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Escola de Matemática Aplicada

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Fish farming and malaria:
A model of mosquito population control

Rio de Janeiro
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A model of mosquito population control**

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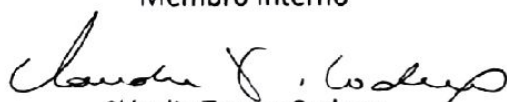
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A minha mãe, por me ensinar o valor do esforço. A meu pai, por me ensinar o valor da curiosidade. A minha orientadora, pelos diversos ensinamentos, cobrança, atenção e paciência. A diversos amigos e amigas que me apoiaram, e já não aguentam mais ouvir sobre mosquitos, malária e equações diferenciais.

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‘With four parameters I can fit an elephant, and with five I can make him wiggle his trunk.’

John von Neumann

Resumo

Estudamos dois problemas matemáticos distintos, mas relacionados, alcançando resultados teóricos e aplicados. Estudamos o problema da malária na região do Alto Juruá, no Acre, propondo um sistema de equações diferenciais (incluindo uma equação impulsiva) como modelo epidemiológico levando em conta a relação entre a falta de manutenção dos tanques de piscicultura e a malária. Para isso, foi organizada uma expedição de campo acompanhando uma equipe da Fundação Oswaldo Cruz, revisaram-se artigos sobre a região e fez-se uma revisão histórica da modelagem matemática da malária. Descrevemos o nosso modelo, integrando a dinâmica vector-hospedeira da malária, o ciclo de vida de mosquitos *Anopheles darlingi* e a limpeza e crescimento da vegetação de borda em tanques de piscicultura. Teoremas sobre o comportamento assintótico do sistema foram deduzidos, e o sistema foi numericamente simulado e analisado. Nossa análise argumenta em favor de empregar campanhas de limpeza de tanques de peixes e campanhas educativas como medidas de controle da malária. Durante a análise, percebeu-se que nosso modelo não satisfazia as condições para aplicar o Teorema de Smith (H. L. Smith. Cooperative systems of differential equations with concave non-linearities. *Nonlinear Analysis: Theory, Methods Applications*, 1986) sobre o comportamento assintótico de equações diferenciais cooperativas e côncavas. Mais especificamente, o teorema assume a continuidade de tempo da função dinâmica, que nosso modelo não satisfaz. A fim de contornar este problema, o background teórico do teorema foi estudado, e o resultado foi estendido para funções com dinâmica apenas mensurável no tempo.

Palavras-chave: malária, epidemiologia, sistemas dinâmicos.

Abstract

We studied two distinct but related mathematical problems, achieving both theoretical and applied results. We studied the problem of malaria in the region of Alto Juruá, Acre, proposing a system of differential equations (including an impulsive equation) as an epidemiological model taking into account the relationship between the lack of maintenance of fish farming tanks and malaria. In order to do that, a field expedition was put together with a team from Oswaldo Cruz Foundation, articles surveying the region were reviewed and a historical review of mathematical modelling of malaria was made. We describe our model, integrating the vector-host dynamics of malaria, the life cycle of *Anopheles darlingi* mosquitoes and fish tanks border vegetation growth and cleaning. Theorems about the asymptotic behaviour of the system were derived, and the system was numerically simulated and analyzed. Our analysis argues in favor of employing fish tank cleaning and educational campaigns as measures of malaria control. During the analysis, it was noticed that our model did not satisfy the conditions to apply Smith's Theorem (H. L. Smith. Cooperative systems of differential equations with concave non-linearities. *Nonlinear Analysis: Theory, Methods Applications*, 1986) concerning the asymptotic behaviour of cooperative, concave differential equations. More specifically, the theorem assumes time continuity of the right-hand side function, which our model did not satisfy. In order to circumvent this problem, the theoretical background of the theorem was studied, and the result was extended to functions with merely time-measurable right-hand side.

Keywords: malaria, epidemiology, dynamic systems.

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Chapter 1

Introduction

The goal of this research is **modelling the impact of fish farming ponds' cleaning frequency in the proportion of population infected with malaria in the Alto Juruá region**, giving conditions for the disease to either be eradicated or to stay endemic. In order to achieve this goal, we propose a model which was inspired by [DT16, RHB⁺15, dRCD⁺15] and will be studied in depth in Chapter 3.

Qualitative results about the asymptotic behaviour of the system were derived. Our main results are Theorem 3.2 and Theorem 3.3. Both theorems provide a sufficient condition in terms of the parameters of the system for determining its asymptotic behaviour. Theorem 3.2 concerns the total mosquito population, with respect to its convergence to a periodic solution or convergence to 0. Conversely, Theorem 3.3 concerns the proportion of population infected with malaria, again with respect to its convergence to a periodic solution or to 0.

Another important result, of a more Theoretical nature, is Theorem 2.22. This theorem concerns a class of cooperative differential equations with time-measurable right-hand side. This theorem provides the abstract backbone of both Theorem 3.2 and Theorem 3.3.

1.1 Mathematical Modelling of Diseases

In this section we expose some of the background information on malaria and modelling of biological phenomena.

Models are mathematical abstractions whose behaviour in some way is similar to some, for instance, physical, economical or biological system¹. The use of mathematical concepts to describe the propagation of diseases can show the likely outcome of an epidemic, or can be used to advise public policy. The structure of the model is associated with the simplifying assumptions made. It is worth noting that models cannot, and should not strive for, reproduce the whole complexity of phenomena. Adequate modelling is an equilibrium between mathematical tractability, attempt at verisimilitude, and the intent of the author. The assumptions made in order to make the model are the cornerstone of this interaction. As with maps, the defining characteristic of models are their usefulness.

We can analyze the procedure of creating models through 4 stages, adapted from [Hes86, Ch 9]:

1. *The Description Stage*, in which some phenomena are chosen to be modelled. The theory which is the backbone of the model depends on the kinds of phenomena to be modelled.
2. *The Formulation Stage*, in which the theory is translated to mathematical equations, which form the basis of the model.
3. *The Ramification Stage*, where the properties of those equations are studied through mathematical analysis;
4. *The Validation Stage*, which is concerned with comparing the results of the ramification stage with the phenomena the model aimed to describe. The comparison can go from a simple check on the reasonableness of numerical results to an experimental test.

¹The relation between a model and its object is similar to the relation between a metaphor and its object. A model can't be true, but can be useful to explain some interaction or make a comparison.

