AN ABSTRACT OF THE THESIS OF

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Title: A Ross-Macdonald Model with Vector Demography

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Patrick De Leenheer

Malaria is a vector-borne disease that has affected humans and other animals for a long time and which has shown high prevalence among different populations. During the beginning of the 20th century, Sir Ronald Ross and George Macdonald developed a model that represents the spread of malaria through the interaction of human and mosquito populations. Throughout this work, we study the vector-host dynamics of Malaria with respect to a model based on the work of Ross and Macdonald, which includes the demography of susceptible mosquitoes. With the help of both classic and modern techniques of dynamical systems, we analyze the different characteristics of the proposed model and its connection to corresponding biological scenarios. Some features of this model are the existence of a unique endemic equilibrium if the basic reproduction number is larger than 1; the global asymptotic stability of this equilibrium, provided a sector condition for the function describing the vector demography holds; and the persistence of Malaria when the basic reproduction number is larger than 1. It is also shown that the endemic equilibrium can be unstable under certain condition.

A Ross-Macdonald Model with Vector Demography

by

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Ricardo Noe Gerardo Reyes Grimaldo, Author

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Academic

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TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

LIST OF FIGURES

A ROSS-MACDONALD MODEL WITH VECTOR DEMOGRAPHY

1. INTRODUCTION

In this chapter we describe the importance of Malaria and also some of the different classical approaches to study its dynamics and spread among the human and mosquito population. We review the work by Sir Ronald Ross [27, 28], and the generalization introduced by George Macdonald [33, 21].

1.1. Biological Background

1.1.1 Malaria

The disease known as *malaria* is a *vector-borne disease*, that is a human infectious disease caused by a parasite, virus or bacteria and that it is transmitted between humans or from animals to humans [23]. Malaria is caused by parasites of the genus *Plasmodium* [1, 21, 25, 26, 27, 29]. There are four members that affect mainly humans: *P. vivax*, *P. falciparum*, *P. malariae* and *P. ovale*.

Malaria is one of the diseases that affect humans with higher prevalence and, deadly when left untreated [26]. The World Health Organization reported in 2016 that 216 million cases of Malaria had occurred worldwide that year, where about 445 000 of these cases resulted in human fatalities [24]. In 2015, 95 countries and territories had ongoing malaria transmission and about 3.2 billion people, almost half of the world's population, were at risk of infection by malaria. Among the characteristics of this disease is that its symptoms appear between 7 and 15 days after the infective mosquito bite [26], whilst normally the disease is treatable, but if not treated within 24 hours malaria can progress to severe illness, often leading to death.

In Asia and Africa the most common *Plasmodium* parasites are *falciparum* and *malariae*; whilst the cases of *vivax* are more frequent in Africa, India and Latin America; finally, the last member *ovale* occurs only in Africa.

The main transmitter or vector of this disease is the female mosquito of the genus *Anopheles*. The life cycle of the malaria is extremely complex, which provides tools for its survival [1, 27, 29]. *P. falciparum* is the most common parasite that affects humans among the four members of *Plasmodium* described above, thus making it the focus of research among epidemiologists [9].

1.1.2 Life Cycle of Malaria Parasite

P. falciparum has a life cycle that is typical among protozoan parasites [1, 29]. The complexity of the life cycle of *P. falciparum* provides it with an advantage for its survival. It is the dependence of Malaria on both vectors and humans that makes it difficult to eradicate. This follows from the fact that even if mosquitoes, the vector transmitter of this disease, are affected through external controls, the infected humans allow the parasite to survive in a given geographical area. It is proven that a simpler life cycle makes an infectious agent more prone to elimination, like smallpox for example [9].

As we mentioned before, the spread of malaria is caused by mosquitoes of the genus *Anopheles*. Nevertheless, only the female *Anopheles* mosquito is capable of biting humans [27]; this is caused by the incapability of the male *Anopheles* to penetrate human skin; the male mosquito feeds only on plant juices and some fruits.

Once a human has been bitten by a mosquito the *Plasmodium* parasite makes its way through the bloodstream towards the liver, where it attaches to the parenchymal cells of the liver [1, 27, 37, 40]. Some members of the *Plasmodium* genus, *P. vivax* and *P. ovale*, can remain dormant in the liver cells for months or even years [26, 40]. In

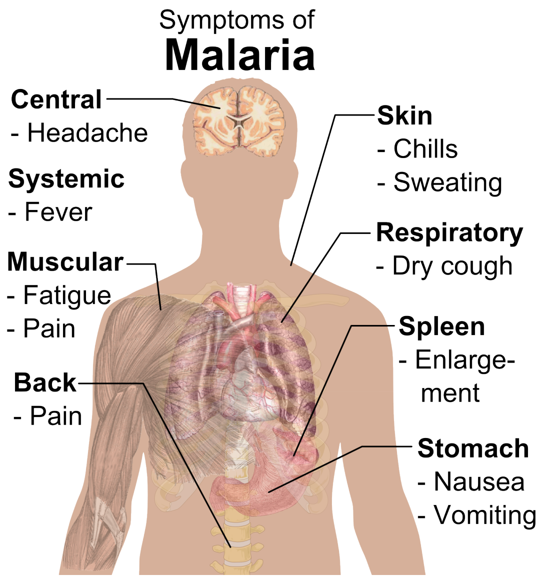


FIGURE 1.1: Main Symptoms of Malaria [8]

the case of *P. falciparum* the incubation period is about 9-14 days [40], during this time the cell replication of the parasite allows it to enter back in the bloodstream where it invades the red blood cells. It is in this stage of the life of the *Plasmodium* parasite where the symptoms of fevers, and chills appear in infected humans, similar to flu-like symptoms or even conditions resembling sepsis and gastroenteritis [9, 40]. In some cases malaria patients can experience headache, fever, shivering, joint pain, vomiting, hemolytic anemia, jaundice, hemoglobin in the urine, retinal damage, and convulsions (cf. Figure 1.1).

Once the *Plasmodium* parasite has infected the erythrocyte, it feeds on the hemoglobin in order to develop to its mature state. After reaching adulthood, it will reproduce and generate more individuals each of which can start the life cycle to infect another red blood cell (cf. Figure 1.2). The second generation of the parasite is ingested by the mosquito along with its blood meal (the parasite is in its gametocyte stage). Once the mosquito achieve its reproductive stage and creates more sporozoites, after 10 to 24 days the mosquito becomes infected thus starting the full life cycle again.

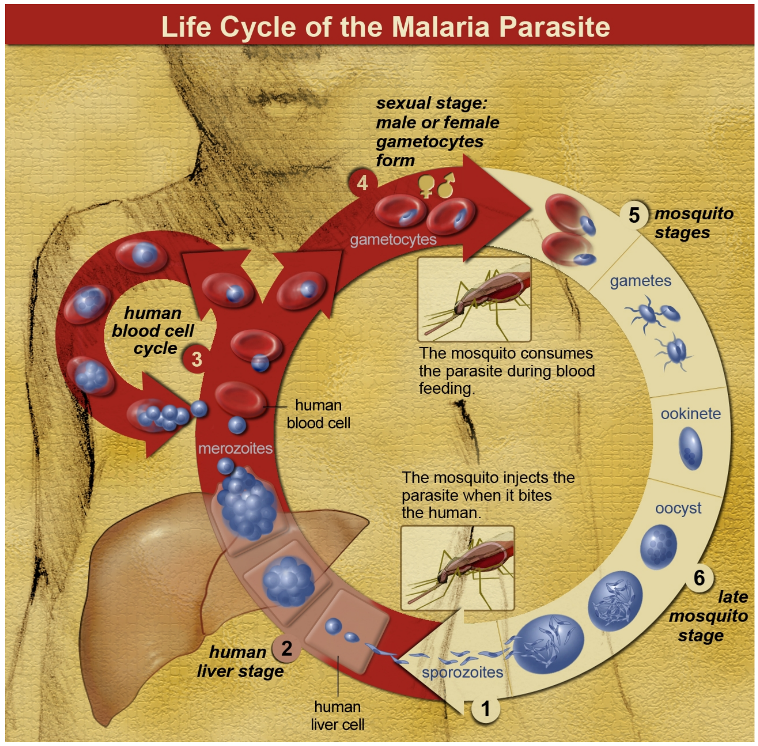


FIGURE 1.2: Life Cycle of the Malaria Parasite [22]

1.2. Mathematical Background

1.2.1 Ross-Macdonald Model

Sir Ronald Ross (1857-1932), who received the Nobel Prize in Physiology and Medicine in 1902, discovered the parasite responsible for Malaria [27, 28]. In his work "The Prevention of Malaria" he showed that transmission of this disease was through mosquito bites and designed a Mathematical Model to predict that malaria can be controlled by maintaining the mosquito population under a certain threshold. Later, George Macdonald improved Ross' model, which concentrated on the distribution of infected human and mosquito populations. This was the earliest attempt to quantitatively understand the dynamics of malarial transmission, and this is now known as the Ross-Macdonald model.

$$\begin{aligned}
\frac{d}{dt}S_h &= \mu_h N - \alpha b\frac{S_h I_v}{N} - \mu_h S_h + \gamma_h I_h \\
\frac{d}{dt}I_h &= \alpha b\frac{S_h I_v}{N} - \mu_h I_h - \gamma_h I_h \\
\frac{d}{dt}S_v &= \mu_v V - b\delta\frac{S_v I_h}{N} - \mu_v S_v + \gamma_v I_v \\
\frac{d}{dt}I_v &= b\delta\frac{S_v I_h}{N} - \mu_v I_v - \gamma_v I_v
\end{aligned} \tag{1.1}$$

where

N	Human population
$S_h(t)$	Number of susceptible humans
$I_h(t)$	Number of infected humans
V	Mosquito population
$S_v(t)$	Number of susceptible vectors
$I_v(t)$	Number of infected vectors
b	average number of mosquito bites per day per mosquito
α	probability that a susceptible human who is bitten, becomes infected
δ	probability that a susceptible mosquito that is bitten, becomes infected
μ_h	Human birth and death rate
γ_h	Human recovery rate
μ_v	mosquito birth and death rate
γ_v	mosquito recovery rate

TABLE 1.1: Parameters of the Ross-Macdonald model

In this model, N and V denote the constant total human and mosquito populations respectively. Individuals that get infected and then recover from the disease become susceptible again. The individual populations are divided in susceptible and infected clases.

We denote $S_h(t)$ and $I_h(t)$ as the number of susceptible and infected humans at time t respectively. Similarly, we denote $S_v(t)$ and $I_v(t)$ to be the number of susceptible and infected female mosquitoes at time t respectively.

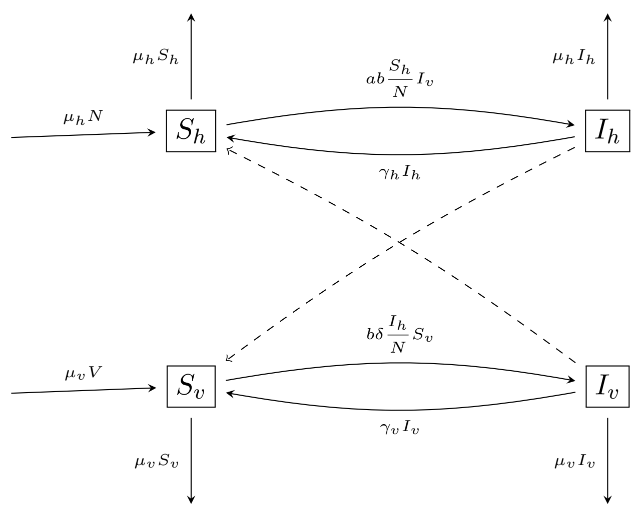


FIGURE 1.3: Transfer diagram for Ross-Macdonald model. Solid arrows indicate transfer. Dashed arrows indicate cross infection.

The parameter b is the average number of mosquito bites per day per mosquito. Thus, daily there are a total of $bI_v(t)$ infectious mosquito bites at time t. Of these, a proportion of $\frac{S_h}{N}$ target susceptible humans, and if successful at infecting (which occurs with probability α), these yield newly infected humans. The parameter α depends on the immunity of the host, the virulency of the parasite and another factors of social nature, economic, etc [1, 6, 27].

Thus, the rate of transmission per unit of time from mosquito to human is given by $\alpha b\dfrac{I_v(t)S_h(t)}{N}$. In a similar way $\delta b\dfrac{I_h(t)S_v(t)}{N}$ is the transmission rate from human to mosquito, where δ denotes the probability that a susceptible mosquito bite yields an infected mosquito.

Finally, infected humans recover at a rate γ_h and the birth rate and death rates of each population are assumed constant, leading to an interaction among the two populations like the one depicted on Figure 1.3.

By defining $m = \frac{V}{N}$, the proportion of female mosquitoes and humans, and by scaling the infected human and vector populations by their respective total populations, $s_h(t) = \frac{S_h(t)}{N}$, $i_h(t) = \frac{I_h(t)}{N}$, $s_v(t) = \frac{S_v(t)}{V}$ and $i_v(t) = \frac{I_v(t)}{V}$, we obtained a scaled version of (1.1) for the proportions of humans and mosquitoes populations:

$$\begin{aligned} \frac{d}{dt}s_h(t) &= \mu_h - \alpha bms_hi_v - \mu_hs_h + \gamma_hi_h \\ \frac{d}{dt}i_h(t) &= \alpha bms_hi_v - \mu_hi_h - \gamma_hi_h \\ \frac{d}{dt}s_v(t) &= \mu_v - \delta bs_vi_h - \mu_vs_v + \gamma_vi_v \\ \frac{d}{dt}i_v(t) &= \delta bs_vi_h - \mu_vi_v - \gamma_vi_v \end{aligned} \tag{1.2}$$

Notice that since $s_h + i_h = 1$ and $s_v + i_v = 1$ we may choose to utilize two of the four variables. We choose i_h and i_v, which are the infected proportions in the human and mosquito populations. We now denote $x = i_h$ and $y = i_v$, so that $s_h = 1 - x$ and $s_v = 1 - y$. Substituting into (1.2) we obtain the following:

$$\begin{aligned} x' &= \alpha bmy(1 - x) - \mu x \\ y' &= b\delta x(1 - y) - \nu y \end{aligned} \tag{1.3}$$

Here, we have defined $\mu = \gamma_h + \mu_h$ and $\nu = \mu_v + \gamma_v$. Note that model (1.3) is defined on the unit square

$$D = \{(x, y)|0 \le x, y \le 1\}.$$

1.2.2 Analysis of the Ross-Macdonald model

Having introduced the Ross-Macdonald model, we can study the qualitative behavior of its solutions in order to predict the prevalence of malaria among a group of individuals. Since the system (1.3) is a planar system of differential equations, it can be studied with classical tools [4, 41] such as phase plane analysis using nullclines and the linearization about equilibria. Nevertheless, the system (1.3) has other interesting properties as discussed in the following theorem.

Theorem 1.2.2.1. *The solutions of system (1.3) remain in D, and the system is cooperative and monotone (cf. Appendix A.).*

Proof. Rewriting the system (1.3) as $\dot{X} = F(X)$ on the rectangle D, we see that if $(x, y) \in \partial D \backslash (0, 0)$ then the vector field $F(X)$ points towards the interior of D, and the origin is a steady state of (1.3). Thus the solutions on D stay in D, implying that they remain bounded.

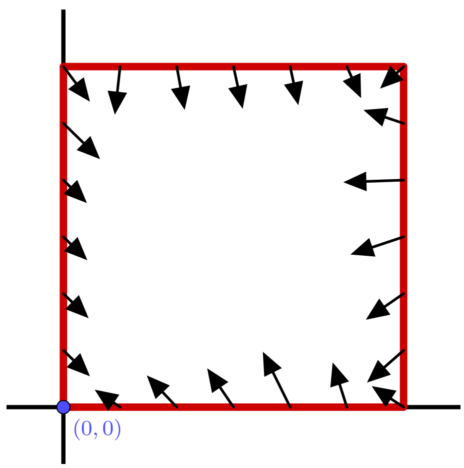


FIGURE 1.4: Vector Field of Ross-Macdonald at ∂D.

