$, $H(S)$ is a continuous function of S. Note that

$$\lim_{S \to \frac{D_I}{\alpha_I}^-} x_I(S) = +\infty,$$

and $x_s\left(\frac{D_I}{\alpha_I}\right) > 0$, and that if $S^0 < \frac{D_I}{\alpha_I}$, then since $x_s(S) > 0$ and $x_I(S) > 0$ for $S \in [\hat{S}, S^0]$, it follows that $H(S^0) < 0$. Hence, there exists a value of $S^* \in (\hat{S}, \min(S^0, \frac{D_I}{\alpha_I}))$ satisfying $H(S^*) = 0$, $x_s(S^*) > 0$, and $x_I(S^*) > 0$. Therefore, E_2 exists.

Now, if E_3 exists, then we have that $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$ and that

$$(S^0 - \frac{D_y}{\alpha_y})D = \frac{\alpha_s \hat{S} \hat{x}_s}{\eta_s} + \frac{\alpha_I \hat{S} \hat{x}_I}{\eta_I} > 0 \Rightarrow S^0 > \frac{D_y}{\alpha_y}.$$

From this, E_{1y} and E_{1x} must also exist and we conclude our argument. ■

Proof of Lemma 4.5.

We will prove that when E_2 and E_3 exist, it follows that $\hat{S} < S^* = \frac{D_y}{\alpha_y}$.

Assuming both E_2 and E_3 exist, we have that any equilibrium of the form of E_2 or E_3 must satisfy $x_s(S) = \frac{-\alpha_I S + D_I + \gamma}{\delta}$, $x_I(S) = \frac{x_S(-D_s + \alpha_s S)}{\delta x_s - \gamma}$, and $y(S) = \left(\frac{\eta_y}{\alpha_y}\right)\left(\frac{S^0 D}{S} - D - \frac{\alpha_s x_s}{\eta_s} - \frac{\alpha_I x_I}{\eta_I}\right)$, where $y(S) > 0$ for E_3 and $y(S) = 0$ for E_2. We also have:

$$\frac{dx_s}{dS} = \frac{-\alpha_I}{\delta}, \qquad \text{and}$$

$$
\begin{aligned}
\frac{dx_I}{dS} &= \frac{\left[\left(\frac{-\alpha_I}{\delta}\right)(-D_s+\alpha_s S)+\alpha_s x_s\right](\delta x_s-\gamma)+\delta\left(\frac{\alpha_I}{\delta}\right)x_s(-D_s+\alpha_s S)}{(\delta x_s-\gamma)^2} \\
&= \frac{\gamma\left[\left(\frac{\alpha_I}{\delta}\right)(-D_s+\alpha_s S)-\alpha_s x_s\right]+\delta\alpha_s x_s^2}{(\delta x_s-\gamma)^2} \\
&= \frac{\frac{\gamma\alpha_I}{\delta}(-D_s+\alpha_s S)+\alpha_s x_s(\delta x_s-\gamma)}{(\delta x_s-\gamma)^2} \\
&= \frac{\gamma\alpha_I(-D_s+\alpha_s S)+\alpha_s(-\alpha_I S+D_I+\gamma)(D_I-\alpha_I S)}{\delta(D_I-\alpha_I S)^2}.
\end{aligned}
$$

Therefore,

$$
\begin{aligned}
\frac{dy}{dS} &= \left(\frac{\eta_y}{\alpha_y}\right)\left(-\frac{S^0 D}{S^2}-\frac{\alpha_s}{\eta_s}\frac{dx_s}{dS}-\frac{\alpha_I}{\eta_I}\frac{dx_I}{dS}\right) \\
&= \left(\frac{\eta_y}{\alpha_y}\right)[-\frac{S^0 D}{S^2}+\frac{\alpha_s\alpha_I}{\eta_s\delta} \\
&\quad -\frac{\alpha_I}{\eta_I}\left(\frac{\gamma\alpha_I(-D_s+\alpha_s S)+\alpha_s(-\alpha_I S+D_I+\gamma)(D_I-\alpha_I S)}{\delta(D_I-\alpha_I S)^2}\right)]
\end{aligned}
$$

Recall that the S component of E_2 must lie in the interval $\left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$, and note that the above expression for $\frac{dy}{dS}$ is always negative for $S \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ and $\hat{S} = \frac{D_y}{\alpha_y} \in \left(\frac{D_s}{\alpha_s}, \frac{D_I}{\alpha_I}\right)$ where E_3 exists. Therefore, in order for $\hat{y} > 0$, it follows that $\hat{S} < S^*$. ■

A Appendix

A.1 General local analysis for E_3

Recall that in the local analysis of E_3 (§4.3.6), we assumed $D = D_s = D_I$ and $\eta_s = \eta_I$. The analysis presented here does not assume anything beyond existence of E_3, i.e. that $\frac{D_s}{\alpha_s} < \frac{D_y}{\alpha_y} < \frac{D_I}{\alpha_I}$ and $S^0 > \frac{D_y}{\alpha_y}\left[\frac{\alpha_s(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})}{\delta\eta_s} + \frac{\alpha_I(D_I+\gamma-\frac{\alpha_I D_y}{\alpha_y})(-D_s+\frac{\alpha_s D_y}{\alpha_y})}{\delta\eta_I(D_I-\frac{\alpha_I D_y}{\alpha_y})} + D\right]$.