In our work, for example, the description stage consists of the current chapter, with its exposition of the context of the phenomenon to be modelled. The formulation stage consists in Section 3.3, in which the actual equations of the model are presented. The ramification stage follows with Section 3.4, where we analyze the properties of our equations. Finally, we validate the model in Section 3.5, with numerical simulation of the equations. It is important to note that simulations are in no way substitutes for empirical validation, they merely give us reason to believe the model to be *internally* consistent.

One prevalent kind of model in mathematical modelling of diseases, or mathematical epidemiology is the compartmental model. A *compartmental model* consists in

- a state space $\Omega \subset \mathbb{R}^n$ in which every axis is associated with a subset or compartment of the population.
- a transfer function $f : \mathbb{R} \times \Omega \mapsto \mathbb{R}^n$, which determines the evolution of the system at time t and state $x(t)$ through the differential equation $\dot{x} = f(t, x(t))$.

The essential assumption of a compartmental model is that individuals inside a same compartment are indistinguishable with regards to the disease.

The history of mathematical epidemiology, can be traced back to the beginning of the 20th century. Microbiological research had recently revealed the mechanisms by which infectious diseases spread among populations, notably in the work by Pasteur and Koch. This, together with statistical developments with regard to epidemiological data, proved to be fertile ground to the development of mathematical epidemiology. The *Mass Action Principle*², which proposes that the rate of spread of a disease is proportional to the product of the density of susceptible individuals times the density of infectious individuals, was the first important theoretical contribution. This idea, due to Hammer, is central to most models of disease dynamics [And13].

Hammer, however, formulated the Mass Action Principle in a discrete time model. It was Ronald Ross (credited with discovering the transmission of malaria by mosquitoes) who

²An idea and name probably borrowed from the theory of chemical reactions.

introduced the principle into a continuous-time model, in his work on malaria dynamics [And13, Ros11]. He proposed his model to support the claim that malaria could be eradicated through reduction of the mosquito population [Bac11]. Ross divided both the human and the mosquito population into two compartments: the *susceptible* and the *infected*. *Infected* humans return to the *susceptible* compartment, giving the model the SIS-SI name. Both populations are assumed constant. We denote the human population as N_h , susceptible humans as S and infected as I . As for the mosquitoes, we denote the whole population as N_m , susceptibles as M_S and infected as M_I .

$$\begin{cases} \dot{S} &= \kappa I - \beta_{vh} \frac{M_I}{N_m} \frac{S}{N_h}, \\ \dot{I} &= \beta_{vh} \frac{M_I}{N_m} \frac{S}{N_h} - \kappa I, \\ \dot{M}_S &= \mu_M M_I - \beta_{hv} \frac{M_S}{N_m} \frac{I}{N_h}, \\ \dot{M}_I &= \beta_{hv} \frac{M_S}{N_m} \frac{I}{N_h} - \mu_M M_I. \end{cases}$$

As $S + I = N_h$, $M_S + M_I = N_m$, and considering both populations normalized to 1, we can simplify the model to the following system of differential equations

$$\begin{cases} \dot{I} &= \beta_{vh} M_I (1 - I) - \kappa I, \\ \dot{M}_I &= \beta_{hv} I (1 - M_I) - \mu_M M_I, \end{cases} \quad (S_0)$$

where I is the *infected human* population, M_I is the *infected mosquito* population, the *susceptible human* population is represented through $(1 - I)$ and the *susceptible mosquito* population through $(1 - M_I)$ [MSS11]. The biological parameters are: β_{vh} and β_{hv} , the vector to host and host to vector transmission rates, respectively; κ , the recovery rate for humans infected with malaria; and μ_M , the mortality rate for mosquitoes. Figure 1.1 shows the compartmental diagram for System (S_0) .

Ross' mathematical models studied malaria transmission reduction through control of its vector. There are two possibilities for this kind of control: reduction of mosquito population, or separation of the mosquitoes from the human host. Through his model, Ross concluded that it was not necessary to completely eliminate the mosquito population to eradicate malaria. In fact, below a critical density of mosquitoes, infection cannot be sustained [M⁺57]. This was

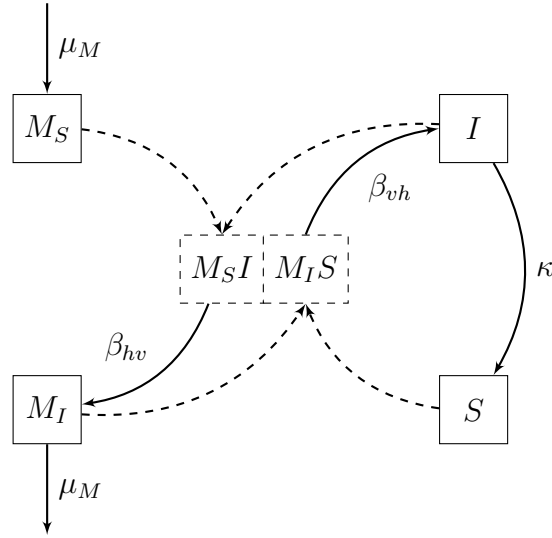


Figure 1.1: Compartmental diagram for Malaria dynamics in System (S_0). With both populations normalized to 1, we can represent S as $1 - I$ and M_S as M_I and drop two equations.

the reason for the World Health Organization to support the use of insecticides in the control of malaria [SLC⁺06].

Following this, came the work of Dietz, Molineaux and Thomas, in which different intervention strategies were compared. Their investigation was framed within the context of the Garki project [MGO⁺80], a research led by the World Health Organization and the Nigerian government that collected data on the epidemiology and control of malaria in northern Nigeria. To this date, the wealth of data collected in the Garki project has not been surpassed. Dietz et al. [DMT74] included the effect of hosts' immune response on transmission rates into their model. This effect is crucial for malaria control, with regards to changing the equilibrium between host and parasite population, specially in regions where eradication is not feasible. Their model was the first to represent the quantitative relationship involving molecular (immune response), microscopic (parasites) and population (hosts) level phenomena as a single differential equations system.

Some other findings of the Garki project, summarized in [MGO⁺80], were the degree to which vector genetic diversity affects control programs based on domiciliary spraying, and the possible loss of parasitological immunity in the aftermath of mass drug administrations. This latter observation was made when the prevalence of *P. falciparum* increased in the first wet season following the intervention. Due to this, the authors advised against the prolonged use

of these control measures, such as in Garki.

Motivated by attempts at the development of a malaria vaccine in the early 80's, epidemiological modelling of malaria started to consider the biological mechanisms associated with different control strategies, changing intervention design and measurement of efficacy. The mechanisms considered were infection blocking, disease modification and transmission blocking, among others. Each mechanism corresponds to a stage in the parasite life cycle, mirroring the search for a viable vaccine target mechanism. A vaccine model that encompass all three mechanisms was proposed by [Ned85, HSS89], based on Dietz' model [DMT74].