Observe that the Jacobian matrix is given by

$$\begin{pmatrix} -\alpha bmy - \mu & \alpha bm(1-x) \\ \delta b(1-y) & -\delta bx - \nu \end{pmatrix} \tag{1.4}$$

which has an associated directed graph that is strongly connected (cf. Figure 1.5). Since the Jacobian matrix has non-negative off-diagonal entries in D, the system (1.3) is cooperative [30, 2, 31]. Then by Theorem A.0.8 we have that the system (1.3) is monotone (cf. [39]). □

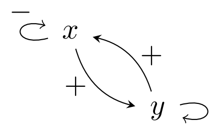


FIGURE 1.5: Directed graph associated to the Jacobian matrix of (1.3)

Kamke's Theorem implies that cooperative systems are monotone (cf. Theorem A.0.7). This means that if the system $\dot{X} = F(X)$, with $X \in \mathbb{R}^n$, is cooperative then its solutions preserve the partial order relation in $\mathbb{R}^n$ given by $(a_1, ..., a_n) \leq (b_1, ..., b_n)$ if and only if $a_i \leq b_i$ for $i = 1, ..., n$. Moreover, since the system (1.3) is planar, it follows from Theorem A.0.9 that all solutions converge to an equilibrium point.

Through a phase plane analysis we obtain that the $x-$nullcline of (1.3) is given by

$$y = f(x) := \frac{\mu}{\alpha bm} \frac{x}{1-x} . \tag{1.5}$$

On the other hand, the $y-$nullcline of (1.3) is given by

$$y = g(x) := \frac{x}{x + \frac{\nu}{\delta b}} . \tag{1.6}$$

Notice that (1.5) and (1.6) are strictly increasing in their respective domains, and the function $g(x) < 1$ for all $x \in \mathbb{R}_+$.

From the nullclines we obtain that the two equilibria of the system (1.3) are the disease-free equilibrium $P_0 = (0, 0)$, and possibly an endemic equilibrium $P_1 = (x^*, y^*)$ where

$$x^* = \frac{\alpha\delta b^2 m - \nu\mu}{\delta b(\alpha bm + \mu)} \quad y^* = \frac{\mu x^*}{\alpha bm(1 - x^*)}.$$

Notice that existence of P_1 in D, implies uniqueness, and P_1 exists in D if and only if $0 < x^* < 1$ and $0 < y^* < 1$.

In order to determine conditions for the existence of P_1, we study the disease-free equilibrium. Notice that the Jacobian matrix (1.4) at P_0 is given by

$$\begin{pmatrix} -\mu & \alpha bm \\ \delta b & -\nu \end{pmatrix} = \begin{pmatrix} 0 & \alpha bm \\ \delta b & 0 \end{pmatrix} - \begin{pmatrix} \mu & 0 \\ 0 & \nu \end{pmatrix} =: \mathcal{F} - \mathcal{V}$$

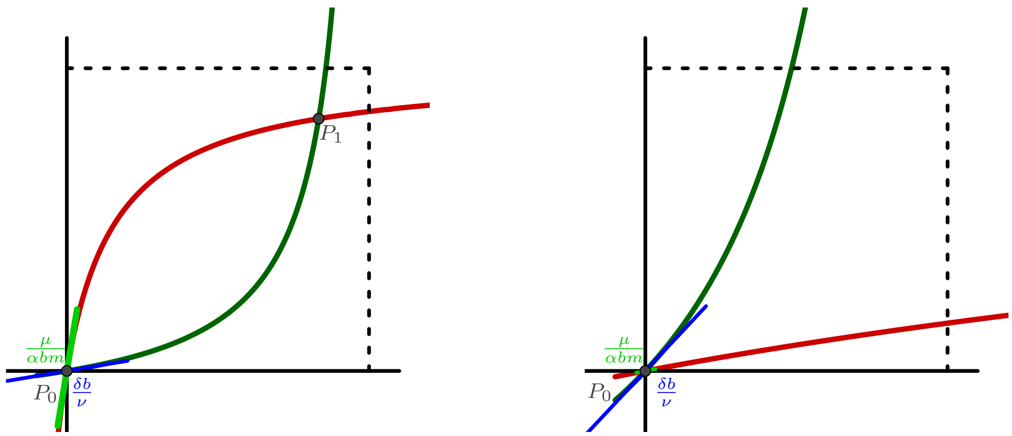
since the Jacobian matrix at the disease-free equilibrium can be expressed as the difference of a non-negative matrix $\mathcal{F}$ and a non-singular Metzler matrix $\mathcal{V}$. By the work of Van den Driessche and Watmough [38] we can define the basic reproductive number R_0 as the spectral radius ρ of the matrix $\mathcal{F}\mathcal{V}^{-1}$:

$$R_0 := \rho(\mathcal{F}\mathcal{V}^{-1}) = \rho\left(\begin{bmatrix} 0 & \frac{\alpha bm}{\nu} \\ \frac{\delta b}{\mu} & 0 \end{bmatrix}\right) = \sqrt{\frac{\delta b}{\nu} \cdot \frac{\alpha bm}{\mu}}$$

Observe that $R_0 = \sqrt{\dfrac{g'(0)}{f'(0)}}$. If $R_0 > 1$ we have that $g'(0) > f'(0)$ then for all sufficiently small $\varepsilon > 0$ we have that $g(\varepsilon) > f(\varepsilon)$. Moreover, since $f(1-\varepsilon) > g(1-\varepsilon)$ for all sufficiently small $\varepsilon > 0$, we have that $f(x) = g(x)$ for some $x \in (0,1)$ proving the existence of P_1 in D.

On the other hand, if $R_0 < 1$ we have that $g'(0) < f'(0)$, since $f(x)$ and $g(x)$ are strictly increasing, and $f(x)$ is a convex function and $g(x)$ is a concave function, we have that $g(x) \neq f(x)$ for all $x \in (0,1)$ thus having that P_1 does not exist in D in this situation (cf. Figure 1.6).

As noted, if $R_0 > 1$ then we have two equilibria in D and when $R_0 < 1$ we have only one equilibrium in D. Thus we need to analize the stability of P_0. Notice that from the Jacobian matrix at P_0, its eigenvalues have negative real part if and only if $R_0 < 1$ [38]. If $R_0 > 1$, one eigenvalue of the Jacobian matrix at P_0 has positive real part. Hence by Theorem A.0.9, P_0 is globally asymptotically stable for $R_0 < 1$. P_0 is unstable if $R_0 > 1$. Thus, if $R_0 > 1$, the nonzero solutions converge to P_1 by Theorem A.0.9 and because the stable manifold of P_0 does not intersect $D \backslash \{P_0\}$. Indeed, this stable manifold is tangential to the eigenvector associated to the negative eigenvalue of the Jacobian matrix at P_0, and this eigenvector does not belong to $\mathbb{R}^2_+$. Moreover P_1 is asymptotically stable in this case.



(a) $R_0 > 1$

(b) $R_0 < 1$

FIGURE 1.6: Phase plane diagram of system (1.3) with $x-$nullcline in green and $y-$nullcline in red.

To appreciate the practical relevance of R_0, we determine the critical mosquito population level V_c, below which the disease will be cleared. Recalling that $m = \frac{V}{H}$, it follows from the definition of R_0

$$V_c = \frac{\nu \mu H}{\alpha \delta b^2}$$

obtained by setting $R_0 = 1$. This is important for control purposes which are often aimed at reducing the mosquito population. Of course there are other control measures, for example lowering the biting rate b (using bed nets, for instance).

2. A ROSS-MACDONALD MODEL WITH VECTOR DEMOGRAPHY

In this chapter we present our model, which is based on the Ross-Macdonald model, but includes the demography of susceptible mosquitoes which is neglected in the original Ross-Macdonald model.

2.1. SIS Version of the Ross-Macdonald Model with vector demography

As we discussed on Chapter 1, the Ross-Macdonald model implies that human and mosquito populations remain constant. Whereas this seems reasonable for the human population, given that the time scale of infection is far shorter than the time scale of human demography, it is far less reasonable for the mosquito population.

Therefore, we shall explicity include the vector demography, representing it as a function $f(S_V)$ that depends on susceptible mosquitoes, i.e. we assume that infected mosquitoes don't reproduce. We also assume that infected mosquitoes don't recover from the infection. This leads to the following extension of the Ross-Macdonald model, framed using an SIS (Susceptible-Infectious-Susceptible) approach:

$$\begin{aligned} \dot{S_H} &= -cI_V\left(\frac{S_H}{S_H+I_H}\right)+rI_H \\ \dot{I_H} &= cI_V\left(\frac{S_H}{S_H+I_H}\right)-rI_H \\ \dot{S_V} &= -dS_V\left(\frac{I_H}{S_H+I_H}\right)+f(S_V) \\ \dot{I_V} &= dS_V\left(\frac{I_H}{S_H+I_H}\right)-\mu I_V \end{aligned} \tag{2.1}$$

where $\mu > 0$, $f(S_V)$ is a function dependent on S_V, for which assumptions will be stated later. The compartmental diagram of this model can be found in Figure 2.1.

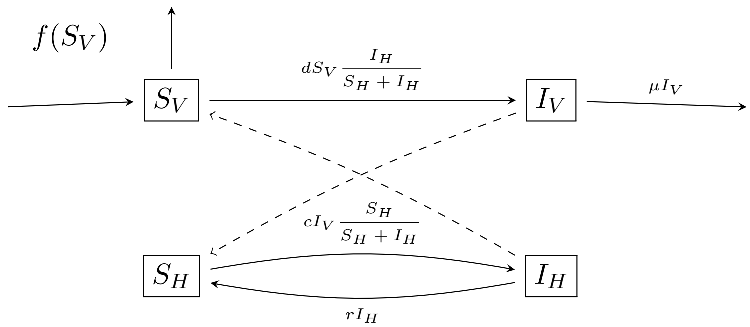


FIGURE 2.1: Transfer diagram for proposed modified Ross-Macdonald model. Solid arrows indicate transfer. Dashed arrows indicate cross infection.

Similarly to the Ross-Macdonald model, we denote $S_H(t)$ and $I_H(t)$ as the number of susceptible and infected humans at time t, $S_V(t)$ and $I_V(t)$ are the number of susceptible and infected female mosquitoes at time t. The parameter c is the successful infection by a mosquito, assuming it bites at the average daily rate. It compares to αb in the original Ross-Macdonald model (1.3). The parameter d can be interpreted similarly. We also assume a constant recovery rate for the human population given by the parameter r, but neglect the recovery of infected mosquitoes. In summary, when comparing the models (1.3) and (2.1) we have that $c = \alpha b$, $d = \delta b$, $r = \gamma_h$, $\mu_h = 0$, $\gamma_v = 0$, $\mu = \mu_v$ and $\mu_v(S_v + I_v) - \mu_v S_v$ is replaced by $f(S_V)$.

As mentioned in Chapter 1, the Ross-Macdonald model implies that the populations of mosquitoes and humans remain constant. Notice from model (2.1) that this is still true for the human population because $\frac{d}{dt}(S_H + I_H) = 0$, but not true for the mosquito population. Indeed, $\frac{d}{dt}(S_V + I_V) = f(S_V) - \mu I_V$ and we won't assume that $f(S_V) = \mu I_V$. Finally, the function $f(S_V)$ is the dynamics of the susceptible vector population in the absence of the infection. This allows us to study different types of population dynamics for the mosquitoes: affine decreasing ($f(S_V) = b - \mu_S S_V$), logistic ($f(S_V) = pS_V(1 - S_V/K)$) or logistic with immigration ($f(S_V) = b + pS_V(1 - S_V/K)$), where all parameters are assumed to be positive, are common examples. Consequently, the mosquito population is not necessarily constant. The conservation of the human population ($S_H + I_H = H$) enables us to reduce model (2.1) to:

$$\dot{S}_V = -\frac{d}{H} S_V I_H + f(S_V) \tag{2.2}$$

$$\dot{I}_V = \frac{d}{H} S_V I_H - \mu I_V \tag{2.3}$$

$$\dot{I}_H = \frac{c}{H} I_V (H - I_H) - r I_H \tag{2.4}$$

We assume that $f(S_V)$ is $\mathcal{C}^1$, that $f(0) \geq 0$, $f(K) = 0$ for some $K > 0$, and that $f(S_V) > 0$ if $0 < S_V < K$, and $f(S_V) < 0$ for $S_V > K$. Consequently, all positive solutions of the equation $\dot{S}_V = f(S_V)$, converge to K, which can be thought of as the carrying capacity.

3. EQUILIBRIA AND STABILITY

In this chapter we study the existence of equilibria of the system (2.2)- (2.4) and conditions for the global stability of the endemic equilibria and the case of local oscillatory instability.

3.1. Boundary and positive equilibria

Theorem 3.1.0.1. *Let $f : \mathbb{R}_+ \to \mathbb{R}$ be $\mathcal{C}^1$, and assume there exists a unique positive $K > 0$ such that*

$$f(S_V) = \begin{cases} > 0, & \text{if } 0 < S_V < K \\ = 0, & \text{if } S_V = K \\ < 0, & \text{if } S_V > K \end{cases}$$

and such that $f'(K) < 0$. If $f(0) = 0$ we also assume that $f'(0) > 0$. Define

$$R_0 := \left(\frac{cd}{\mu r} \frac{K}{H} \right)^{1/2}$$

Then:

- *If $f(0) > 0$, then (2.2)-(2.4) has exactly one equilibrium $E_1 = (K, 0, 0)$ on the boundary of $\mathbb{R}^3_+$, which is locally asymptotically stable if $R_0 < 1$, but unstable if $R_0 > 1$.*
- *If $f(0) = 0$, then (2.2)-(2.4) has two equilibria $E_0 = (0, 0, 0)$ and $E_1 = (K, 0, 0)$ on the boundary of $\mathbb{R}^3_+$. E_0 is unstable, and E_1 is locally asymptotically stable if $R_0 < 1$, but unstable if $R_0 > 1$.*
- *If $R_0 \leq 1$, there are no positive steady states.*
- *If $R_0 > 1$, then there exists at least one positive steady state. Moreover, if f in $\mathcal{C}^2$ and $f''(S_V) < 0$ for all S_V in $\mathbb{R}_+$, then there is exactly one positive steady state.*

Proof. Equilibria of the system (2.2)-(2.4) are solutions of

$$\frac{d}{H}S_V I_H = f(S_V) \tag{3.1}$$

$$\frac{d}{H}S_V I_H = \mu I_V \tag{3.2}$$

$$rI_H = \frac{c}{H}I_V(H - I_H) \tag{3.3}$$

- **Case 1:** $f(0) > 0$. Suppose that (S_V, I_V, I_H) is a boundary equilibrium. Then necessarily $S_V > 0$ by (3.1). If $I_H = 0$, then $I_V = 0$ as well by (3.2). Similarly, if $I_V = 0$, then $I_H = 0$, also by (3.2). Finally, since $I_H = 0$, it follows from (3.1) that S_V must equal K. In summary $E_1 = (K, 0, 0)$ is the only boundary steady state of (2.2)- (2.4).

- **Case 2:** $f(0) = 0$. If (S_V, I_V, I_H) is a boundary equilibrium, and if $S_V = 0$, then $I_V = I_H = 0$ by (3.2) and (3.3). Thus, $E_0 = (0, 0, 0)$ is a boundary steady state. If $S_V > 0$, then the same argument as in Case 1, shows that necessarily this boundary equilibrium is $E_1 = (K, 0, 0)$.