The Jacobian matrix for E_3 is:

$$J_{E_3} = \begin{bmatrix} -D - \frac{\alpha_s}{\eta_s}\hat{x}_s - \frac{\alpha_I}{\eta_I}\hat{x}_I - \frac{\alpha_y}{\eta_y}\hat{y} & -\frac{\alpha_s}{\eta_s}\hat{S} & -\frac{\alpha_I}{\eta_I}\hat{S} & -\frac{\alpha_y}{\eta_y}\hat{S} \\ \alpha_s\hat{x}_s & -D_s + \alpha_s\hat{S} - \delta\hat{x}_I & -\delta\hat{x}_s + \gamma & 0 \\ \alpha_I\hat{x}_I & \delta\hat{x}_I & -D_I + \alpha_I\hat{S} + \delta\hat{x}_s - \gamma & 0 \\ \alpha_y\hat{y} & 0 & 0 & -D_y + \alpha_y\hat{S} \end{bmatrix},$$

which simplifies to

$$\begin{bmatrix} -\frac{S^0 D}{\hat{S}} & -\frac{\alpha_s}{\eta_s}\hat{S} & -\frac{\alpha_I}{\eta_I}\hat{S} & -\frac{\alpha_y}{\eta_y}\hat{S} \\ \alpha_s\hat{x}_s & -\frac{\gamma\hat{x}_I}{\hat{x}_s} & -\delta\hat{x}_s + \gamma & 0 \\ \alpha_I\hat{x}_I & \delta\hat{x}_I & 0 & 0 \\ \alpha_y\hat{y} & 0 & 0 & 0 \end{bmatrix}.$$

The characteristic equation is of the form $\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0$, where

$$\begin{aligned} a_1 &= \frac{S^0 D}{\hat{S}} + \frac{\gamma\hat{x}_I}{\hat{x}_s}, \\ a_2 &= \frac{\gamma S^0 D\hat{x}_I}{\hat{x}_s\hat{S}} + \frac{\alpha_s^2\hat{x}_s\hat{S}}{\eta_s} + \delta^2\hat{x}_s\hat{x}_I - \gamma\delta\hat{x}_I + \frac{\alpha_I^2\hat{x}_I\hat{S}}{\eta_I} + \frac{\alpha_y^2\hat{y}\hat{S}}{\eta_y}, \\ a_3 &= \frac{\delta^2 S^0 D\hat{x}_s\hat{x}_I}{\hat{S}} - \frac{S^0 D\delta\gamma\hat{x}_I}{\hat{S}} + \frac{\alpha_s\alpha_I\delta\hat{S}\hat{x}_s\hat{x}_I}{\eta_I} \\ &\quad - \frac{\alpha_s\alpha_I\delta\hat{S}\hat{x}_s\hat{x}_I}{\eta_s} + \frac{\alpha_s\alpha_I\gamma\hat{S}\hat{x}_I}{\eta_s} + \frac{\alpha_I^2\gamma\hat{S}(\hat{x}_I)^2}{\eta_I\hat{x}_s} + \frac{\alpha_y^2\gamma\hat{S}\hat{x}_I\hat{y}}{\eta_y\hat{x}_s}, \qquad \text{and} \end{aligned}$$

$$a_4 = \left(\frac{(\alpha_y)^2 \delta \hat{S} \hat{x}_I \hat{y}}{\eta_y}\right)(\delta \hat{x}_s - \gamma).$$

By the Routh-Hurwitz criterion for fourth order polynomials, all roots of the characteristic equation have negative real part if and only if: $a_1 > 0$, $a_3 > 0$, $a_1 a_2 > a_3$, $a_4 > 0$, and $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$ [15] [18] [30].

Under our assumption that $\eta_s \geq \eta_I$, all the coefficients are positive provided E_3 exists, i.e. that $\hat{x}_s \geq \frac{\gamma}{\delta}$. As in the case of E_2, it is difficult to prove that $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$. However, in all of our numerical simulations and bifurcation diagrams using XPPAUT [16], when E_3 exists it appears to be locally asymptotically stable. For an example of coexistence of all three species at equilibrium, see Figure 3. Also refer to the bifurcation diagrams for the full system (1), in Figures 4 and 5.

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