Another development in malaria research was the introduction of heterogeneous mosquito behaviour. Kingsolver [Kin87] discriminated in his model mosquito behaviour towards malaria-infected and non-infected humans. As it seems, humans infected with malaria attract more mosquitoes than non-infected humans. This changes the dynamics of the disease and, consequently, modifies the equilibria, showing the importance of taking biological phenomena into consideration.

Current research started to take into account genetic phenomena, such as: genetic suitability as vector, *Plasmodium* and *Anopheles* evolution, introduction of genetically modified vectors or parasites into the environment. Studying the life cycle of the parasite inside the vector shows the existence of several vector traits that are potential barriers to pathogen development [BJC00]. Knowing which genes control those traits provides the opportunity to develop new control strategies. With regards to evolution, understanding the selective pressures that affect both parasite and vector can help to explain some undesirable consequences of large scale interventions, such as resistance to drugs or pesticides [CF03, SLC⁺06]. Therefore, this knowledge can lead to better design of control strategies. In parallel to this, techniques for genetic manipulation of mosquitoes and parasites open the possibility of controlling the disease through introduction of genetically altered vectors and pathogens in the environment [GS04, MLKM05, SAHTG03]. This idea is subject to heated debate regarding the evolutionary possibilities and constraints, the virulence trajectory of the parasite, the impact on the environment and the actual impact on disease morbidity and spread [Cur94, Spi94, RK94, BK02, BK03].

Some macroscopic phenomena that affect malaria dynamics are spatial heterogeneity, and social and economic incentives. Differences in regional environment's potential for malaria provides a spatial dimension to modelling, which affects phenomena at great scale [LCMS03]. This spatial heterogeneity promotes permanence in host-parasite systems, forming "islands" where the disease persists. Malaria in Brazil is an example of this, as the disease is mostly restricted to the amazon river basin, and even in that region, highly focused in a small number of municipalities [RHB⁺15, dRCD⁺15]. Finally, social and economics incentives are included in the model due to the importance of population-wide measures in the control of vector-based diseases. Such is the example of dengue fever control through the removal of potential *Aedes aegypti* larvae breeding sites and malaria control through fish farming tanks management, which is the subject matter of this thesis.

1.2 Cooperative Dynamical Systems

Differential equations are equations which relate the derivative $\dot{x}(t)$ to the value $x(t)$ of some function, in an equation of form

$$\dot{x}(t) = f(t, x(t)) \quad (1.1)$$

where f is a given function. The use of differential equations is widespread in science, with applications ranging from physics and engineering to economy or biology. When t represents time, the differential equation represents the time evolution of some system, which is called a *dynamical system*. System (S_0) is an example of a dynamical system.

A dynamical system given by a differential equation is characterized by:

- a set X , which is the state space of the equation,
- a function $f : \mathbb{R} \times X \mapsto X$, which determines the behaviour of the system for a given time $t \in \mathbb{R}$ and a given state $x \in X$.

We can observe this in Figure 1.2. In this graph, a particular case of system (S_0) is considered. The dynamics are indicated with blue arrows. The state space is $[0, 1]^2$. Three trajectories

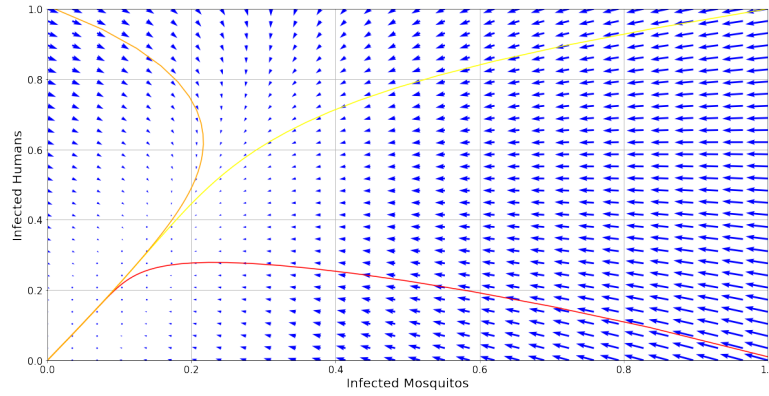


Figure 1.2: Illustration of the behaviour in a dynamical system.

are plotted for different initial conditions, in red, yellow and orange, respectively. Note that at every point the vector field is tangent to the trajectory.

An introduction to the theory of dynamical systems, with many applications can be found in e.g. [Str18, HSD12], and references therein. More in-depth study of ordinary differential equations can be found in [CL55, Har02], and for the Carathéodory solutions that we consider here, we refer to the introductory chapter of [BP07].

During Chapter 2, we concern ourselves with differential equations governed by a *monotone, concave, cooperative* function f , which is *measurable* w.r.t. t and *Lipschitz continuous* w.r.t. x . We conclude Chapter 2 with Theorem 2.22, giving an algebraic criteria for the asymptotic behaviour of this kind of system. This development is important as the model for malaria control that we propose (introduced in next section, and analyzed in Chapter 3) has these properties. The theory of concave, cooperative differential equations systems, continuous in both x and t was developed in [Smi86, Jif90]. Our main result is an extension of that of [Jif90] for dynamics f that are merely measurable w.r.t. time.

Two well-known and widely used threshold values from the literature on mathematical modelling of biological phenomena are the *basic offspring number* and the *basic reproduction number*. Both are significant because their value determines the asymptotic behaviour of a biological model. The *basic offspring number* \mathcal{N} is a value derived from the parameters which determines the growth of a population, and is interpreted as the average number of offspring

that an individual produces during its lifetime[YMG⁺09, FG14]. When $\mathcal{N} < 1$, the population tends to go extinct, while for $\mathcal{N} \geq 1$ the population persists (i.e. it is viable). The *basic reproduction number* \mathcal{R}_0 for a disease is interpreted as the average amount of new infections an infected person causes if introduced in a completely susceptible population. In standard compartmental models (see e.g. [VdDW02]), when $\mathcal{R}_0 > 1$, it is possible for the disease to become endemic. Conversely, when $\mathcal{R}_0 < 1$ the disease goes extinct, with the infected state variables converging to zero. Their mathematical definitions are given in the next section.

1.3 Methodology

This work ranges from the application of mathematical theory on the real world problem of endemic malaria in the Alto Juruá region to the theoretical problem of extending a theorem to a larger class of functions.