To establish the local stability properties of E_0 and E_1 in both cases, we consider the Jacobian matrix:

$$Jac = \begin{pmatrix} -\frac{d}{H}I_H + f'(S_V) & 0 & -\frac{d}{H}S_V \\ \frac{d}{H}I_H & -\mu & \frac{d}{H}S_V \\ 0 & \frac{c}{H}(H - I_H) & -\frac{c}{H}I_V - r \end{pmatrix} \tag{3.4}$$

At $E_1 = (K, 0, 0)$, which exists in both cases,

$$Jac(E_1) = \begin{pmatrix} f'(K) & 0 & -\frac{d}{H}K \\ 0 & -\mu & \frac{d}{H}K \\ 0 & c & -r \end{pmatrix}$$

The eigenvalues of $Jac(E_1)$ are $f'(K)$, which is negative by assumption, and the eigenvalues of the 2×2 matrix

$$\begin{pmatrix} -\mu & \frac{d}{H}K \\ c & -r \end{pmatrix} = \begin{pmatrix} 0 & \frac{d}{H}K \\ c & 0 \end{pmatrix} - \begin{pmatrix} \mu & 0 \\ 0 & r \end{pmatrix} = \mathcal{F} - \mathcal{V}$$

The latter matrix has two eigenvalues with negative real part if and only if

$$R_0 := \rho(\mathcal{F}\mathcal{V}^{-1}) = \left(\frac{cd}{\mu r}\frac{K}{H}\right)^{1/2} < 1 \qquad \text{(cf. [38])}.$$

It has an eigenvalue with positive real part if and only if

$$R_0 > 1\,.$$

These observations establish the claimed stability properties of E_1.

In case $f(0) = 0$, the Jacobian matrix at $E_0 = (0, 0, 0)$ is:

$$Jac(E_0) = \begin{pmatrix} f'(0) & 0 & 0 \\ 0 & -\mu & 0 \\ 0 & c & -r \end{pmatrix},$$

which has one positive eigenvalue $f'(0)$, and two negative eigenvalues. Therefore, E_0 is unstable.

Next we look for possible equilibria (S_V, I_V, I_H) which must satisfy the equations (3.1)-(3.3). Dividing (3.2) by (3.3), and solving for I_H, yields:

$$I_H = H\left(1 - \frac{1}{R_0^2}\frac{K}{S_V}\right). \tag{3.5}$$

From (3.2) we can solve for I_V and by using the value of I_H above we obtain

$$I_V = \frac{1}{\mu}\frac{d}{H}S_V I_H = \frac{d}{\mu}\left(S_V - \frac{K}{R_0^2}\right). \tag{3.6}$$

Substituting this in (3.1) yields:

$$f(S_V) = d\left(S_V - \frac{K}{R_0^2}\right) \tag{3.7}$$

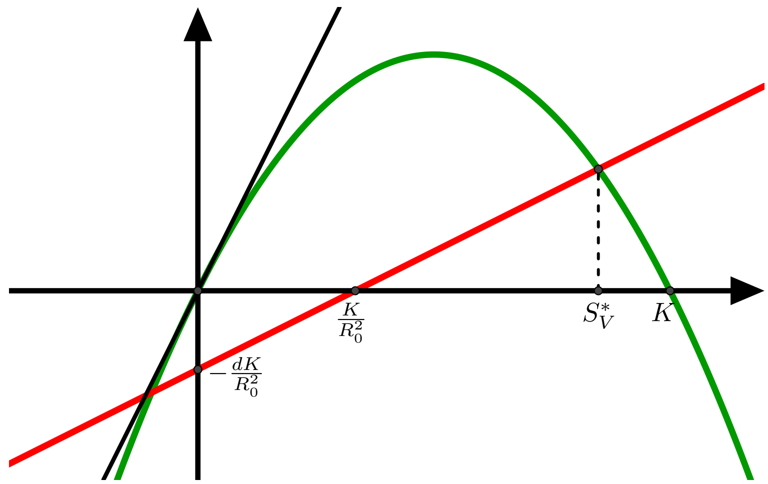
- If $R_0 < 1$, then $\dfrac{K}{R_0^2} > K$, hence any solution S_V to (3.7) occurs at a value S_V that is larger than K. But this implies that $f(S_V) < 0$, and then (3.1) cannot be met for a positive value of I_H. Thus if $R_0 < 1$, there are no positive equilibria. If $R_0 = 1$, then $S_V = K$ is the only solution of (3.7). But then $f(S_V) = 0$, hence $I_V = I_H = 0$ must hold by (3.1) and (3.2).

- If $R_0 > 1$, then $\dfrac{K}{R_0^2} < K$. Then $f\left(\frac{K}{R_0^2}\right) > 0$, and $0 = f(K) < d\left(K - \dfrac{K}{R_0^2}\right)$, hence by the intermediate value theorem, there exists at least one postive solution S_V to (3.7), and S_V belongs to $\left(\dfrac{K}{R_0^2}, K\right)$. Notice that (3.5) then implies that $I_H > 0$, and from (3.2) then follows that $I_V > 0$. Thus, if $R_0 > 1$, there exists at least one positive steady state.

To see that when f is $\mathcal{C}^2$ and $f''(S_V) < 0$ for all S_V in $\mathbb{R}_+$, there is exactly one positive state, we argue by contradiction. First, notice that the steady state equations (3.1)-(3.3) imply that if (S_V^1, I_V^1, I_H^1) and (S_V^2, I_V^2, I_H^2) are distinct positive steady states, then necessarily $S_V^1 \neq S_V^2$ (Indeed, if S_V^1 and S_V^2 were equal, so would I_H^1 and I_H^2 by (3.1) and then also I_V^1 and I_V^2 by (3.2)). Assume without loss of generality that $S_V^1 < S_V^2$. Since S_V^1 and S_V^2 solve (3.7), and since we know that $R_0 > 1$ must hold, there follows that

$$\frac{K}{R_0^2} < S_V^1 < S_V^2 < K\,.$$

Define $g(S_V) = f(S_V) - d\left(S_V - \dfrac{K}{R_0^2}\right)$. Thus, $g(S_V^1) = g(S_V^2) = 0$, and $g''(S_V) < 0$ for all S_V. Since $g\left(\dfrac{K}{R_0^2}\right) > 0 = g(S_V^1)$, there exist an S_V^* in $\left(\dfrac{K}{R_0^2}, S_V^1\right)$ such that $g'(S_V^*) < 0$ by the mean value theorem. Since $g(S_V^1) = g(S_V^2) = 0$, there exists an S_V^{**} in (S_V^1, S_V^2) such that $g'(S_V^{**}) = 0$. Thus, we have found $S_V^* < S_V^{**}$ with $g'(S_V^*) < 0$, yet $g'(S_V^{**}) = 0$. This contradicts that $g''(S_V) < 0$ for all S_V. In summary, when f is $\mathcal{C}^2$ and $f''(S_V) < 0$ for all S_V in $\mathbb{R}_+$, there is exactly one positive steady state (see figure below).



□

3.2. Extinction of the disease. Global stability of the disease free equilibrium when $R_0 < 1$

Throughout our studies for the system (2.2)-(2.4), we need to point out the importance of two sets:

$$\Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\} \tag{3.8}$$

which is the state space of the system (2.2)-(2.4) and the cone

$$\mathcal{K} = \{(S_V, I_V, I_H) \in \mathbb{R}^3 \mid S_V\,, I_H \geq 0\,,\ I_V \leq 0\}\,. \tag{3.9}$$

endowed with the partial order $\leq_{\mathcal{K}}$ given by $x \leq_{\mathcal{K}} y$ if $x_1 \leq y_1$, $x_2 \geq y_2$ and $x_3 \leq y_3$.

Theorem 3.2.0.1. *The system (2.2)-(2.4) is competitive with respect to the cone $\mathcal{K}$ (cf. (3.9)). (cf. [30], p. 49)*

Proof. Consider the system (2.2)-(2.4) with its state space Ω and partial order $\mathcal{K}$. Recall that the Jacobian matrix of system (2.2)-(2.4) at an arbitrary point of Ω has the following sign structure (cf. (3.4)):

$$\begin{pmatrix} * & 0 & - \\ + & * & + \\ 0 & + & * \end{pmatrix} \tag{3.10}$$

where some of the off-diagonal entries (+ or -) can be zero at points on the boundary of Ω. The matrix (3.10) is sign-symmetric, i.e., for every $i \neq j$ the product of the (i, j)th and (j, i)th entry is nonnegative. The incidence graph associated with this matrix, where edges between the nodes are labeled with a sign accordingly to the sign on the corresponding entry on the Jacobian matrix (see Figure 3.1), satisfies the following property: every closed loop in this graph possesses an odd number of edges with - signs. This property implies that the system is competitive (cf. [30], pp. 48-50).

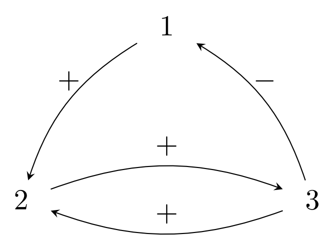


FIGURE 3.1: Incidence graph associated to the matrix (3.10)

Alternatively, the change of variables $(S_V, I_V, I_H) \to (S_V, T, I_H)$, with $T = -I_V$, results in the system

$$\dot{S}_V = f(S_V) - \frac{d}{H} S_V I_H$$
$$\dot{T} = -\frac{d}{H} S_V I_H - \mu T$$
$$\dot{I}_H = -\frac{c}{H} T(H - I_H) - r I_H$$

whose Jacobian matrix has nonpositive off-diagonal terms on the relevant domain, making it a competitive system with respect to the usual, componentwise partial order. $\square$

The relevance for the system (2.2)-(2.4) to be competitive relies on the theory developed by Morris W. Hirsch and Hal L. Smith [10, 11, 12, 14, 13, 15, 30]. A specific consequence of the theory of competitive systems is a generalization of the Poincaré-Bendixson Theorem (cf. Theorem A.0.10) to dimension 3, see Theorem A.0.12. This allows us to conclude, for example, that a compact limit set of a competitive system in $\mathbb{R}^3$ which contains no steady states is a periodic orbit.

Theorem 3.2.0.2. *If $R_0 < 1$, then the disease free equilibrium $E_1 = (K, 0, 0)$ is globally asymptotically stable with respect to all initial conditions when $f(0) > 0$; when $f(0) = 0$, E_1 is globally asymptotically stable with respect to all initial conditions not on the invariant $(I_V, I_H)-$plane.*

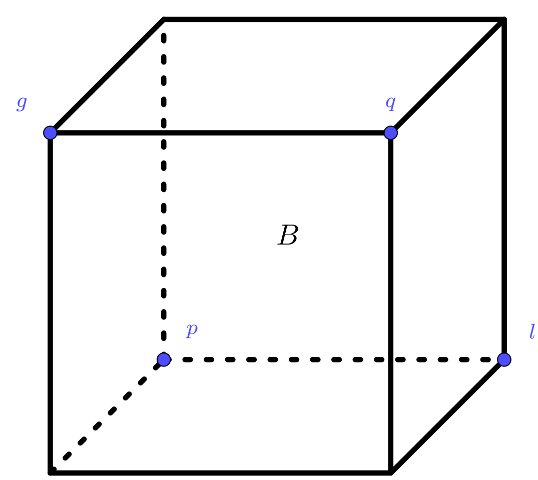
Proof. Let $f(0) > 0$. If E_1 is not Globally Asymptotically Stable then there exists $X_0 \in \Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\}$ such that the solution $X(t) = (S_V(t), I_V(t), I_H(t))$ starting at X_0, does not converge to E_1, i.e. $X(t) \not\to E_1$. We then have two cases: $E_1 \in \omega(X_0)$ or $E_1 \notin \omega(X_0)$.

If $\omega(X_0) \ni E_1$, since E_1 is locally asymptotically stable (cf. Theorem 3.1.0.1), then $\omega(X_0) = \{E_1\}$. Contradicting that $X(t) \not\to E_1$.

If $\omega(X_0) \not\ni E_1$, then no equilibria belong to $\omega(X_0)$ because E_1 is the only equilibrium of system (2.2)-(2.4). Then by Theorem A.0.12, we have that $\omega(X_0)$ is a periodic orbit, since (2.2)-(2.4) is competitive by Theorem 3.2.0.1.

We claim that the periodic orbit given by $\omega(X_0)$ must belong to $int(\Omega)$. Indeed, it is easy to check that solutions that start on the boundary of Ω but not on the S_V-axis enter $int(\Omega)$ instantaneously. This implies that points on this part of the boundary of Ω cannot belong to a periodic orbit. It is also clear that no point on the invariant S_V-axis belongs to a periodic orbit.

Now, since $\omega(X_0) \subset int(\Omega)$ and $\omega(X_0)$ is compact, there is a box B that contains $\omega(X_0)$ and whose sides are parallel to the coordinate planes and also lies in $int(\Omega)$. B can be expressed as a closed order interval with respect to the usual order given by the positive orthant $\mathbb{R}^3_+$ (defining an order cone), $\leq$, say $B = [\mathbf{p}, \mathbf{q}] = \{x \in \mathbb{R}^3 \mid p \leq x \leq q\}$. Now, since the boundary of $\mathbb{R}^3_+$ and the boundary of $\mathcal{K}$ are parallel to each other, we can find a homomorphism between the closed order interval $[\mathbf{p}, \mathbf{q}]$ and some closed order interval with respect to the order $\leq_{\mathcal{K}}$. Indeed, the closed order interval $[\mathbf{p}, \mathbf{q}]$ defines a parallelepiped in $int(\Omega)$ where one of its spatial diagonals joins the points p and q. Let us consider the sides parallel to the $(S_V, I_H)-$plane and let g and l be the points diagonal opposite to p and q on their respective sides. Due to the order $\leq_{\mathcal{K}}$ these points g and l define the same box B over the order $\leq_{\mathcal{K}}$ with its respective closed interval $B = [\mathbf{l}, \mathbf{g}]_{\mathcal{K}} = \{x \in \mathbb{R}^3 \mid l \leq_{\mathcal{K}} x \leq_{\mathcal{K}} g\}$ (see figure below).



Since the periodic orbit $\omega(X_0)$ is such that $\omega(X_0) \subset [\mathbf{l}, \mathbf{g}]_{\mathcal{K}} \subset int(\Omega)$ then by Theorem A.0.14, B must contain a steady state of (2.2)-(2.4). However, E_1 is the only steady state of the system (since $R_0 < 1$ and $f(0) > 0$, see Theorem 3.1.0.1) and $E_1 \notin B$. Therefore $\omega(X_0)$ cannot be a periodic orbit, a contradiction.

Therefore E_1 is globally asymptotically stable in this case.

Let $f(0) = 0$. If E_1 is not Globally Asymptotically Stable then there exists $X_0 \in$

$\Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\}$ but not on the invariant $(I_V, I_H)-$plane such that the solution $X(t) = (S_V(t), I_V(t), I_H(t))$ starting at X_0, does not converge to E_1. We have the same two cases as when $f(0) > 0$, the case when $E_1 \in \omega(X_0)$ follows in an analogous way. The difference occurs when $E_1 \notin \omega(X_0)$. In this case, since we have an additional equilibrium on the S_V-axis, $E_0 = (0, 0, 0)$ (cf. Theorem 3.1.0.1) we have to determine if also E_0 is, or is not in $\omega(X_0)$. We claim that $E_0 \notin \omega(X_0)$. Indeed, suppose that $E_0 \in \omega(X_0)$. Since X_0 is a hyperbolic equilibrium, the Butler-McGehee Lemma (cf. Theorem A.0.11) implies that $\omega(X_0)$ contains a point of $W^u(E_0)\backslash\{E_0\}$, which is the open segment on the S_V-axis connecting E_0 and E_1. By the invariance and closedness of $\omega-$limit sets, $\omega(X_0)$ must then also contain E_1, a contradiction. The rest of the proof now proceeds as in the case where $f(0) > 0$: since $\omega(X_0)$ does not contain either of the system's two equilibria E_0 or E_1, it must be a periodic orbit by Theorem A.0.12. This leads to a contradiction as before, and we conclude that E_1 is globally asymptotically stable. □

3.3. Global Stability of the endemic equilibrium

Theorem 3.3.0.1. *Let* $X^* = (S_V^*, I_V^*, I_H^*)$ *be a positive steady state (or equilibrium) of the system (2.2)-(2.4). Then* X^* *is globally asymptotically stable with respect to initial conditions in* $int(\mathbb{R}^3_+)$*, if*

$$(S_V - S_V^*)(f(S_V) - f(S_V^*)) \leq 0\,, \qquad \text{for all } S_V \text{ (cf. Figure 3.2).} \tag{3.11}$$

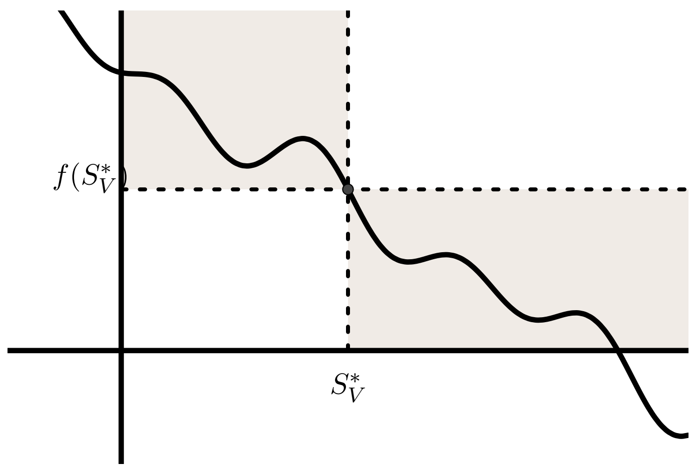


FIGURE 3.2: Graphic representation of the condition $(S_V - S_V^*)(f(S_V) - f(S_V^*)) \leq 0$.