In order to model the situation in Alto Juruá, tentative model structures were proposed through discussions, with their form inspired by [MSS11, DT16]. The local phenomena to be included in the model were selected from [dRCD⁺15, RHB⁺15]. The model evolved through trial-and-error, by balancing the range of phenomena incorporated in it and its mathematical tractability. Our system includes two different kinds of carrying capacities for larvae, representing two classes of fish farming ponds: those with larvae predatory fish and those without. Both carrying capacities depend on the percentage of borders covered by vegetation, which is modelled to obey a differential equation containing jumps or, more precisely called, 'impulses'. Our final model is given by the following system:

$$\left\{ \begin{array}{lcl} \dot{V}(t) & = & r(1 - V); \text{ for } t \neq n\tau; \\ \Delta V(t) & = & -\gamma(H(t))V(t), \text{ for } t = n\tau, \ n \in \mathbb{N}; \\ \dot{M}_S & = & \nu(L_w + L_p) - \beta_{hv}IM_S - \mu_M M_S; \\ \dot{M}_I & = & \beta_{hv}IM_S - \mu_M M_I; \\ \dot{L}_p & = & \alpha \frac{K_p(V)}{K_w(V) + K_p(V)}(M_I + M_S) \left(1 - \frac{L_p}{K_p(V)}\right) - (\nu + \mu_L + \mu_p(1 - V))L_p; \\ \dot{L}_w & = & \alpha \frac{K_w(V)}{K_w(V) + K_p(V)}(M_I + M_S) \left(1 - \frac{L_w}{K_w(V)}\right) - (\nu + \mu_L)L_w; \\ \dot{S} & = & -\beta_{vh}SM_I + \kappa I; \\ \dot{I} & = & \beta_{vh}SM_I - \kappa I. \end{array} \right. \quad (S_3)$$

The system variables are vegetation V , susceptible mosquito population M_S , infected mosquito population M_I , larvae population on ponds with predatory fish L_p , larvae population on ponds without predatory fish L_w , proportion of susceptible population S , and proportion of infected I . Biological meaning of the parameters is given in Table 1.1.

Our system is a composition of a population model for mosquitoes and an epidemiological model for malaria. For System S_3 , the basic offspring number for the mosquito population assumes the form

$$\mathcal{N} \doteq \frac{\alpha\nu}{\mu_M(\nu + \mu_L)}, \quad (1.2)$$

while the basic reproduction number of malaria is given by

$$\mathcal{R}_0 \doteq \frac{\beta_{hv}\beta_{vh}M}{\kappa\mu_M}. \quad (1.3)$$

During the course of writing this work, a visit was made to the Alto Juruá region, together with a team from Oswaldo Cruz Foundation. The author and the thesis advisor accompanied the team through group activities about the problem of malaria, with local teachers and fish farmers. During the activities, estimates of the numerical values of some parameters were made

Parameter	Biological Meaning
K	Aquatic stage carrying capacity of the environment.
K_p	Aquatic stage carrying capacity of fishing ponds with predatory fish, as a function of border vegetation.
K_w	Aquatic stage carrying capacity of fishing ponds without predatory fish, as a function of border vegetation.
α	Mean number of eggs per mosquito which become larvae.
ν	Aquatic to adult transition rate.
μ_L	Aquatic stage basic mortality rate.
μ_p	Added mortality due to predatory fish.
μ_M	Adult mosquito mortality rate.
κ	Recovery rate for infected individuals.
β_{vh}	Mosquito to human infection rate.
β_{hv}	Human to mosquito infection rate.
r	Rate of growth of vegetation.
H	Proportion of population cleaning the vegetation as function of time.
γ	Proportion of vegetation removed as function of H .

Table 1.1: Biological meaning of the parameters.

through interviews and collective activities with the fish farmers. This visit helped to improve the form of the model with the first-hand experience of the situation in Alto Juruá, and the exchange of ideas with the Oswaldo Cruz Foundation research team. The visit also brought to mind the importance of this work, due to the impact the disease has in the population, and the somewhat controversial nature of the relation between fish farming tanks and malaria to local politics.

Numerical values for parameters of the system were taken from a review of the literature, from works such as [dRCD⁺15, RHB⁺15, AFG12, BHA11, And13, MSS11, Ros11, Kam12], and, as already mentioned above, from estimates taken during the field visit. Numerical experiments were implemented in Python using consumer grade computing equipment. The computing language was chosen due to convenience, as the language has well-known numerical and plotting libraries such as NumPy and Matplotlib. A computation notebook with the code used can be

found in the url https://github.com/fjpAntunes/NB_Malaria_Acre

For the theoretical development leading to Theorem 2.22, Smith and Jifa's article were studied in depth. By reproducing the proofs step by step, it was possible to determine at which point the assumption of continuity was necessary. As it happens, it was necessary to prove existence and uniqueness of solutions of initial value problems. Therefore, using Carathéodory's existence theorem, it was possible to extend the theorem to time measurable functions.

1.3.1 Organization of the Thesis

The following work is divided in 4 chapters. The first one is this introduction. Chapter 2 is dedicated to the study of cooperative systems with concave nonlinearities, Chapter 3 to the mathematical modelling and analysis of malaria in Acre. Chapter 4 concludes the work.

The goal of Chapter 2 is to prove Theorem 2.22 that yields the convergence result included in Chapter 3. During Chapter 2, we concern ourselves with differential equations with a *periodic, monotone, concave, cooperative* dynamics f that is *measurable* w.r.t. t and *Lipschitz continuous* w.r.t. x (The meaning of each term will be given in the introduction of Chapter 2). Theorem 2.22 provides a sufficient condition in terms of the principal minors of the Jacobian matrix at 0 of the function f for the convergence of the trajectories either to a periodic orbit (with strictly positive components) or to zero. These conditions are applied in the qualitative analysis of the asymptotic behaviour of our malaria model, given in Chapter 3.

Theorem 2.22 is an extension to a larger domain of functions of a result due to [Jif90] that was applied in [DT16]. Studying [DT16], it was noted that this result does not apply to differential equations systems with right-hand side that are merely measurable with respect to time. A careful study of [Jif90, Smi86] led to the structure of Chapter 2. Basic properties needed for the proof of Theorem 2.22, such as existence and uniqueness of solutions for differential equations with the desired kind of f are derived following [BP07, Ch 2]. Some topics which play a key part in the proof were studied in more depth as e.g. Kamke's Theorem in [Kra68, Cop65], and Perron-Frobenius theory in [BP94, BG59].

Chapter 2

Cooperative Systems with Time-measurable Dynamics and Concave Nonlinearities: Well-posedness and Asymptotic Behaviour

2.1 Theoretical Framework

In this chapter, we study the limiting behaviour of periodic, cooperative, concave systems of the form

$$\dot{x} = F(t, x), \tag{2.1}$$

where $F : \mathbb{R} \times \mathbb{R}_+^n \rightarrow \mathbb{R}_+^n$ is a *measurable* function with respect to t , and continuous with respect to x . The main result of this chapter is Theorem 2.22, which concerns algebraic criteria for determining the asymptotic behaviour of systems such as (2.1). Our contribution is an extension of a result given in [Jif90], but for dynamics F that are merely measurable with respect to t , instead of continuous. This extension is then applied to the result in Chapter 3 to study the behaviour of System (S_3), as its right-hand side is piecewise continuous in t . Cooperative

systems are of special concern in mathematical biology, as they are used to model the dynamics of species with multiple life-cycle stages. In order to prove Theorem 2.22, this chapter follows the structure of works such as [Smi86, Jif90]. The overall structure of the proof and the chapter is as follows: first, we recall some results regarding existence and uniqueness of Carathéodory solutions, as well as some results about continuity and differentiability of solutions w.r.t. initial conditions. This is done in Section 2.2. Afterwards, in Section 2.3 conditions for convergence of iterated applications of a convenient class of operators are given. We finish the section by transforming these conditions into criteria over the principal minors of the Jacobian matrix of F . Section 2.4 concludes the chapter, and states Theorem 2.22, which is the main result of this chapter to be later applied in Chapter 3.

2.1.1 Literature Review

The theory of concave, cooperative differential equations with *continuous* right hand side is developed in a series of papers due to Hirsch, Smith and Jifa [Hir85, Smi86, Jif90]. Hirsch's [Hir85] main result concerns autonomous cooperative systems and states that for this kind of system there is no attracting non-constant periodic solution; and, if the system is also irreducible¹, then its flow approaches the equilibrium set for almost every starting point x .

In Smith [Smi86], a criteria for the asymptotic behaviour of the non-autonomous system of the form $\dot{x} = F(x, t)$, for a continuous with respect to both t and x , periodic in t , cooperative and concave function F is developed. Smith's result states that the asymptotic behaviour is determined by the linear stability of the trivial solution $x(t) \equiv 0$. If the trivial solution is linearly stable, then it is globally asymptotically attractive. Conversely, if it is unstable, then there exists a periodic solution which is globally asymptotically attractive.

In [Jif90], Jifa weakens the irreducibility condition in Smith's result from the irreducibility of the Jacobian for every (t, x) in $\mathbb{R} \times \mathbb{R}_+^n$ to the irreducibility at $(t, 0)$ for any $t \in \mathbb{R}$, and gives a sufficient algebraic condition involving the principal minors of the Jacobian matrices for global

¹ A system is *irreducible* if the Jacobian matrix of F cannot be transformed by permutation of rows and columns into a block upper triangular matrix.

asymptotic convergence to 0, or for global asymptotic convergence to some periodic orbit.

Under appropriate regularity assumptions, we can still prove existence and uniqueness of Carathéodory solutions, as well as differentiability with respect to the initial conditions. [CL55]. These properties will be enough to extend the results of Smith and Jifa to systems such as (2.1).

2.1.2 Definitions and Preliminary Results

In this section, we introduce some notation and preliminary results which will be used throughout the chapter. We will make use of the following notation: if $x, y \in \mathbb{R}^n$, we write $x < y$ and $x \leq y$ if the inequalities hold component-wise. If x and y are $n \times n$ matrices, then the inequalities should hold entry-wise. We use $x \lneq y$ if $x \leq y$ and $x \neq y$, this is, when the inequality is strict for at least one component (or entry). If $x < y$, we define $[x, y] := \{z : x \leq z \leq y\}$, $(x, y] := \{z : x < z \leq y\}$ and $(x, y) = \{z : x < z < y\}$.

Let Ω be an open set in $\mathbb{R} \times \mathbb{R}^n$. Our objective is to study the asymptotic behaviour of solutions to *concave, cooperative, irreducible* systems such as

$$\dot{x} = F(t, x), \tag{2.2}$$

where $F: \Omega \rightarrow \mathbb{R}^n$ is differentiable w.r.t. x , measurable and τ -periodic w.r.t. the variable t .

In equation (2.2), F is called *concave* if $0 < x < y$ implies

$$\partial_x F(t, x) \succeq \partial_x F(t, y),$$

where $\partial_x F(t, x)$ denotes the Jacobian matrix of F with respect to x at time t . Conversely, the system is called *cooperative* if

$$\frac{\partial F_i}{\partial x_j}(t, x) \geq 0,$$

for $i \neq j$, for $(t, x) \in \Omega$. This is equivalent to saying that $\partial_x F(t, x)$ has non-negative off-diagonal terms.² Informally, being *cooperative* means that an increase in any variable does not imply a

² Analogously, an $n \times n$ -matrix A is *cooperative* if each off-diagonal term is nonnegative.

slower growth in other variables, and may even imply faster growth, while being *concave* means that the greater the variable, the less its increase accelerates growth rate.

A *Cauchy problem* (or initial value problem) is a differential equation such as (2.2) equipped with an initial condition (t_0, x_0) . By a *Carathéodory solution* to a Cauchy problem, we mean an absolutely continuous function $t \mapsto \mathbf{x}(t, t_0, x_0)$ defined on some interval $[t_0, t_1]$ which satisfies (2.2) almost everywhere, and such that $\mathbf{x}(t_0, t_0, x_0) = x_0$. We may write $\mathbf{x}(t)$ if both t_0 and x_0 are implicit from the context.

In the following development, we employ the mapping

$$T : \mathbb{R}^n \mapsto \mathbb{R}^n, \quad T(x_0) := \mathbf{x}(t, t_0, x_0), \quad (2.3)$$

for a given $t > t_0$. T is called a *Poincaré Map* for (2.2). We will delineate conditions under which this mapping is well defined, and conditions under which this mapping is differentiable. Following that, we will analyze the convergence of $\lim_{n \rightarrow \infty} T^n(x_0)$ for x_0 in some given interval $[0, p]$, and employ these results to the study of solutions for system equation (2.2).

For a linear, τ -periodic system, we call *Floquet multipliers* the eigenvalues of the Poincaré map for $t = \tau$ [Kra68].

For the mapping T in (2.3) to be well-defined, we require that, for each x_0 there is a unique $T(x_0)$. This occurs if solutions for (2.2) are unique given an initial condition, which is the result of Theorem 2.3. Throughout the chapter, we assume the following regularity conditions.