Proof. For the system (2.2)-(2.4), we will prove that a Lyapunov function exists. The steady state equations for the steady state $X^* = (S_V^*, I_V^*, I_H^*)$ are:

$$f(S_V^*) = \frac{d}{H} S_V^* I_H^* = \mu I_V^* \tag{3.12}$$

$$r I_H^* = \frac{c}{H} I_V^* (H - I_H^*) \tag{3.13}$$

We define the function

$$V = \int_{S_V^*}^{S_V} 1 - \frac{S_V^*}{x} dx + \int_{I_V^*}^{I_V} 1 - \frac{I_V^*}{x} dx + \alpha \int_{I_H^*}^{I_H} 1 - \frac{I_H^*}{x} dx\,, \tag{3.14}$$

where α is a positive constant, defined later. Notice that

$$
\begin{aligned}
\dot{V} &= \left(1 - \frac{S_V^*}{S_V}\right)\dot{S}_V + \left(1 - \frac{I_V^*}{I_V}\right)\dot{I}_V + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\dot{I}_H \\
&= \left(1 - \frac{S_V^*}{S_V}\right)\left(-\frac{d}{H}S_V I_H + f(S_V)\right) + \left(1 - \frac{I_V^*}{I_V}\right)\left(\frac{d}{H}S_V I_H - \mu I_V\right) \\
&\quad + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)\left(-\frac{d}{H}S_V I_H + f(S_V) + f(S_V^*) - f(S_V^*)\right) + \left(1 - \frac{I_V^*}{I_V}\right)\left(\frac{d}{H}S_V I_H - \mu I_V\right) \\
&\quad + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) + \left(1 - \frac{S_V^*}{S_V}\right)f(S_V^*) + \frac{d}{H}S_V^* I_H - \mu I_V - \frac{d}{H}\frac{I_V^* S_V I_H}{I_V} \\
&\quad + \mu I_V^* + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) + \left(1 - \frac{S_V^*}{S_V}\right)f(S_V^*) + \frac{d}{H}S_V^* I_H^* \frac{I_H}{I_H^*} - \mu I_V^* \frac{I_V}{I_V^*} \\
&\quad - \frac{d}{H}S_V^* I_H^* \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*} + \mu I_V^* + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) + 2\mu I_V^* - \frac{S_V^*}{S_V}\mu I_V^* + \mu I_V^* \frac{I_H}{I_H^*} - \mu I_V^* \frac{I_V}{I_V^*} - \mu I_V^* \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*} \\
&\quad + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) + \mu I_V^*\left(2 - \frac{S_V^*}{S_V} + \frac{I_H}{I_H^*} - \frac{I_V}{I_V^*} - \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}\right) \\
&\quad + \alpha\left(1 - \frac{I_H^*}{I_H}\right)\left(\frac{c}{H}I_V(H - I_H) - rI_H\right) \\
&= \left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) + \mu I_V^*\left(2 - \frac{S_V^*}{S_V} + \frac{I_H}{I_H^*} - \frac{I_V}{I_V^*} - \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}\right) \\
&\quad + \alpha\left(cI_V - \frac{cI_V I_H}{H} - rI_H - \frac{cI_H^* I_V}{I_H} + \frac{cI_H^* I_V}{H} + rI_H^*\right)
\end{aligned}
$$

We want to take advantage of a common factor for μI_V^* and to simplify the term rI_H^*, and set

$$
\alpha = \frac{\mu I_V^*}{rI_H^*}
$$

Then notice that

$$\begin{aligned}
\dot{V} &= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(2-\frac{S_V^*}{S_V}+\frac{I_H}{I_H^*}-\frac{I_V}{I_V^*}-\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}\right)\\
&\quad + \frac{\mu I_V^*}{r I_H^*}\left(cI_V - \frac{cI_V I_H}{H} - rI_H - \frac{cI_H^* I_V}{I_H} + \frac{cI_H^* I_V}{H} + rI_H^*\right)\\
&= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(2-\frac{S_V^*}{S_V}+\frac{I_H}{I_H^*}-\frac{I_V}{I_V^*}-\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}\right)\\
&\quad + \mu I_V^*\left(\frac{cI_V}{rI_H^*} - \frac{cI_V I_H}{HrI_H^*} - \frac{I_H}{I_H^*} - \frac{cI_V}{rI_H} + \frac{cI_V}{Hr} + 1\right)\\
&= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(3-\frac{S_V^*}{S_V}-\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}-\frac{I_V I_H^*}{I_V^* I_H}\right)\\
&\quad + \mu I_V^*\left(\frac{I_V I_H^*}{I_V^* I_H} - \frac{I_V}{I_V^*} + \frac{c}{rI_H^*}I_V - \frac{cI_H}{HrI_H^*}I_V - \frac{c}{rI_H}I_V + \frac{c}{Hr}I_V\right)\\
&= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(3-\left(\frac{S_V^*}{S_V}+\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}+\frac{I_V I_H^*}{I_V^* I_H}\right)\right)\\
&\quad + \mu I_V^* I_V\left(\frac{I_H^*}{I_V^* I_H} + \frac{c}{rI_H^*} + \frac{c}{Hr} - \frac{1}{I_V^*} - \frac{cI_H}{HrI_H^*} - \frac{c}{rI_H}\right)
\end{aligned}$$

Notice that (3.13) gives us the following relations:

$$\begin{aligned}
\frac{I_H^*}{I_V^*} &= \frac{c}{rH}(H-I_H) = \frac{c}{r} - \frac{cI_H}{rH}\\
\frac{1}{I_V^*} &= \frac{c}{I_H^* r} - \frac{cI_H}{rHI_H^*}
\end{aligned}$$

by substituting in the last term of $\dot{V}$ we obtain

$$\begin{aligned}
\dot{V} &= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(3-\left(\frac{S_V^*}{S_V}+\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}+\frac{I_V I_H^*}{I_V^* I_H}\right)\right)\\
&\quad + \mu I_V^* I_V\left(\frac{c}{I_H r} - \frac{c}{rH} + \frac{c}{rI_H^*} + \frac{c}{Hr} - \frac{c}{I_H^* r} + \frac{cI_H}{rHI_H^*} - \frac{cI_H}{rHI_H^*} - \frac{c}{rI_H}\right)\\
&= \left(1-\frac{S_V^*}{S_V}\right)(f(S_V)-f(S_V^*)) + \mu I_V^*\left(3-\left(\frac{S_V^*}{S_V}+\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}+\frac{I_V I_H^*}{I_V^* I_H}\right)\right)
\end{aligned}$$

Let us notice that $3-\left(\frac{S_V^*}{S_V}+\frac{I_V^* S_V I_H}{I_V S_V^* I_H^*}+\frac{I_V I_H^*}{I_V^* I_H}\right) \leq 0$ as a consequence of the inequality of arithmetic and geometric means. Since by hypothesis we know that $f(S_V)$ satisfies:

$$(S_V - S_V^*)(f(S_V)-f(S_V^*)) \leq 0\,,$$

there follows that $\dot{V} \leq 0$.

Let us observe that V is a Lyapunov function (cf. Definition A.0.9), since $V = 0$ if $X = X^*$, $V > 0$ if $X \neq X^*$. Moreover, from what deducted above we have that $\dot{V} \leq 0$, then by the Lyapunov Theorem (cf. TheoremA.0.3) we know that X^* is stable.

We also claim that every sublevel set $\{X \in int(\mathbb{R}^3_+) \mid V(X) \leq V_0\}$, where $V_0 \geq 0$ is an arbitrary constant, is a compact subset of $\text{int}(\mathbb{R}^3_+)$. Indeed, according to (3.14), $V(X) = V_1(S_V) + V_2(I_V) + V_3(I_H)$, and every $V_i(\cdot)$ is non-negative and strictly convex on $\text{int}(\mathbb{R}_+)$, and such that $V_i(z) \to +\infty$ as $z \to 0^+$, or $z \to +\infty$. This implies that all sublevel sets of each $V_i(z)$, are compact in $\text{int}(\mathbb{R}_+)$, from which the claim follows.

The fact that $\dot{V} \leq 0$, together with the compactness of the sublevel sets of $V(X)$ implies that these sublevel sets are forward invariant. Since they are compact sets, this implies in particular that every solution of (2.2)-(2.4) in $\text{int}(\mathbb{R}^3_+)$ is bounded, enabling an application of LaSalle's Invariance Principle (cf. TheoremA.0.15). Notice that $\dot{V} = 0$ if and only if both

$$\left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) = 0 \qquad \text{and} \qquad \left(3 - \left(\frac{S_V^*}{S_V} + \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*} + \frac{I_V I_H^*}{I_V^* I_H}\right)\right) = 0$$

From our condition in (3.11), we have that $\left(1 - \frac{S_V^*}{S_V}\right)(f(S_V) - f(S_V^*)) = 0$ if and only if

$$\frac{S_V^*}{S_V} = 1\,.$$

Substituting this in the second term of $\dot{V}$ yields:

$$\begin{aligned} 3 - \left(\frac{S_V^*}{S_V} + \frac{I_V^* S_V I_H}{I_V S_V^* I_H^*} + \frac{I_V I_H^*}{I_V^* I_H}\right) = 0 \\ 3 - \left(1 + \frac{I_V^* I_H}{I_V I_H^*} + \frac{I_V I_H^*}{I_V^* I_H}\right) = 0 \\ 2 = \frac{I_V^* I_H}{I_V I_H^*} + \frac{I_V I_H^*}{I_V^* I_H} \end{aligned}$$

The equation above can be rewritten as $2 = x + x^{-1}$ by setting $x = \frac{I_V^* I_H}{I_V I_H^*}$, and the only solution of this equation is $x = 1$. Therefore,

$$\frac{I_V^* I_H}{I_V I_H^*} = 1\,.$$

Thus, the subset of $\mathbb{R}^3_+$ where $\dot{V}$ vanishes is

$$E = \left\{ (S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid \frac{S_V^*}{S_V} = 1\,,\; \frac{I_V^* I_H}{I_V I_H^*} = 1 \right\}.$$

We claim that the largest invariant set in E is $\{E_1\}$. To see this, let $(S_V(t), I_V(t), I_H(t))$ be a solution in E. Then $S_V(t) = S_V^*$ for all t. Consequently, $\dot{S}_V(t) = 0$, and then (2.2) implies that $I_H(t) = \frac{H}{d}\frac{f(S_V^*)}{S_V^*}$ for all t. But then $I_H(t) = I_H^*$ for all t. Then $\dot{I}_H(t) = 0$ for all t, and (2.4) implies that $I_V(t) = \frac{H}{c} r \frac{I_H^*}{H - I_H^*}$ for all t, or equivalently that $I_V(t) = I_V^*$ for all t. □

3.4. (In)Stability of the positive steady state when mosquitoes grow logistically

Lemma 3.4.0.1. *Let $X^* = (S_V^*, I_V^*, I_H^*)$ be a positive steady state (or equilibrium) of the system (2.2)-(2.4). Then X^* is locally asymptotically stable with respect to initial conditions in int($\mathbb{R}^3_+$), provided that $f'(S_V^*) < 0$.*

Proof. Given a positive steady state for the system (2.2)-(2.4), we can evaluate the Jacobian matrix (3.4) at the positive equilibrium. Moreover, by taking advantage of the equations (3.1), (3.5) and (3.6) we know that

$$\frac{d}{H} I_H^* = \frac{f(S_V^*)}{S_V^*}\,, \qquad \frac{c}{H}(H - I_H^*) = \frac{cK}{R_0^2 S_V^*} \qquad \text{and} \qquad -\frac{c}{H} I_V^* - r = -r R_0^2 \frac{S_V^*}{K}\,.$$

This allows us to express the Jacobian matrix in terms of S_V^*

$$J = \begin{pmatrix} f'(S_V^*) - \frac{f(S_V^*)}{S_V^*} & 0 & -\frac{d}{H} S_V^* \\ \frac{f(S_V^*)}{S_V^*} & -\mu & \frac{d}{H} S_V^* \\ 0 & \frac{cK}{R_0^2 S_V^*} & -\frac{r R_0^2 S_V^*}{K} \end{pmatrix},$$

whose characteristic polynomial is given by

$$\begin{aligned}
p(\lambda) = &\left(\lambda + \frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)(\lambda+\mu)\left(\lambda + rR_0^2\frac{S_V^*}{K}\right) + \frac{f(S_V^*)}{S_V^*}\frac{cdK}{HR_0^2} \\
&- \frac{cdK}{HR_0^2}\left(\lambda - f'(S_V^*) + \frac{f(S_V^*)}{S_V^*}\right) \\
=&\lambda^3 + \lambda^2\left(rR_0^2\frac{S_V^*}{K} + \mu + \frac{f(S_V^*)}{S_V^*} - f'(S_V)\right) \\
&+ \lambda\left(\mu rR_0^2\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right) + \left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)\right) \\
&+ \mu rR_0^2\left(\frac{f(S_V^*)}{K} - f'(S_V^*)\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right)\right) \\
=:&\ \lambda^3 + a_2\lambda^2 + a_1\lambda + a_0
\end{aligned}$$

Notice that $a_2 > 0$ given that $f'(S_V) < 0$. Moreover, as a result of Theorem 3.1.0.1, for the first component of the positive equilibrium holds that $\frac{S_V^*}{K} > \frac{1}{R_0^2}$ and $f(S_V^*) > 0$. Hence $a_0 > 0$ and also $a_1 > 0$, and thus the Routh table associated to the characteristic polynomial above is given by

$$\begin{array}{cc}
1 & a_1 \\
a_2 & a_0 \\
\dfrac{a_2a_1 - a_0}{a_2} & 0 \\
a_0 &
\end{array}$$

Hence by the Routh-Hurwitz test (cf. [41], p. 14) we have that the equilibrium E^* is stable given that $0 < \frac{a_1a_2 - a_0}{a_2}$.

$$\begin{aligned}
a_1a_2 - a_0 = &-\mu rR_0^2\left(\frac{f(S_V^*)}{K} - f'(S_V^*)\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right)\right) + \left(rR_0^2\frac{S_V^*}{K} + \mu + \frac{f(S_V^*)}{S_V^*} - f'(S_V)\right) \\
&\times\left(\mu rR_0^2\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right) + \left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)\right)
\end{aligned}$$

$$= -\mu r R_0^2 \frac{f(S_V^*)}{K} - f'(S_V)\left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)$$
$$+\left(rR_0^2\frac{S_V^*}{K} + \mu + \frac{f(S_V^*)}{S_V^*}\right)\left(\mu r R_0^2\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right) + \left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)\right)$$
$$= \left(rR_0^2\frac{S_V^*}{K} + \frac{f(S_V^*)}{S_V^*}\right)\left(\mu r R_0^2\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right) + \left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)\right)$$
$$+\mu\left(\mu r R_0^2\left(\frac{S_V^*}{K} - \frac{1}{R_0^2}\right) + \mu\frac{S_V^*}{S_V^*} - f'(S_V^*)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)\right)$$
$$- f'(S_V^*)\left(\frac{f(S_V^*)}{S_V^*} - f'(S_V^*)\right)\left(rR_0^2\frac{S_V^*}{K} + \mu\right)$$

Since $f'(S_V^*) < 0$ and $\frac{1}{R_0^2} < \frac{S_V^*}{K} < 1$ all the terms in the last equation above are positive, and thus $a_1 a_2 - a_0 > 0$. Hence by the Routh-Hurwitz test we know that X^* is locally asymptotically stable. $\square$

The strictly positive equilibrium is globally stable given the sector condition $(S_V - S_V^*)(f(S_V) - f(S_V^*)) \leq 0$, for all S_V. This raises the question of what happens when the sector condition fails.