Basic Assumptions: $F : \Omega \mapsto \mathbb{R}^n$ satisfies the following conditions:

$$\begin{cases} t \mapsto F(t, x) \text{ defined on } \Omega_x = \{t : (t, x) \in \Omega\} \text{ is measurable } \forall x, \\ x \mapsto F(t, x) \text{ defined on } \Omega_t = \{x : (t, x) \in \Omega\} \text{ is continuous for a.e. } t. \end{cases} \quad (\text{A})$$

and, for any compact set $K \subset \Omega$, there exist positive constants C_K, L_K such that:

$$\begin{cases} |F(t, x)| \leq C_k, \\ |F(t, x) - F(t, y)| \leq L_k |x - y|, \end{cases} \quad \text{for all } (t, x), (t, y) \in K. \quad (\text{B})$$

Two notions that will be useful are *forward invariance* and *global asymptotic attractiveness*. They are defined as follows. Let $g : \Omega \mapsto \mathbb{R}^n$, and consider the Cauchy problem

$$\dot{x}(t) = g(x(t)), \quad x(t_0) = x_0 \quad (2.4)$$

Definition 2.1 (Forward invariant set). *If a set $\mathcal{K} \subset \mathbb{R}^n$ is such that for every $x_0 \in \mathcal{K}$, the solution to the Cauchy problem (2.4) with $x(t_0) = x_0$ has $x(t) \in \mathcal{K}$ for every $t > t_0$ for which the solution $x(\cdot)$ is defined, then we say that \mathcal{K} is a forward invariant set for g .*

Remark. The definition means that trajectories that at some time t_0 are inside a forward invariant set remain inside that set for every $t \geq t_0$.

Definition 2.2 (Globally Asymptotic Attractive). *We say that a trajectory $\mathbf{x} : \mathbb{R} \mapsto \mathbb{R}^n$ is globally asymptotic attractive if, for every $x_0 \in \Omega$, the solution $x(\cdot)$ to (2.4) satisfies*

$$\lim_{n \rightarrow \infty} \max_{t \in [n, \infty)} |\mathbf{x}(t) - x(t)| = 0. \quad (2.5)$$

Remark. What this means informally is that after a long period of time the system follows the global asymptotic attractive solution, and the initial condition does not influence the "long term behaviour" of the system.

We say that a $n \times n$ -matrix A is *cooperative* if its off-diagonal entries are non negative, that is $a_{ij} \geq 0$, for $i \neq j$. The Jacobian matrix of a cooperative system is a cooperative matrix.

Any $k \times k$ -submatrix of A formed by deleting $n - k$ rows of A , and the corresponding $n - k$ columns is called a *principal submatrix* of A , and its determinant is called a *principal minor* of order k . If the $n - k$ removed lines and columns are the last ones, we say that the resulting

matrix is a *leading principal submatrix*, and the determinant is the *leading principal minor*.

If the retained rows and columns of A are given by

$$1 \leq i_1 < i_2 < \dots < i_k \leq n, \quad (2.6)$$

then the principal submatrix is denoted by

$$A \begin{pmatrix} i_1 & i_2 & \dots & i_k \end{pmatrix}. \quad (2.7)$$

Next we present some results from Perron-Frobenius theory of non-negative matrices which will be used later on. Let $\rho(A)$ denote the spectral radius of a matrix A , and $s(A) := \max \operatorname{Re} \lambda$, where λ runs through the eigenvalues of A .

Theorem 2.1 (Perron-Frobenius). *Let A be a cooperative matrix. Then the following assertions hold*

1. $s(A)$ is a non-negative eigenvalue of A and there exists a corresponding non-negative eigenvector. Moreover, if A is irreducible, then to $s(A)$ there corresponds a positive eigenvector.
2. If $A \leq B$ then $s(A) \leq s(B)$. Furthermore, if A is irreducible and $A \neq B$, then $s(A) < s(B)$.
3. If B is a principal submatrix of A , then $s(B) \leq s(A)$. If A is irreducible, then the inequality is strict for $k < n$.
4. $s(A) < \lambda$ if and only if all principal minors of $\lambda I - A$ are positive; this is equivalent to stating that all leading principal minors of $\lambda I - A$ are positive.
5. $s(A) < 0$ if, and only if, for a positive vector $r > 0$, there is a vector $x > 0$ such that $Ax + r = 0$
6. If λ is an eigenvalue of A , then $\lambda - 1$ is an eigenvalue of $A - I$. From the maximality of $s(A)$, it follows that $s(A) - 1 = s(A - I)$

Due to Perron-Frobenius Theorem, if $A \geq 0$, then $\rho(A) = s(A)$. Some sources for matrix theory and the theory of non-negative matrices are [BP94, BG59].

We present also *Kamke's Theorem*, which will be used throughout the chapter.

Theorem 2.2 (Kamke's Theorem). *Let $x(t)$ and $y(t)$ be solutions of*

$$\dot{x} = F(t, x)$$

and

$$\dot{y} = G(t, y)$$

respectively, where both systems are assumed to have the uniqueness of solutions property for initial value problems. Assume both $x(t)$ and $y(t)$ belong to a domain $D \subset \mathbb{R}^n$ for $[t_0, t_1]$, in which one of the two systems is cooperative and

$$F(t, z) \leq G(t, z), \quad \text{for } (t, z) \in [t_0, t_1] \times D \quad (2.8)$$

then, $x(t_0) \leq y(t_0)$ implies $x(t_1) \leq y(t_1)$. If $F = G$ and $x(t_0) < y(t_0)$, then $x(t_1) < y(t_1)$.

In-depth study of the theory behind Kamke's Theorem can be found in [Kra68, Cop65].

2.2 On Caratheódory Solutions

In this section, we recall some results which are the basic requirements for the development of our proof. We present existence and uniqueness results for Cauchy problems with right-hand side functions that are merely measurable with relation to time. Section 2.2.1 will employ these results to prove that a Poincaré map T for our desired class of functions is well-defined, continuous and differentiable.

We begin with the following theorem [Rud06, BP07, CL55].

Theorem 2.3 (Carathéodory's Existence Theorem). *Given a mapping $g: \mathbb{R} \times \Omega \rightarrow \mathbb{R}^n$ satisfying (A) and (B), consider the Cauchy problem:*

$$\dot{x} = g(t, x), \quad x(t_0) = x_0, \quad (2.9)$$

for some $(t_0, x_0) \in \Omega$. The following holds:

1. *There exists an $\epsilon > 0$ such that (2.9) has a local solution $x(\cdot)$ defined for $t \in [t_0, t_0 + \epsilon]$.*
2. *Assume that the function g is defined on the entire space $\mathbb{R} \times \mathbb{R}^n$, and there exist constants C, L such that*

$$|g(t, x)| \leq C, \quad |g(t, x) - g(t, y)| \leq L|x - y|, \quad \text{for all } (t, x), (t, y) \in \mathbb{R} \times \mathbb{R}^n. \quad (2.10)$$

Then, for every $t_1 > t_0$, the initial value problem (2.9) has a global unique solution $\mathbf{x}(\cdot, t_0, x_0)$ defined on $t \in [t_0, t_1]$. Moreover, the solution depends continuously on the initial data x_0 .