A common assumption is that populations grow logistically. Notice that the usual logistic growth $f(S_V) = pS_V\left(1 - \frac{S_V}{K}\right)$ does not satisfy the condition provided for global stability, since the sector condition fails near $S_V = 0$ as $0 < S_V^* < K$.

Hence we assume that $f(S_V) = pS_V\left(1 - \frac{S_V}{K}\right)$ where $p > 0$ and $K > 0$ denote the maximal per capita growth rate, and K the carrying capacity of mosquitoes respectively.

From Theorem 3.1.0.1 we have found the unique positive equilibrium E^* whenever $R_0^2 > 1$. By using a similar approach to the one used on Lemma 3.4.0.1, we can compute the Jacobian matrix to determine the stability of this equilibrium. Our first goal is to express the Jacobian in (3.4) using S_V^* only and to avoid explicit reference to I_V^* and I_H^*. Notice that $f'(S_V) = p\left(1 - 2\frac{S_V}{K}\right)$. Now, by using (3.1) we have that

$$\frac{d}{H} I_H^* = \frac{f(S_V^*)}{S_V^*} = p\left(1 - \frac{S_V^*}{K}\right)$$

this implies that

$$-\frac{d}{H}I_H^* + f'(S_V^*) = -p\left(1 - \frac{S_V^*}{K}\right) + p\left(1 - 2\frac{S_V^*}{K}\right) = -p\frac{S_V^*}{K}\,.$$

Also, from (3.5),

$$c\left(\frac{H - I_H^*}{H}\right) = c\frac{1}{R_0^2}\frac{K}{S_V^*}\,,$$

and from (3.6),

$$\frac{c}{H}I_V^* = \frac{cd}{\mu H}\left(S_V^* - \frac{K}{R_0^2}\right) = \frac{cdK}{\mu r H}\left(\frac{rS_V^*}{K}\right) - \frac{cdK}{\mu r H}\frac{r}{R_0^2} = rR_0^2\frac{S_V^*}{K} - r\,,$$

yielding

$$-\frac{c}{H}I_V^* - r = -rR_0^2\frac{S_V^*}{K}$$

These relations help us to express the Jacobian matrix at the positive equilibrium E^* in terms of S_V^* only:

$$Jac_{E^*} = \begin{bmatrix} -p\frac{S_V^*}{K} & 0 & -\frac{dK}{H}\frac{S_V^*}{K} \\ p\left(1 - \frac{S_V^*}{K}\right) & -\mu & \frac{dK}{H}\frac{S_V^*}{K} \\ 0 & c\frac{1}{R_0^2}\frac{K}{S_V^*} & -rR_0^2\frac{S_V^*}{K} \end{bmatrix} = \begin{bmatrix} -pz^* & 0 & -\frac{dK}{H}z^* \\ p(1 - z^*) & -\mu & \frac{dK}{H}z^* \\ 0 & c\frac{1}{R_0^2 z^*} & -rR_0^2 z^* \end{bmatrix}$$

where $z^* = \dfrac{S_V^*}{K}$, so $z^* \in \left(\dfrac{1}{R_0^2}, 1\right)$.

Notice that the characteristic polynomial of the above matrix is given by

$$\begin{aligned} T(\lambda) = &\begin{vmatrix} \lambda + pz^* & 0 & \frac{dK}{H}z^* \\ -p(1 - z^*) & \lambda + \mu & -\frac{dK}{H}z^* \\ 0 & -c\frac{1}{R_0^2 z^*} & \lambda + rR_0^2 z^* \end{vmatrix} \\ =&(\lambda + pz^*)(\lambda + \mu)(\lambda + rR_0^2 z^*) + (p(1 - z^*))\left(\frac{c}{R_0^2 z^*}\right)\left(\frac{dK}{H}z^*\right) \\ &- (\lambda + pz^*)\left(\frac{dK}{H}z^*\right)\left(\frac{c}{R_0^2 z^*}\right) \\ =&\lambda^3 + (pz^* + \mu + rR_0^2 z^*)\lambda^2 + (pz^*\mu + prR_0^2(z^*)^2 + \mu rR_0^2 z^* - \mu r)\lambda \\ &+ pr\mu(R_0^2(z^*)^2 - 2z^* + 1) \\ =&\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 \end{aligned}$$

Note that $a_2 > 0$, and $a_0 > 0$ because $R_0^2 > 1$. The Routh table associated to the characteristic polynomial above is given by

$$\begin{array}{cc} 1 & a_1 \\ a_2 & a_0 \\ \dfrac{a_2 a_1 - a_0}{a_2} & 0 \\ a_0 & \end{array}$$

Hence by the Routh-Hurwitz test (cf. [41], p. 14) we have that the equilibrium E^* is stable given that

$$0 < \frac{a_1 a_2 - a_0}{a_2},$$

and unstable if this inequality is reversed. We thus need to find the sign of $a_1 a_2 - a_0$:

$$\begin{aligned} a_2 a_1 - a_0 = &\left(\frac{S_V^*}{K}\right)^2 \left(\mu + rR_0^2 \frac{S_V^*}{K}\right) p^2 + (\mu r)\left(R_0^2 \frac{S_V^*}{K} - 1\right)\left(\mu + rR_0^2 \frac{S_V^*}{K}\right) \\ &+ \left[\left(\frac{S_V^*}{K}\right)\left\{\mu^2 + \mu r R_0^2 \frac{S_V^*}{K} + \left(rR_0^2 \frac{S_V^*}{K}\right) + \mu r \left(R_0^2 \frac{S_V^*}{K} - 1\right)\right\} - \mu r \left(1 - 2\frac{S_V^*}{K}\right)\right] p \\ = &\left(\frac{S_V^*}{K}\right)^2 \left(\mu + rR_0^2 \frac{S_V^*}{K}\right) p^2 + (\mu r)\left(R_0^2 \frac{S_V^*}{K} - 1\right)\left(\mu + rR_0^2 \frac{S_V^*}{K}\right) \\ &+ \left[\left(\frac{S_V^*}{K}\right)\left\{\mu^2 + 2\mu r R_0^2 \frac{S_V^*}{K} + \left(rR_0^2 \frac{S_V^*}{K}\right)^2 + \mu r\right\} - \mu r\right] p \\ = &\left(\frac{S_V^*}{K}\right)^2 \left(\mu + rR_0^2 \frac{S_V^*}{K}\right) p^2 + \left[\left(\frac{S_V^*}{K}\right)\left\{\left(\mu + rR_0^2 \frac{S_V^*}{K}\right)^2 + \mu r\right\} - \mu r\right] p \\ &+ (\mu r)\left(R_0^2 \frac{S_V^*}{K} - 1\right)\left(\mu + rR_0^2 \frac{S_V^*}{K}\right) \\ = &\alpha p^2 + \beta p + \gamma . \end{aligned}$$

Note that $\alpha > 0$ and $\gamma > 0$ $\left(\text{because } \dfrac{S_V^*}{K} > \dfrac{1}{R_0^2}\right)$. In order to make E^* unstable, we need to show that $\beta < 0$ and $\beta^2 - 4\alpha\gamma > 0$. Notice that for all sufficiently small S_V^*/K we have that

$$\beta = \left[\left(\frac{S_V^*}{K}\right)\left\{\left(\mu + rR_0^2 \frac{S_V^*}{K}\right)^2 + \mu r\right\} - \mu r\right] < 0$$

this also makes that $\gamma < 0$. On the other hand, notice that

$$\beta^2 - 4\alpha\gamma = \left[\left(\frac{S_V^*}{K}\right)\left\{\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2 + \mu r\right\} - \mu r\right]^2 - 4\left(\frac{S_V^*}{K}\right)^2\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2(\mu r)\left(R_0^2\frac{S_V^*}{K} - 1\right)$$

$$= \left(\frac{S_V^*}{K}\right)^2\left[\left(\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2 + \mu r - \frac{\mu r}{\left(\frac{S_V^*}{K}\right)}\right)^2 - 4\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2(\mu r)\left(R_0^2\frac{S_V^*}{K} - 1\right)\right]$$

$$= \left(\frac{S_V^*}{K}\right)^2\left[\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2 + \mu r\left(1 - \frac{1}{\frac{S_V^*}{K}}\right) + 2\left(\mu + rR_0^2\frac{S_V^*}{K}\right)\sqrt{(\mu r)\left(R_0^2\frac{S_V^*}{K} - 1\right)}\right]$$

$$\times\left[\left(\mu + rR_0^2\frac{S_V^*}{K}\right)^2 + \mu r\left(1 - \frac{1}{\frac{S_V^*}{K}}\right) - 2\left(\mu + rR_0^2\frac{S_V^*}{K}\right)\sqrt{(\mu r)\left(R_0^2\frac{S_V^*}{K} - 1\right)}\right]$$

From the last expression the last two factors can be made negative, by choosing S_V^*/K sufficiently small, due to the term $-\mu r\frac{1}{\frac{S_V^*}{K}}$ in each factor. This implies that $\beta^2 - 4\alpha\gamma > 0$. Thus, $a_2a_1 - a_0 < 0$, and by the Routh-Hurwitz test, the steady state $E^* = (S_V^*, I_V^*, I_H^*)$ is unstable.

Lemma 3.4.0.2. *Given the system (2.2)-(2.4) with* $f(S_V) = pS_V\left(1 - \frac{S_V}{K}\right)$ *and* $R_0 > 1$. *The positive steady state* $E^* = (S_V^*, I_V^*, I_H^*)$ *is unstable for* S_V^*/K *sufficiently small for all values of* p *belonging to some interval.*

We claim that S_V^*/K can be made sufficiently small. Indeed by solving the equation $d\left(S_V - \frac{K}{R_0^2}\right) = pS_V\left(1 - \frac{S_V}{K}\right)$ for $\frac{S_V}{K}$, we obtain the solution $\frac{S_V^*}{K}$:

$$\frac{S_V^*}{K} = \frac{p - d + \sqrt{(d-p)^2 + 4\frac{pd}{R_0^2}}}{2p}. \tag{3.15}$$

To see that $\frac{S_V^*}{K}$ can be made arbitrarily small, consider the special case where $p = d$ is arbitrary. Then $\frac{S_V^*}{K} = \frac{1}{R_0}$. Thus if R_0 is arbitrarily large, then $\frac{S_V^*}{K}$ is arbitrarily small.

4. PERSISTENCE OF THE DISEASE

In this chapter we establish that system (2.2)-(2.4) is a persistent dynamical system when $R_0 > 1$.

Persistence is an important notion in the study of population biology and epidemiology. It implies the endemicity of the disease; or in other words, the long term prevalence of a disease.

In order to establish persistence, we first have to show that solutions are and ultimately uniformly bounded (cf. Definition A.0.16), following the techniques discussed in [5] and [35].

Lemma 4.0.0.1. *The set $\Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\}$ is forward invariant for system (2.2)-(2.4). Moreover there exists $P > 0$ such that for all solutions (S_V, I_V, I_H) in Ω, holds that $S_V(t)$, $I_V(t) < P$ for all large t, that is, the solutions of the system (2.2)-(2.4) are ultimately uniformly bounded in Ω (cf. Definition A.0.16).*

Proof. The positive invariance of Ω follows from the fact that whenever any of the state variables equals zero, the corresponding component of the vector field generated by the system (2.2)-(2.4) is nonnegative, and whenever $I_H = H$, the corresponding I_H component is nonpositive. That is, if $S_V = 0$ we know by (2.2) that $\dot{S}_V = f(0) \geq 0$ from the definition of $f(S_V)$ in Theorem 3.1.0.1; if $I_V = 0$ then by (2.2) we have that $\dot{I}_V = \frac{d}{H} S_V I_H \geq 0$ for $S_V, I_H \in \mathbb{R}_+$; and if $I_H = 0$ then by (2.4) follows that $\dot{I}_H = cI_V \geq 0$ for $I_V \in \mathbb{R}_+$; and if $I_H = H$, then $\dot{I}_H = -rH \leq 0$. Therefore, Ω is positively invariant by the Nagumo Theorem (cf. Theorem A.0.16).

In order to prove that the solutions are ultimately uniformly bounded, firstly notice that for any initial condition, $I_H(t) \in [0, H]$ for all $t \in \mathbb{R}_+$ by the forward invariance of Ω.

Now, since $\dot{S}_V = f(S_V) - \frac{d}{H} S_V I_H$ we know that $\dot{S}_V \leq f(S_V)$, and this implies that if $S_V > K$ then $f(S_V) < 0$ and for any fixed $\varepsilon > 0$ we have that $S_V(t) \leq K + \varepsilon$ for all $t >> 1$. Let $M = \max_{S_V \in \mathbb{R}_+} \{f(S_V)\}$. Notice that by adding (2.2) and (2.3) we obtain that

$$\dot{S}_V + \dot{I}_V = f(S_V) - \mu I_V \leq M - \mu I_V \,,$$

let $A > 0$ be such that $A\mu > M + \varepsilon$ and notice that as long as $S_V(t) + I_V(t) \geq A + K + \varepsilon$ for $t >> 1$ then

$$-\mu I_V(t) \leq \mu S_V(t) - \mu(A + K + \varepsilon) \leq \mu(K + \varepsilon) - \mu(A + K + \varepsilon) \leq -\mu A \,.$$

This implies that for $t >> 1$ we have $\dot{S}_V + \dot{I}_V \leq M - \mu I_V \leq M - \mu A < -\varepsilon$. Therefore $S_V(t) + I_V(t) \leq A + K + \varepsilon$ for $t >> 1$, thus proving that all solutions of (2.2)-(2.4) are uniformly bounded for t sufficiently large. For simplicity let us fix $\varepsilon = 1$ and define $P := A + K + 1$. □

Having proved the positive invariance of Ω and the ultimate uniform boundedness of the solutions of (2.2)-(2.4), we proceed to prove the uniform strong persistence of the system (cf. Definition B.0.1).

Theorem 4.0.0.1. *If $R_0 > 1$, then there exists $\varepsilon > 0$, independent of initial conditions satisfying $(S_V(0), I_V(0), I_H(0))$ in $\Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\}$, such that $\liminf_{t\to\infty} X(t) > \varepsilon$ for $X = S_V$, I_V, I_H.*

Proof. This result follows from applying Theorem 4.6 in [35] (cf. Theorem B.0.3). Let $\mathcal{X} = \Omega$, $\mathcal{X}_1 = int(\Omega)$, $\mathcal{X}_2 = \partial\Omega$ and $B = \{(S_V, I_V, I_H) \in \Omega \mid 0 \leq S_V \leq P\,, 0 \leq I_V \leq P\,, 0 \leq I_H \leq H$.

To see that $int(\Omega)$ is positively invariant, we argue by contradiction. Suppose $X(0)$ in $int(\Omega)$ is such that $X(T) \notin int(\Omega)$, for some $T > 0$. Let T be the smallest such time. Since Ω is forward invariant, it follows that $X(T) \in \partial\Omega$.

If $f(0) > 0$, then $X(T)$ must belong to the S_V-axis because the vector field points to $int(\Omega)$ elsewhere on $\partial\Omega$. But the S_V-axis is forward and backward invariant. This leads to a contradiction to the existence and uniqueness of solutions of ODEs, because at least two distinct backward solutions starting in $X(T)$ would exist.

If $f(0) = 0$, then $X(T)$ must belong to either the S_V-axis of the $(I_V, I_H)-$plane. This also leads to a contradiction to the existence and uniqueness property of solutions of ODEs.

Notice that since Ω is positively invariant and the solutions of (2.2)-(2.4) are ultimately uniformly bounded (cf. Lemma 4.0.0.1), all solutions $(S_V(t), I_V(t), I_H(t))$ that start in Ω ultimately enter the compact set B and remain there. It is with the help of these two properties that we claim the conditions of compactness $(\mathbf{C}_{4.2})$ in Definition B.0.11 hold. Indeed, the ultimately uniformly boundedness of solutions guarantee that for any initial condition $(S_V, I_V, I_H) \in \Omega$, the solution $(S_V(t), I_V(t), I_H(t)) \in B$ for $t >> 1$, implying that $d((S_V(t), I_V(t), I_H(t)), B) \to 0$ as $t \to \infty$. Now, for any $\delta > 0$ we notice that $B \cap \{(S_V, I_V, I_H) \in \Omega \mid d((S_V, I_V, I_H), \partial\Omega) < \delta\}$ is bounded, thus having compact closure.

We need to determine the following set

$$\Omega_2 = \bigcup_{y \in Y_2} \omega(y)\,, \qquad Y_2 = \{(S_V, I_V, I_H) \in \mathcal{X}_2 \mid (S_V(t), I_V(t), I_H(t)) \in \mathcal{X}_2 \ \forall t > 0\}\,, \quad (4.1)$$

where $\omega((S_V, I_V, I_H))$ is the omega limit set of the solution $(S_V(t), I_V(t), I_H(t))$ starting in (S_V, I_V, I_H). From this point onward we have to consider two distinct cases: if $f(0) = 0$ and if $f(0) > 0$ (cf. Theorem 3.1.0.1).

If $\mathbf{f(0) > 0}$, the system (2.2)-(2.4) has only one equilibrium in $\partial\Omega$ which is $E_1 = (K, 0, 0)$. Moreover, the set $\{(S_V, I_V, I_H) \in \Omega \mid I_V = 0\,, I_H = 0\}$ is invariant, but any other solution starting on $\partial\Omega$ but not on the S_V-axis leaves $\partial\Omega$. Consequently, clearly $Y_2 = \{(S_V, I_V, I_H) \in \partial\Omega \mid I_V = 0\,, I_H = 0\}$. Moreover $\Omega_2 = \{E_1\}$, because all solutions starting on the S_V-axis, converge to E_1. Recall that the Jacobian matrix for (2.2)-(2.4) at E_1 is given by

$$J_1 = \begin{pmatrix} f'(K) & 0 & -\frac{d}{H}K \\ 0 & -\mu & \frac{d}{H}K \\ 0 & c & -r \end{pmatrix}.$$

Since $f'(K) < 0$, E_1 is a hyperbolic equilibrium, making $\{E_1\}$ an isolated covering of Ω_2 (see Definition B.0.8), and since no homoclinic connection of E_1 to itself exists on the S_V-axis, $\{E_1\}$ is an acyclic covering of Ω_2 (see Definition B.0.10).

There remains to show that E_1 is a weak repeller for $int(\Omega)$, i.e. for every solution $(S_V(t), I_V(t), I_H(t))$ starting in $int(\Omega)$, there must hold that:

$$\limsup_{t\to\infty} d((S_V(t), I_V(t), I_H(t)), E_1) > 0\,. \tag{4.2}$$

We claim that this holds if the stable manifold of E_1, denoted $W^s(E_1)$, does not intersect $int(\Omega)$. Indeed, if (4.2) does not hold for some solution $(S_V(t), I_V(t), I_H(t))$ that starts in $int(\Omega)$ then, since Ω is positively invariant for the system (2.2)-(2.4),

$$\liminf_{t\to\infty} d((S_V(t), I_V(t), I_H(t)), E_1) = \limsup_{t\to\infty} d((S_V(t), I_V(t), I_H(t)), E_1) = 0$$

and $\lim_{t\to\infty} (S_V(t), I_V(t), I_H(t)) = E_1$; which cannot happen if $W^s(E_1) \cap int(\Omega) = \emptyset$.

We claim that $W^s(E_1) \cap int(\Omega) = \emptyset$. Recall that E_1 is unstable if $R_0 > 1$ (cf. Theorem 3.1.0.1). Notice that the Jacobian matrix at E_1, J_1, has one eigenvalue with positive real part (denoted λ_+) and two eigenvalues with negative real part ($f'(K)$ and one denoted λ_-, with the possibility of $f'(K) = \lambda_-$). The stable eigenspace of E_1 can be determined, as mentioned above $(1,0,0)^T$ is an eigenvector of J_1 associated to $f'(K)$. If $\lambda_- \neq f'(K)$ then the eigenvector associated to λ_- is of the form $(*, v_2, v_3)^T$ where v_2 and v_3 hold

$$\begin{pmatrix} -\mu & \frac{dK}{H} \\ c & -r \end{pmatrix} \begin{pmatrix} v_2 \\ v_3 \end{pmatrix} = \lambda_- \begin{pmatrix} v_2 \\ v_3 \end{pmatrix}. \tag{4.3}$$

Notice that if $\lambda_- = f'(K)$ then $f'(K)$ is a repeated eigenvalue, and an associated generalized eigenvector posseses the same structure $(*, v_2, v_3)^T$.

We claim that in both cases the vector $(v_2, v_3)^T \notin \mathbb{R}^2_+$. The matrix in (4.3) is an irreducible Metzler matrix (a Metzler matrix is a matrix with nonnegative off-diagonal entries). An interesting property of the matrix in (4.3) is that by adding the positive multiple of the identity matrix $(\mu + r)\mathcal{I}$, we obtain a nonnegative irreducible matrix for which the Perron-Frobenius Theorem holds. This implies that the matrix in (4.3) has a positive real eigenvalue which is larger than the real part of any other eigenvalue, i.e. a dominant eigenvalue. The dominant eigenvalue is λ_+ and by the Perron-Frobenius theorem we know that every eigenvector that is not associated to the dominant eigenvalue is not in the positive quadrant in our case. This means that $(v_2, v_3) \notin \mathbb{R}^2_+$, which implies that the (generalized) eigenspace associated to E_1 does not intersect $int(\Omega)$. Therefore $W^s(E_1) \cap int(\Omega) = \emptyset$, and thus E_1 is a weak repeller for $int(\Omega)$. Then by Theorem B.0.3 we obtain that $\partial\Omega$ is a uniform strong repeller for $int(\Omega)$, thus proving the existence of some $\varepsilon > 0$, such that $\liminf_{t\to\infty} X(t) > \varepsilon$ for $X = S_V,\ I_V,\ I_H$ when $f(0) > 0$.

If $\mathbf{f(0)} = \mathbf{0}$, the system (2.2)-(2.4) has two equilibria in $\partial\Omega$ which are $E_0 = (0, 0, 0)$ and $E_1 = (K, 0, 0)$. The set $\{(S_V, I_V, I_H) \in \Omega \mid I_V = 0\,, I_H = 0\}$ is still invariant as in the case when $f(0) > 0$, but we also have that the set $\{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\}$ is invariant. This last fact follows from the equations (2.2)- (2.4) when $S_V = 0$, we have that $\dot{S}_V = 0$ thus any solution starting in the set $\{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\}$ remains there. But notice that when $S_V = 0$, $\dot{I}_V = -\mu I_V$ and $I_H = -rI_H$, thus all the solutions starting in $\{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\}$ converge to E_0.

Now, any solution starting on $\partial\Omega$ but not in the set $\{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\} \cup \{(S_V, I_V, I_H) \in \Omega \mid I_V = 0\,, I_H = 0\}$ leaves $\partial\Omega$. This allows us to define the set $Y_2 = \{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\} \cup \{(S_V, I_V, I_H) \in \Omega \mid I_V = 0\,, I_H = 0\}$, and then also $\Omega_2 = \{E_0, E_1\}$. Indeed, solutions which start on the S_V-axis, different from E_0, clearly converge to E_1, and as we remarked above, solutions starting on the $(I_V, I_H)-$plane converge to E_0. Moreover, recall that the Jacobian matrix at E_0 is

$$J_0 = \begin{pmatrix} f'(0) & 0 & 0 \\ 0 & -\mu & 0 \\ 0 & c & -r \end{pmatrix}$$

which has one positive eigenvalue $f'(0)$ and two negative eigenvalues. Which implies that E_0 is a hyperbolic equilibrium. Note that the unstable manifold of E_0 is the open segment between E_0 and E_1 on the S_V-axis, and the stable manifold of E_0 consists of the $(I_V, I_H)-$plane in Ω.

Given the corresponding stable and unstable manifolds for E_0 and E_1 we know that E_0 and E_1 are hyperbolic equilibria. Clearly, there are no homoclinic or heteroclinic connections in Y_2 between these two equilibria. Thus $M = \{E_0\} \cup \{E_1\}$ is an acyclic isolated covering of Ω_2.

For this case it remains to show that E_0 and E_1 are weak repellers for $int(\Omega)$, i.e. for every solution $(S_V(t), I_V(t), I_H(t))$ starting in $int(\Omega)$

$$\limsup_{t\to\infty} d((S_V(t), I_V(t), I_H(t)), E_k) > 0 \, . \qquad k = 0, 1 \, . \tag{4.4}$$

The fact that E_1 is a weak repeller is exactly the same as in the case that $f(0) > 0$. On the other hand, we have proved that $W^s(E_0)$, does not intersect $int(\Omega)$, since $W^s(E_0) = \{(S_V, I_V, I_H) \in \Omega \mid S_V = 0\}$, and thus E_0 is also a weak repeller for $int(\Omega)$. Then by Theorem B.0.3 we obtain that $\partial\Omega$ is a uniform strong repeller for $int(\Omega)$, i.e. that there exists $\varepsilon > 0$, such that $\liminf_{t\to\infty} X(t) > \varepsilon$ for $X = S_V$, I_V, I_H when $f(0) = 0$. □

5. GLOBAL ASPECTS OF OSCILLATORY BEHAVIOR IN THE MODEL

We have seen that the system (2.2)-(2.4) possesses a unique positive steady state, E^*, whenever $R_0 > 1$ (cf. Theorem 3.1.0.1), and that when $f(S_V) = pS_V(1 - S_V/K)$ this positive steady state can be unstable (cf. Lemma 3.4.0.2). The persistence result in Theorem 4.0.0.1 implies that the omega limit set of a solution which is initiated in the interior of $\Omega = \{(S_V, I_V, I_H) \in \mathbb{R}^3_+ \mid S_V \geq 0\,, I_V \geq 0\,, 0 \leq I_H \leq H\}$ ultimately stays away from the boundary of Ω. In this chapter we will show that for the unstable case introduced in Lemma 3.4.0.2 the solutions that do not start on the invariant part of the boundary of Ω, and also not on the stable manifold of the endemic equilibrium, have an omega limit set that it is a periodic orbit. Moreover, there always exists a stable periodic orbit if $f(S_V)$ is analytic.

Theorem 5.0.0.1. *Suppose that $R_0 > 1$. If $f(0) > 0$, then the omega limit set of any solution not initiated on the invariant S_V-axis, either contains E^* or is a periodic orbit.*

If $f(0) = 0$, the same conclusion holds if in addition, the solution is also not initiated on the invariant $(I_V, I_H)-$plane.

Proof. Let $f(0) > 0$. Let X_0 be an initial condition not on the S_V-axis. Since $R_0 > 1$, Theorem 4.0.0.1 implies the omega limit of a solution, that does not start in the S_V-axis, cannot contain a point on the S_V-axis. Because there is only one steady state in Ω which does not belong to the S_V-axis, E^*, the Poincaré-Bendixson Theorem for competitive systems in dimension 3 (cf. Theorem A.0.12) guarantees that the omega limit set either contains E^* or is a periodic orbit.

Similarly, if $f(0) = 0$ and $R_0 > 1$. For any initial condition X_0 that is not on the S_V-axis nor the $(I_V, I_H)-$plane, its omega limit cannot contain a point on these invariant sets by Theorem 4.0.0.1. By Theorem 3.1.0.1 there is only one steady state in Ω that does not belong to either the S_V-axis nor the $(I_V, I_H)-$plane, E^*. Theorem A.0.12 guarantees that the omega limit set either contains E^* or is a periodic orbit. □

Theorem 5.0.0.2. *Let $f(S_V) = pS_V(1 - S_V/K)$, $R_0 > 1$, and suppose that S_V^*/K is sufficiently small and that an appropriate value of p are chosen, such that the steady state E^* is hyperbolic and unstable (cf. Lemma 3.4.0.2). Then there exists an orbitally asymptotically stable periodic orbit. Every solution except those whose initial data on the one dimensional stable manifold of E^*, or on the S_V-axis, or the $(I_V, I_H)-$plane approaches a nontrivial periodic orbit.*

Proof. This result follow from Theorem B.0.4 (cf. [32]). Notice that the vector field given by (2.2)-(2.4) is analytic in $\mathbb{R}^3_+$. Let us consider as domain the interior of Ω and recall that the only steady state in this set is E^*. Since $R_0 > 1$, by Lemma 4.0.0.1 the solutions of the system (2.2)-(2.4) are ultimately uniformly bounded, and by Theorem 4.0.0.1 the system (2.2)-(2.4) is uniformly strongly persistent. Therefore the system (2.2)-(2.4) holds the dissipative condition of Theorem B.0.4. By Lemma 3.4.0.2 we have that the Jacobian matrix at E^* has two eigenvalues with positive real part and one negative eigenvalue. Since the determinant of a matrix is the product of its eigenvalues, the Jacobian matrix at E^* has negative determinant. Moreover, the Jacobian matrix at E^* is irreducible:

$$Jac_{E^*} = \begin{bmatrix} -p\frac{S_V^*}{K} & 0 & -\frac{dK}{H}\frac{S_V^*}{K} \\ p\left(1 - \frac{S_V^*}{K}\right) & -\mu & \frac{dK}{H}\frac{S_V^*}{K} \\ 0 & c\frac{1}{R_0^2}\frac{K}{S_V^*} & -rR_0^2\frac{S_V^*}{K} \end{bmatrix}.$$

Finally, recall that the system(2.2)-(2.4) is competitive (cf. Theorem 3.2.0.1) in Ω, hence also in $int(\Omega)$, and therefore by Theorem B.0.4 there exists at least a periodic orbit that is orbitally asymptotically stable. Now, since the Jacobian matrix at E^* is irreducible, appliying Perron-Frobenius Theorem to see that the dominant eigenvalue, which is the negative eigenvalue of the Jacobian matrix, has a positive eigenvector with respect to the partial order $\leq_{\mathcal{K}}$, i.e., $v \geq_{\mathcal{K}} 0$. Therefore by Theorem A.0.13 we have that the forward orbits of the appropriately restricted initial conditions approach a periodic orbit. $\square$

An example of this behavior can be generated through numerical simulations. Consider the following parameter values for system (2.2)-(2.4):

$$d = 5\,, \quad H = 100\,, \quad \mu = 0.2\,, \quad r = 0.5\,, \quad p = 0.5\,, \quad K = 30\,, \quad c = 1\,.$$

This set of parameters yields $R_0^2 = 15$, thus providing the existence of the positive equilibrium (cf. Theorem 3.1.0.1), and it is given by $E^* = (2.2042, 5.1057, 9.2653)$ with Jacobian matrix

$$\begin{pmatrix} -0.0367 & 0 & -0.1102 \\ 0.4633 & -0.2 & 0.1102 \\ 0 & 0.9073 & -0.5511 \end{pmatrix}.$$

The eigenvalues of the Jacobian matrix are: $\lambda_1 = 0.01213 + 0.2395i$, $\lambda_2 = 0.01213 - 0.2395i$ and $\lambda_3 = -0.8121$. Therefore, E^* is an unstable hyperbolic equilibrium.

We obtain that the solutions of the system (2.2)-(2.4), for an initial conditions close to the equilibrium, are given by

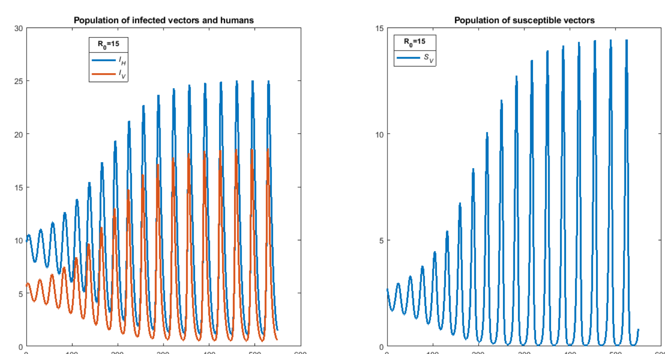


FIGURE 5.1: Solution for the system (2.2)-(2.4) near the positive steady state

The solution starting at $E^* + (1/2, 1/2, 1/2)$ appear to converge to a stable limit cycle, in accordance with Theorem 5.0.0.2.