Proof. We begin by proving statement 2. In what follows, the initial condition $x_0 \in \mathbb{R}^n$ plays the role of a parameter. Let $C_+[t_0, t_1], \mathbb{R}^n$ be the space of all continuous functions from $[t_0, t_1]$ into \mathbb{R}^n with the norm:

$$\|x(\cdot)\|_+ = \max_{t_0 \leq t \leq t_1} e^{-2Lt} |x(t)|, \quad (2.11)$$

which is equivalent to the usual C^0 -norm

$$\|x(\cdot)\| = \max_{t_0 \leq t \leq t_1} |x(t)|. \quad (2.12)$$

Define the mapping $\psi: \mathbb{R}^n \times C_+[t_0, t_1], \mathbb{R}^n \rightarrow C_+[t_0, t_1], \mathbb{R}^n$ as:

$$\psi(x_0, w(\cdot))(t) = x_0 + \int_{t_0}^t g(s, w(s)) ds, \quad t \in [t_0, t_1]. \quad (2.13)$$

As g is not continuous, we need to show that the mapping $s \rightarrow g(s, w(s))$ is integrable. In order to do that, consider a sequence of piecewise constant functions $\{w_\nu\}_{\nu \geq 1}$ with:

$$w_\nu(t) = w\left(t_0 + \frac{j(t_1 - t_0)}{\nu}\right) \text{ if } t \in \left[t_0 + \frac{j(t_1 - t_0)}{\nu}, t_0 + \frac{(j+1)(t_1 - t_0)}{\nu}\right], \text{ for } j \in \{0, 1, 2, \dots, \nu-1\} \quad (2.14)$$

From assumption (A), the maps $t \rightarrow g(t, w_\nu(t))$ are all measurable. From our global assumption (2.10), we have:

$$\lim_{\nu \rightarrow \infty} |g(t, w(t)) - g(t, w_\nu(t))| \leq \lim_{\nu \rightarrow \infty} L|w(t) - w_\nu(t)| = 0, \quad (2.15)$$

which shows that the function $t \rightarrow g(t, w(t))$ is a limit of a sequence of measurable maps, hence measurable itself. As g is globally bounded by C , the integral in (2.13) is well defined, and continuous on t . Hence, ψ is well defined, and its image is contained in $C_+[t_0, t_1], \mathbb{R}^n$.

Our next step is to show that ψ is a contraction in $C_+[t_0, t_1], \mathbb{R}^n$. From the definition of the norm in $C_+[t_0, t_1], \mathbb{R}^n$, we have:

$$|w(s) - w'(s)| \leq \|w - w'\|_+ e^{2Ls} \text{ for all } s \in [t_0, t_1].$$

From the Lipschitz continuity condition in (2.10):

$$\begin{aligned} e^{-2Lt} |\psi(x_0, w)(t) - \psi(x_0, w')(t)| &= e^{-2Lt} \left| \int_{t_0}^{t_1} g(s, w(s)) - g(s, w'(s)) ds \right| \\ &\leq e^{-2Lt} \int_{t_0}^t L|w(s) - w'(s)| ds \\ &\leq e^{-2Lt} \int_{t_0}^t L e^{2Ls} e^{-2Ls} |w(s) - w'(s)| ds \\ &\leq e^{-2Lt} \int_{t_0}^t L e^{2Ls} \|w - w'\|_+ ds \\ &= \frac{(1 - e^{-2L(t-t_0)})}{2} \|w - w'\|_+ \\ &< \frac{\|w - w'\|_+}{2}, \end{aligned} \quad (2.16)$$

which holds for all $t \in [t_0, t_1]$. Therefore, it follows that

$$\|\psi(x_0, w) - \psi(x_0, w')\|_{\dagger} \leq \frac{1}{2} \|w - w'\|_{\dagger}. \quad (2.17)$$

Applying Banach's Contraction Mapping Theorem [BP07, A.1], there exists a unique continuous mapping $x_0 \mapsto \mathbf{x}(\cdot, t_0, x_0)$ which is a fixed point for ψ :

$$\mathbf{x}(t, t_0, x_0) = \psi(x_0, \mathbf{x}) = x_0 + \int_{t_0}^t g(s, \mathbf{x}(s, t_0, x_0)) ds. \quad (2.18)$$

It follows that \mathbf{x} is the solution to (2.9), proving statement 2.

Now, in order to prove 1, consider the set

$$K := \{(t, x) : |t - t_0| \leq \epsilon, |x - x_0| \leq \epsilon\}, \quad (2.19)$$

where $\epsilon > 0$ is small enough for $K \subset \Omega$. Let $h : \mathbb{R} \times \mathbb{R}^n \mapsto [0, 1]$ be a smooth function such that $h \equiv 1$ on K and $h \equiv 0$ outside some larger compact set K' such that $K \subset K' \subset \Omega$. The function

$$g^\dagger(t, x) := \begin{cases} g(t, x)h(t, x), & \text{if } (t, x) \in \Omega, \\ 0, & \text{if } (t, x) \notin \Omega, \end{cases} \quad (2.20)$$

satisfies both (A) and (B), together with (2.10), as it vanishes outside K' . By statement 2, there exists a solution $x(\cdot)$ to the Cauchy problem

$$\dot{x}(t) = g^\dagger(t, x(t)), \quad x(t_0) = x_0, \quad (2.21)$$

defined on an arbitraly large interval $[t_0, t_1]$.

As K is a neighborhood of (t_0, x_0) , for some small $\epsilon > 0$, the point $(t, x(t)) \in K$ for $t \in [t_0, t_0 + \epsilon]$. From (2.20), g and g^\dagger coincide inside K , which means that $x(\cdot)$ provides a solution to the original problem (2.9) restricted to the interval $[t_0, t_0 + \epsilon]$. This concludes the proof. \square

Remark. Statement 2 on Theorem 2.3 straightforwardly proves *existence* for every $t_1 > t_0$, *uniqueness* and *continuity* at the price of a restrictive global condition. Conversely, in statement 1 we know there is some time interval $[t_0, t_0 + \epsilon]$ over which a solution is defined. The rest of the current section concerns the situation in statement 1, with regards to

- conditions for the local solution to be unique, and
- how far can we extend the interval over which the solution is defined, i.e. for which $t_1 > t_0$ there is a solution $\mathbf{x}(\cdot)$ defined over $[t_0, t_1]$.