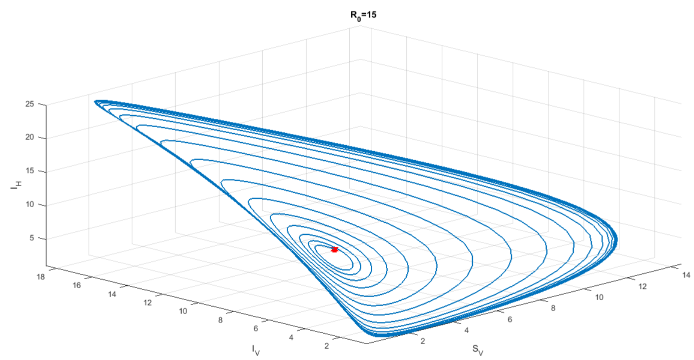


FIGURE 5.2: Orbit of solution with initial condition at $E^* + (1/2, 1/2, 1/2)$ appearing to converge to a stable limit cycle

6. CONCLUSIONS

Throughout this work we have studied the vector-host dynamics of Malaria with respect to a model, based on the work of Ronald Ross and George Macdonald, which includes the demography of susceptible mosquitoes.

We have analyzed the effects of including the vector demography in the classic Ross-Macdonald model. With the study of our main model we determined the existence of a unique endemic equilibrium whenever $R_0 > 1$ and the asymptotic stability of the disease-free equilibrium whenever $R_0 \leq 1$. We also provided a specific condition for the demography of susceptible vectors, such that when holds and given $R_0 > 1$ the epidemic equilibrium is globally asymptotically stable. When this condition fails, the disease can exhibit sustained oscillations when $R_0 > 1$.

Moreover, when $R_0 > 1$ we have proved that for our main model the solutions for endemic initial conditions persist for arbitrarily large values of t. This has an important comparisson to the endemicity of Malaria and its prevalence among both human and mosquito populations, as often reported by the World Health Organization [26].

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APPENDICES

A. APPENDIX Monotone Dynamical Systems

In this Appendix we list several definitions and key results concerning dynamical systems and monotone dynamical systems. We refer the reader to the work of Hal Smith [30] for more details.

Among the different results referred to here we will consider the autonomous system of ordinary differential equations

$$x' = f(x) \tag{A.1}$$

where f is continuously differentiable in an open subset $D \subset \mathbb{R}^n$. We also denote by $\phi_t(x)$ the solution of (A.1) that starts at the point x at $t = 0$. Then nonnegative cone $\mathbb{R}^n_+$ provides with a partial order given by $y \leq x$ if $x - y \in \mathbb{R}^n_+$. We write $x < y$ if $x \leq y$ and $x_i < y_i$ for some i and we write $x << y$ if $x_i < y_i$ for all i. The (closed) order interval determined by $u, v \in \mathbb{R}^n$ is the closed set $[\mathbf{u}, \mathbf{v}] = \{x \in \mathbb{R}^n \mid u \leq x \leq v\}$ which may be empty.

Definition A.0.1 (**Monotone Dynamical System** cf. [30], p. 2)**.** *We say that the system (A.1) is monotone if whenever $x, y \in D$ satisfy $x \leq y$ and the solutions $\phi_t(x)$ and $\pi_t(y)$ are defined and are hold that $\phi_t(x) \leq \phi_t(y)$ for all $t \geq 0$.*

We say that is strictly monotone if $x < y$ implies that $\phi_t(x) < \phi_t(y)$ for all $t \geq 0$.

We say that the system is strongly monotone if $x < y$ implies that $\phi_t(x) << \phi_t(y)$ for all $t \geq 0$.

Definition A.0.2 (**Equilibrium Solution** cf. [41], p. 5)**.** *An equilibrium solution of (A.1) is a point $\bar{x} \in \mathbb{R}^n$ such that $f(\bar{x}) = 0$, i.e., a solution which does not change in time. We also refer to an equilibrium solution to be a fixed point, rest point, critical point or steady state.*

Definition A.0.3 (**Lyapunov Stability** cf. [41], p. 7)**.** *Let $x(t)$ be any solution of (A.1), we say that $x(t)$ is stable (or Lyapunov stable) if, given $\varepsilon > 0$, there exists a*

$\delta = \delta(\varepsilon) > 0$ *such that, for any other solution,* $y(t)$*, of (A.1) satisfying* $|x(t_0) - y(t_0)| < \delta$*, then* $|x(t) - y(t)| < \varepsilon$ *for* $t > t_0$*,* $t_0 \in \mathbb{R}$*.*

Definition A.0.4 (**Asymptotic Stability** cf. [41], p. 7)**.** *Let* $x(t)$ *be any solution of (A.1), we say that* $x(t)$ *is asymptotically stable if it is Liapunov stable and for any other solution,* $y(t)$*, of (A.1), there exists a constant* $b > 0$ *such that, if* $|x(t_0) - y(t_0)| < b$*, then* $\lim_{t\to\infty} |x(t) - y(t)| = 0$*.*

Definition A.0.5 (**Positive Orbit** cf. [41], p. 8)**.** *Let* x_0 *be a fixed point of (A.1), the positive orbit through the point* x *fot* $t \geq t_0$ *is given by*

$$\mathcal{O}^+(x_0, t_0) = \{x \in \mathbb{R}^n \mid x = \bar{x}(t),\, t \geq t_0,\, \bar{x}(t_0) = x_0\} \ . \tag{A.2}$$

Recall that the distance between the an arbitrary point $p \in \mathbb{R}^n$ and a set $S \subset \mathbb{R}^n$ is given by $d(p, S) = \inf_{x \in S} |p - x|$.

Definition A.0.6 (**Orbital Stability** cf. [41], p. 9)**.** *Let* $x(t)$ *be any solution of (A.1), we say that* $x(t)$ *is orbitally stable if, given* $\varepsilon > 0$*, there exists a* $\delta = \delta(\varepsilon) > 0$ *such that, for any other solution,* $y(t)$*, of (A.1), satisfying* $|x(t_0) - y(t_0)| < \delta$*, then* $d(y(t), \mathcal{O}^+(x_0, t_0)) < \varepsilon$ *for* $t > t_0$*.*

Definition A.0.7 (**Asymptotic Orbital Stability** cf. [41], p. 9)**.** *Let* $x(t)$ *be any solution of (A.1), we say that* $x(t)$ *is asymptotically orbitally stable if it is orbitally stable and for any other solution* $y(t)$*, of (A.1), there exists a constant* $b > 0$ *such that, if* $|x(t_0) - y(t_0)| < b$*, then* $\lim_{t\to\infty} d(y(t), \mathcal{O}^+(x_0, t_0)) = 0$*.*

Theorem A.0.1 (cf. [41], p. 11)**.** *Let* $x(t)$ *be any solution of (A.1) and let* $Df(x)$ *be the Jacobian matrix of (A.1) at* $x(t)$ *(the linearization of this system). Suppose all of the eigenvalues of* $Df(x)$ *have negative real parts. Then the equilibrium solution* x *of (A.1) is asymptotically stable.*

Definition A.0.8 (**Hyperbolic Fixed Point** cf. [41], p. 12)**.** *Let x be a fixed point of (A.1). Then x is called a hyperbolic fixed point if none of the eigenvalues of $Df(x)$ have zero real part.*

Theorem A.0.2 (**Hartman-Grobman Theorem** cf. [4], p. 27)**.** *If x_0 is a hyperboic rest point for the autonomous differential equation (A.1), then there is an open set U containing x_0 and a homeomorphism H with domain U such that the orbits of the differential equation (A.1) are mapped by H to orbits of the linearized system $\dot{x} = Df(x_0)(x - x_0)$ in the set U.*

Definition A.0.9 (**Lyapunov function** cf. [4], p. 28)**.** *Let x_0 be a fixed point of (A.1). A continuous function $V : U \to \mathbb{R}$, where $U \subseteq \mathbb{R}^n$ is an open set with $x_0 \in U$, is called a Lyapunov function for the differential equation (A.1) at x_0 if*

(i) $V(x_0) = 0$,

(ii) $V(x) > 0$ *for* $x \in U \backslash \{x_0\}$,

(iii) the function V is continuously differentiable on the set $U \backslash \{x_0\}$, and, on this set, $\dot{V}(x) := gradV(x) \cdot f(x) \leq 0$.

The function V is called a strict Lyapunov function if, in addition,

(iv) $\dot{V}(x) < 0$ *for* $x \in U \backslash \{x_0\}$.

Theorem A.0.3 (**Lyapunov Stability Theorem** cf. [4], p. 29)**.** *If there is a Lyapunov function defined in an open neighborhood of a fixed point of the differential equation (A.1), then the fixed point is stable. If, in addition, the Lyapunov function is a strict Lyapunov function, then the fixed point is asymptotically stable.*

Definition A.0.10 (**Invariant Set** cf. [4], p. 34)**.** *A set $S \subseteq \mathbb{R}^n$ is called an invariant set for the differential equation (A.1) if, for each $x \in S$, the solution $t \mapsto \phi_t(x)$, defined* *on its maximal interval of existence, has its image in S. Alternatively, the orbit passing through each $x \in S$ lies in S. In addition, S is called an invariant manifold if S is a manifold.*

Definition A.0.11 (**Stable Manifold** cf. [4], p. 36)**.** *The stable manifold of a fixed point x_0 ($W^s(x_0)$) for an autonomous differential equation with flow ϕ_t is the set of all points x in the domain of definition of ϕ_t such that $\lim_{t\to\infty} \phi_t(x) = x_0$. The unstable manifold of x_0 ($W^u(x_0)$) is the set of all points x in the domain of definition of ϕ_t such that $\lim_{t\to-\infty} \phi_t(x) = x_0$.*

Theorem A.0.4 (**Stable Manifold Theorem** cf. [34], p. 261)**.** *Suppose that $f \in \mathcal{C}^k$ in the system (A.1), has a fixed point x_0 with corresponding Jacobian A. Then, there is a neighborhood $U(x_0) = x_0 + U$ and functions $h^s \in \mathcal{C}^k(E^s(x_0) \cap U, E^u(x_0))$ and $h^u \in \mathcal{C}^k(E^u(x_0) \cap U, E^s(x_0))$, where $E^s(x_0)$ and $E^u(x_0)$ are the linear stable and unstable manifolds respectively, such that*

$$W^s(x_0) \cap U(x_0) = \{x_0 + a + h^s(a) \mid a \in E^s(x_0) \cap U\},$$
$$W^u(x_0) \cap U(x_0) = \{x_0 + a + h^u(a) \mid a \in E^u(x_0) \cap U\}.$$

Both h^s and h^u, and their Jacobians vanish at x_0, that is, $W^s(x_0)$ and $W^u(x_0)$ are tangent to their respective linear counterpart E^s and E^u at x_0. Moreover,

$$|\phi_t(x) - x_0| \leq Ce^{-t\alpha}, \quad t \geq 0, \quad x \in W^s(x_0)$$
$$|\phi_t(x) - x_0| \leq Ce^{t\alpha}, \quad -t \geq 0, \quad x \in W^u(x_0)$$

for any $\alpha < \min\{|Re(\alpha_j)| \mid \alpha_j \in \sigma(A), Re(\alpha_j) \neq 0\}$ and some $C > 0$ depending on α.

Theorem A.0.5 (**Stable Manifold Theorem addendum if fixed point is hyperbolic** cf. [34], p. 261)**.** *Suppose that $f \in \mathcal{C}^k$ in the system (A.1), has a hyperbolic fixed point x_0. Then there is a neighborhood $U(x_0)$ such that $\mathcal{O}^+(x, t_0) \subset U(x_0)$ (respectively*

$\mathcal{O}^-(x,t_0) \subset U(x_0)$) if and only if $x \in W^s(x_0)$ ($x \in W^u(x_0)$). In particular

$$U^s(x_0) = \{\phi_t(x) \mid x \in W^s(x_0), t \geq 0\},$$

$$U^u(x_0) = \{\phi_t(x) \mid x \in W^u(x_0), -t \geq 0\}.$$

where $U^s(x_0)$ and $U^u(x_0)$ are the stable and unstable set at x_0 respectively.

Definition A.0.12 (**ω and α limit set** cf. [4], p. 92)**.** *Suppose that ϕ_t is a flow on $\mathbb{R}^n$ and $p \in \mathbb{R}^n$. A point x in $\mathbb{R}^n$ is called an omega limit point ($\omega-$limit point) of the orbit through p if there is a sequence of numbers $t_1 \leq t_2 \leq t_3 \leq \cdots$ such that $\lim_{i\to\infty} t_i = \infty$ and $\lim_{i\to\infty} \phi_{t_i}(p) = x$. The collection of all such omega limit points is denoted $\omega(p)$ and is called the omega limit set ($\omega-$limit set) of p. Similarly the $\alpha-$limit set $\alpha(p)$ is defined to be the set of all limits $\lim_{i\to\infty} \phi_{t_i}(p)$ where $t_1 \geq t_2 \geq t_3 \geq \cdots$ and $\lim_{i\to\infty} t_i = -\infty$.*

Theorem A.0.6 (cf. [4], p. 92)**.** *The omega limit set of a point is closed and invariant.*

Definition A.0.13 (**Cooperative and Competitive Systems** cf. [31], p.370)**.** *A dynamical system (A.1) is cooperative if $\dfrac{\partial f_i}{\partial x_j}(x) \geq 0, i \neq j,\ x \in D$. We say the system is competitive if $\dfrac{\partial f_i}{\partial x_j}(x) \leq 0, i \neq j,\ x \in D$.*

Definition A.0.14 (**Kamke condition** cf. [30] p. 32)**.** *Given the system (A.1) we say that f is of type K in D if for each i, $f_i(a) \leq f_i(b)$ for any two points a and b in D satisfiying $a \leq b$ and $a_i = b_i$.*

Theorem A.0.7 (**Kamke's Theorem** cf. [30], p. 32)**.** *Let f be type K on D and $x_0, y_0 \in D$. Let $<_r$ denote one any of the relations $\leq$, $<$ or $<<$. If $x_0 <_r y_0$, $t > 0$ and $\phi_t(x_0)$ and $\phi_t(y_0)$ are defined, then $\phi_t(x_0) <_r \phi_t(y_0)$.*

Theorem A.0.8 (cf. [39], p.268)**.** *Let $\pi(x,t)$ denote the dynamical system generated by the autonomous system of differential equations (A.1). If (A.1) is cooperative in D, then π is a monotone dynamical system with respect to $\leq$ in D. If (A.1) is cooperative and irreducible in D, then π is a strongly monotone system with respect to $\leq$ in D.*

Theorem A.0.9 (cf. [30], p. 35)**.** *All bounded solutions of a cooperative system in* $\mathbb{R}^2$ *converge to an equilibrium point.*

Theorem A.0.10 (**Generalized Poincaré-Bendixson Theorem** cf. [34], p. 215 and [41], p. 120)**.** *Let* M *be a positively invariant region for the vector field generated by (A.1) in* $\mathbb{R}^2$ *and where the vector field has a finite number of fixed points. Let* $p \in M$*, and consider* $\omega(p)$*. Then one of the following possibilities holds.*

- $\omega(p)$ *is a fixed point;*
- $\omega(p)$ *is a closed orbit;*
- $\omega(p)$ *consists of a finite number of fixed points* $p_1, \ldots, p_n$ *and orbits* γ *with* $\alpha(\omega) = p_i$ *and* $\omega(\gamma) = p_j$*.*

Theorem A.0.11 (**Butler-McGehee Lemma** cf. [19], p. 261, [42], p. 16 and [39], p. 12)**.** *Let* P *be a hyperbolic equilibrium of the system (A.1). Suppose* $P \in \omega(x)$*,* $\{P\} \neq \omega(x)$*, the omega limit set of* $\mathcal{O}^+(x, t_0)$*,* $x \in \mathbb{R}^n$*. Then there exists points* $q \in W^s(P) \cap \omega(x)$ *and* $\hat{q} \in W^u(P) \cap \omega(x)$*, where* $W^s(P)$*,* $W^u(P)$ *are stable and unstable manifold of equilibrium* P*, respectively.*

Theorem A.0.12 (cf. [16] and [30], p. 41)**.** *A compact limit set of a competitive or cooperative system in* $\mathbb{R}^3$ *that contains no equilibrium points is a periodic orbit.*

Theorem A.0.13 (cf. [16] and [30], p. 43)**.** *Suppose that* $D \subset \mathbb{R}^3$ *contains a unique equilibrium* p *for the competitive system (A.1) and it is hyperbolic. Suppose further that its stable manifold* $W^s(p)$ *is one-dimensional and tangent at* p *to a vector* $v >> 0$*. If the orbit of* $q \in D \backslash W^s(p)$ *has compact closure in* D*, then* $\omega(q)$ *is a nontrivial periodic orbit.*

Theorem A.0.14 (cf. [30], p. 44)**.** *Let* γ *be a non-trivial periodic orbit of a competitive system in* $D \subset \mathbb{R}^3$ *and suppose that there exists* p*,* q *with* $p << q$ *such that*

$$\gamma \subset [\mathbf{p}, \mathbf{q}] \subset D\,.$$

Then $K = \{x \in \mathbb{R}^3 \mid x$ *is not related to any point* $y \in \gamma\} = (\gamma + \mathbb{R}^3_+)^c \cap (\gamma - \mathbb{R}^3_+)^c$ *is an open subset of* $\mathbb{R}^3$ *consisting of two connected components, one bounded and one unbounded. The bounded component,* $K(\gamma)$*, is homeomorphic to the open unit ball in* $\mathbb{R}^3$*.* $K(\gamma) \subset [\mathbf{p}, \mathbf{q}]$*, is positively invariant and its closure contains an equilibrium.*

Theorem A.0.15 (**LaSalle Invariance Principle** cf. [20], p.128)**.** *Let* $\Omega \subset D$ *be a compact set that is positively invariant with respect to (A.1). Let* $V : D \to \mathbb{R}$ *be a continuously differentiable function such that* $\dot{V}(x) \leq 0$ *in* Ω*. Let* E *be the set of all points in* Ω *where* $\dot{V}(x) = 0$*. Let* M *be the largest invariant set in* E*. Then every solution starting in* Ω *approaches* M *as* $t \to \infty$*.*

Theorem A.0.16 (**Nagumo Theorem** cf. [17], p. 304)**.** *Let* K *be a closed subset of a* $\mathcal{C}^2$ *manifold* M *and let* f *be a vector field on* M *which is Lipschitz continuous. The following conditions are equivalent:*

- *Any integral curve of* f *starting in* K *remains in* K*, i.e.* K *is positively invariant.*
- $\langle f(m), v\rangle \leq 0$ *for any exterior normal vector* v *at a point* m *in* K*.*

Definition A.0.15 (**Ultimate boundedness** cf. [3], p. 154)**.** *Let* $\pi(x)$ *be a dynamical system defined on a locally compact metric space* X*, we say that pi is ultimately bounded if there exists a compact set* $K \subset X$ *with nonempty* $\omega-$*limit set* $\omega(x_0)$ *and such that* $\omega(x_0) \subset K$ *for each* $x_0 \in X$*, i.e. whenever there exists a compact global attractor in* X*.*

Definition A.0.16 (cf. [20], p. 169)**.** *The solutions of (A.1) are*

- uniformly bounded *if there exists a positive constant* c*, independent of* $t_0 \geq 0$ *and for every* $a \in (0, c)$*, there is* $\beta = \beta(a) > 0$*, independent of* t_0*, such that*

$$\|x(t_0)\| \leq a \Rightarrow \|x(t)\| \leq \beta\,, \qquad \forall t \geq t_0\,. \tag{A.3}$$

- *globally uniformly bounded if (A.3) holds for arbitrarily large* a.
- *uniformly ultimately bounded with ultimate bound* b *if there exists positive constants* b *and* c, *independent of* $t_0 \geq 0$, *and for every* $a \in (0, c)$, *there is* $T = T(a, b) \geq 0$, *independent of* t_0, *such that*

$$\|x(t_0)\| \leq a \Rightarrow \|x(t)\| \leq b\,, \qquad \forall t \geq t_0 + T\,. \tag{A.4}$$

- *globally uniformly ultimately bounded if (A.4) holds for arbitrarily large* a.

Theorem A.0.17 (**Perron-Frobenius** cf. [18], p. 534)**.** *Let* $A \in M_{n\times n}$ *be irreducible and nonnegative, and suppose that* $n \geq 2$. *Then*

- $\rho(A) > 0$, *where* $\rho(A)$ *is the spectral radius of* A.
- $\rho(A)$ *is an algebraically simple eigenvalue of* A.
- *there is a unique real vector* $x = [x_i]$ *such that* $Ax = \rho(A)x$ *and* $x_1 + \cdots + x_n = 1$*; this vector is positive*
- *there is a unique real vector* $y = [y_i]$ *such that* $y^T A = \rho(A)y^T$ *and* $x_1y_1 + \cdots + x_ny_n = 1$*; this vector is positive.*

B. APPENDIX Persistence Theory

On this section we list different definitions and results key on the study of dynamical systems and persistent dynamical systems. We refer to the reader to the more in depth work of Hal Smith [31, 39] and Horst Thieme [31, 35, 36].

Let X be an arbitrary nonempty set, $J \subset [0, \infty)$ and $\rho : X \to \mathbb{R}_+$.

Definition B.0.1 (cf. [31], p. 61). *A semiflow $\Phi : J \times X \to X$ is called* weakly $\rho-$persistent, *if*

$$\limsup_{t\to\infty} \rho(\Phi(t,x)) > 0 \qquad \forall x \in X,\ \rho(x) > 0.$$

Φ *is called* strongly $\rho-$persistent, *if*

$$\liminf_{t\to\infty} \rho(\Phi(t,x)) > 0 \qquad \forall x \in X,\ \rho(x) > 0.$$

A semiflow $\Phi : J \times X \to X$ is called uniformly weakly $\rho-$persistent, *if there exists some $\varepsilon > 0$ such that*

$$\limsup_{t\to\infty} \rho(\Phi(t,x)) > \varepsilon \qquad \forall x \in X,\ \rho(x) > 0.$$

Φ *is called* uniformly strongly $\rho-$persistent, *if there exists some $\varepsilon > 0$ such that*

$$\liminf_{t\to\infty} \rho(\Phi(t,x)) > \varepsilon \qquad \forall x \in X,\ \rho(x) > 0.$$

Definition B.0.2 (cf. [31], p. 62). *A semiflow $\Phi : J \times X \to X$ is called* $\rho-$dissipative, *if there exists some $c > 0$ such that*

$$\limsup_{t\to\infty} \rho(\Phi(t,x)) < c \qquad \forall x \in X\,.$$

Φ *is called* weakly $\rho-$dissipative, *if there exists some $c > 0$ such that*

$$\liminf_{t\to\infty} \rho(\Phi(t,x)) < c \qquad \forall x \in X\,.$$

Φ *is called* $\rho-$permanent, *if Φ is both $\rho-$dissipative and uniformly $\rho-$persistent.*

Definition B.0.3 (cf. [31], p. 335). *A semiflow $\Phi : J \times X$ is called periodic, with period $\eta > 0$, if*

$$\Phi(t+\eta, x) = \Phi(t,x) \qquad \forall x \in X\,.$$

Theorem B.0.1 (cf. [31], p. 335). *Let $\Phi : J \times X \to X$ be a periodic semiflow, X a metric space with metric d and Φ continuous. Let $\rho : X \to \mathbb{R}_+$ be uniformly continuous. Then Φ is uniformly $\rho-$persistent whenever it is uniformly weakly $\rho-$persistent and a closed subset B of X exists with the following properties:*

(a) *For all* $x \in X$, $\rho(x) > 0$, $d(\Phi(t,x), B) \to 0$ *as* $t \to \infty$.

(b) *If* $0 < \varepsilon_1 < \varepsilon_2 < \infty$, *the intersection* $B \cap \{\varepsilon_1 \leq \rho(x) \leq \varepsilon_2\}$ *is compact.*

(c) *If* $y \in B$ *and* $\rho(y) > 0$, *there exist no* $t > r > 0$ *such that* $\rho(\Phi(r,y)) = 0$ *and* $\rho(\Phi(t,y)) > 0$.

Definition B.0.4 (cf. [35] p. 2)**.** *Let* (X, d) *be a metric space with metric* d *and let* X *be the union of two disjoint subsets* X_1 *and* X_2. *Consider* Φ *to be a continuous semiflow on* X_1, *i.e., a continuous mapping* $\Phi : [0,\infty) \times X_1 \to X_1$ *such that*

$$\Phi_t \circ \Phi_s = \Phi_{t+s} \quad t, s \geq 0 ; \qquad \Phi_0(x) = x , \quad x \in X_1 .$$

Φ_t *denotes the mapping from* X_1 *to* X_1 *given by* $\Phi_t(x) = \Phi(t,x)$. *Recall that for a point* $x \in X$ *and a subset* Y *of* X, *the distance from* x *to* Y *is given by* $d(x,Y) = \inf_{y \in Y} d(x,y)$. *Let* Y_2 *be a subset of* X_2

- Y_2 *is called a* weak repeller *for* X_1 *if*

$$\limsup_{t\to\infty} d(\Phi_t(x_1), Y_2) > 0 \qquad \forall x_1 \in X_1 .$$

- Y_2 *is called a* strong repeller *for* X_1 *if*

$$\liminf_{t\to\infty} d(\Phi_t(x_1), Y_2) > 0 \qquad \forall x_1 \in X_1 .$$

- Y_2 *is called a* uniform weak repeller *for* X_1 *if there exists some* $\varepsilon > 0$ *such that*

$$\limsup_{t\to\infty} d(\Phi_t(x_1), Y_2) > \varepsilon \qquad \forall x_1 \in X_1 .$$

- *Y_2 is called a uniform strong repeller for X_1 if there exists some $\varepsilon > 0$ such that*

$$\liminf_{t\to\infty} d(\Phi_t(x_1), Y_2) > \varepsilon \qquad \forall x_1 \in X_1 .$$

Typically X_1 is open, and X_2 is considered the "boundary" of X. The dynamical system Φ is called (uniformly) weakly or (uniformly) strongly persistent if X_2 is a (uniform) weak or (uniform) strong repeller for X_1.

Definition B.0.5 (cf. [7])**.** *The continuous flow $\mathcal{F} = (X, \mathbb{R}, \Phi)$ is point dissipative over a nonempty set $M \subset X$ if there exists a compact set $N \subset X$ such that for any $y \in M$, there exists $t(y) > 0$ such that for any $t \geq t(y)$, $\Phi_t(y) \in int(N)$.*

Theorem B.0.2 (cf. [7], p. 593)**.** *Let E be a closed, positively invariant subset of X with nonempty interior $int(E)$ and ∂E. Suppose there exists $\alpha > 0$ such that $\mathcal{F}$ is point dissipative on $\{x \mid x \in X\,,\ d(x, \partial E) \leq \alpha\} \cap int(E)$. Then one of the following statements holds.*

- *The boundary ∂E is not isolated.*
- *There exists $y \in int(E)$ such that $\omega(y) \subset \partial E$.*
- *There exists $\varepsilon > 0$ such that for any $x \in int(E)$, $\lim_{t\to\infty} d(\Phi_t(x), \partial E) \geq \varepsilon$.*

Definition B.0.6 (cf. [35], pp. 422-423)**.** *The $\omega-$limit set of a point y is defined*

$$\omega(y) = \bigcap_{t\geq 0} \overline{\Phi([t,\infty) \times \{y\})} .$$

An element $y \in X$ has a full orbit, if there is a function $x(t)$, $-\infty < t < \infty$, such that $x(0) = y$ and $x(t+s) = \Phi_t(x(s))$ for all $t \geq 0$, $s \in \mathbb{R}$. The $\alpha-$limit set of a full orbit $x(t)$ is defined by

$$\alpha(x) = \bigcap_{t\geq 0} \overline{x((-\infty, -t])} .$$

Recall that a subset M of X is called forward invariant *if and only if $\Phi_t(M) \subset M$, $t > 0$, and* invariant *if and only if $\Phi_t(M) = M$, $t > 0$.*

Definition B.0.7 (cf. [35], p. 423)**.** *A compact invariant subset M of $Y \subseteq X$ is called an* isolated compact invariant set in Y *if there is an open subset U of X such that there is no invariant set $\tilde{M}$ with $M \subseteq \tilde{M} \subseteq U \cap Y$ except M. U is called an* isolating neighborhood *of M.*

Definition B.0.8 (cf. [35], p. 425)**.** *A finite covering $M = \cup_{k=1}^{m} M_k$ in X_2 is called* isolated *if the sets M_k are pairwise disjoint subsets of X_2, which are isolated compact invariant sets in X.*

Definition B.0.9 (cf. [35], p. 425)**.** *A set $M \subset X_2$ is said to be* chained *(in X_2) to another (not necessarily different) set $N \subset X_2$, symbolically $M \mapsto N$, if there is some $y \in X_2$, $y \notin M \cup N$, and a full orbit through y in X_2 whose $\alpha-$limit set is contained in M and whose $\omega-$limit set is contained in N.*

Definition B.0.10 (cf. [35], p. 425)**.** *A finite covering $M = \cup_{k=1}^{m} M_k$ is called* cyclic *if, after possible renumbering, $M_1 \mapsto M_1$ or $M_1 \mapsto M_2 \mapsto \cdots \mapsto M_k \mapsto M_1$ for some $k \in \{2, \ldots, m\}$. M is called an* acyclic covering *otherwise.*

Definition B.0.11. *From the work described in [35] we define the following compactness conditions.*

($\mathbf{C}_{4.1}$) *There exists $\delta > 0$ with the following properties:*

- *If $x \in X$ such that $d(\Phi_t(x), X_2) < \delta$ for all $t \geq 0$, then the forward orbit of x has compact closure in X.*
- *If x_n is a sequence in X satisfying*

$$\limsup_{t\to\infty} d(\Phi_t(x_n), X_2) \to 0\,, \qquad n \to \infty$$

then $\bigcup_{n\in\mathbb{N}} \omega(x_n)$ has compact closure.

$(\mathbf{C}_{4.2})$ *There exists $\delta > 0$ and a subset B of X with the following properties:*

- *If $x \in X$ and $d(x, X_2) < \delta$, then $d(\Phi_t(x), B) \to 0$, $t \to \infty$.*
- *The intersection $B \cap B_\delta(X_2)$ of B with the $\delta-$neighborhood of X_2, $B_\delta(X_2) := \{x \in X \mid d(x, X_2) < \delta\}$ has compact closure.*

Theorem B.0.3 (cf. [35], p. 426)**.** *Let X_1 be open in X and forward invariant under Φ. Further, let the compactness assumption $(\mathbf{C}_{4.2})$ hold. Assume that Ω_2,*

$$\Omega_2 = \bigcup_{y \in Y_2} \omega(y)\,, \qquad Y_2 = \{x \in X_2 \mid \Phi_t(x) \in X_2 \ \forall t > 0\}\,,$$

has an acyclic isolated covering $M = \cup_{k=1}^{m} M_k$ such that each part M_k of M is a weak repeller for X_1. Then X_2 is a uniform strong repeller for X_1.

Theorem B.0.4 (cf. [32])**.** *Let the following conditions hold for the system (A.1)*

- *The system is dissipative: For each $x \in D$, $\mathcal{O}^+(x,t)$ has compact closure in D. Moreover, there exists a compact subset B of D with the property that for each $x \in D$ there exists $T(x) > 0$ such that $x(t,x) \in B$ for $t \geq T(x)$.*
- *The system is competitive and irreducible in D.*
- *D is an open, convex subset of $\mathbb{R}^3$*
- *D contains a unique equilibrium point x^* and $\det(Df(x^*)) < 0$.*
- *f is analytic in D.*

If x^* is unstable then there is at least one but no more than finitely many periodic orbits for (A.1) and at least one of these is orbitally asymptotically stable.

INDEX