Theorem 2.4 bellow will be used to prove *uniqueness* of solutions.

Theorem 2.4 (Gronwall's lemma). *Let $z(\cdot)$ be an absolutely continuous non-negative function such that*

$$z(t_0) \leq \gamma, \quad \dot{z}(t) \leq \alpha(t)z(t) + \beta(t), \quad \text{for a.e. } t \in [t_0, t_1], \quad (2.22)$$

for some integrable functions α, β , and some constant $\gamma \geq 0$. Then for every $t \in [t_0, t_1]$, the following holds

$$z(t) \leq \gamma \exp \left(\int_{t_0}^t \alpha(s) ds \right) + \int_{t_0}^t \beta(s) \exp \left(\int_{t_0}^s \alpha(\sigma) d\sigma \right) ds. \quad (2.23)$$

Proof. Consider the absolutely continuous function

$$\psi(t) := \exp \left(- \int_{t_0}^t \alpha(s) ds \right) \left[z(t) - \int_{t_0}^t \beta(s) \exp \left(\int_s^t \alpha(\sigma) d\sigma \right) ds \right]. \quad (2.24)$$

After some calculations, its time derivative can be written as

$$\dot{\psi}(t) = \exp \left(- \int_{t_0}^t \alpha(s) ds \right) [\dot{z}(t) - \alpha(t)z(t) - \beta(t)], \quad (2.25)$$

which, by (2.22) implies $\dot{\psi}(t) \leq 0$ for almost every t . Therefore, $\psi(t) \leq \psi(t_0) = z(t_0) = \gamma$. From the definition of ψ , we get (2.23). \square

Armed with Gronwall's Lemma, we turn to Theorem 2.5.

Theorem 2.5 (Uniqueness of solutions). *Let $g : \Omega \mapsto \mathbb{R}^n$ satisfy conditions (A) and (B), as in Theorem 2.3. Let $x_1(\cdot)$ and $x_2(\cdot)$ be solutions of (2.9) defined on the intervals $[t_0, t_1], [t_0, t_2]$ respectively. If $t' = \min\{t_1, t_2\}$, then $x_1(t) = x_2(t)$ for $t \in [t_0, t']$.*

Proof. Consider the compact set

$$K := \{(t, x_1(t)), (t, x_2(t)) : t \in [t_0, t']\}, \quad (2.26)$$

From (B), there exist a Lipschitz constant L_K such that

$$|g(t, x_1(t)) - g(t, x_2(t))| = |\dot{x}_1(t) - \dot{x}_2(t)| \leq L_K |x_1(t) - x_2(t)| \quad \text{for a.e } t \in [t_0, t']. \quad (2.27)$$

Consider the function $z(t) := |x_1(t) - x_2(t)|$. Then z satisfies

$$z(t_0) = 0, \quad \dot{z}(t) \leq |\dot{x}_1(t) - \dot{x}_2(t)| \leq L_K z(t) \quad \text{for a.e } t \in [t_0, t']. \quad (2.28)$$

Applying Gronwall's Lemma 2.4 with $\alpha \equiv L_K, \beta \equiv \gamma = 0$, we have $z(t) \leq 0$ for every $t \in [t_0, t']$.

The conclusion follows. □

Remark. Theorem 2.5 concerns uniqueness *given some time interval* over which the solution is defined. The problem of how far we can extend the solution, i.e. finding the maximal time $t^* > t_0$ for which the solution is defined on $[t_0, t^*]$ is the subject of Theorem 2.6 below.

Theorem 2.6 (Maximal Solutions). *Under the hypothesis of Theorem 2.3, let $t^* > t_0$ be the supremum of all times t_1 such that (2.9) has a solution $x(\cdot)$ defined on $[t_0, t_1]$. Then, either $t^* = \infty$ or*

$$\lim_{t \rightarrow t^*_-} \left(|x(t)| + \frac{1}{d((t, x(t)), \partial\Omega)} \right) = \infty. \quad (2.29)$$

Proof. Assume $t^* < \infty$. If (2.29) does not hold, then there exists a sequence $t_n \rightarrow t^*$ and

$M, \epsilon > 0$ such that, for every $n \geq 1$,

$$|x(t_n)| \leq M, \quad d((t_n, x(t_n)), \partial\Omega) \geq \epsilon. \quad (2.30)$$

By possibly taking a subsequence, we can assume $x(t_n)$ converges to a point x_∞ , with $(t^*, x_\infty) \in \Omega$. Define

$$K := \{(t, x) : |t - t^*| \leq \rho, \quad |x - x_\infty| \leq \rho\}, \quad (2.31)$$

with $\rho > 0$ small enough for $K \subset \Omega$, and define $g^\dagger : \mathbb{R} \times \mathbb{R}^n \mapsto \mathbb{R}^n$ as in (2.20), with $g^\dagger \equiv g$ on K , and such that there exists constants $C, L \geq 1$ with

$$|g^\dagger(t, x)| \leq C, \quad |g^\dagger(t, x) - g^\dagger(t, y)| \leq L|x - y|, \quad \text{for all } t, x, y. \quad (2.32)$$

Choose $\delta > 0$ small enough, and n large enough so that

$$(2C + 1)\delta \leq \rho, \quad |x_n - x_\infty| \leq \delta, \quad t^* - t_n \leq \delta. \quad (2.33)$$

Consider the Cauchy problem

$$\dot{y}(t) = g^\dagger(t, y(t)), \quad y(t_n) = x(t_n). \quad (2.34)$$

From statement 2 of Theorem 2.3, the latter equation has a solution $y(\cdot)$ defined on $[t_n, t^* + \delta]$.

We can then extend the solution $x(\cdot)$ by setting

$$\hat{x}(t) := \begin{cases} x(t), & \text{if } t_0 \leq t \leq t_n, \\ y(t), & \text{if } t_n \leq t \leq t^* + \delta. \end{cases} \quad (2.35)$$

As $|\dot{y}(t)| \leq C$, for $t \in [t_n, t^* + \delta]$ we have

$$|y(t) - x_\infty| \leq |y(t) - y(t_n)| + |x(t_n) - x_\infty| \leq C|t - t_n| + \delta \leq 2C\delta + \delta \leq \rho. \quad (2.36)$$

This implies that, for all $t \in [t_n, t^* + \delta]$, $(t, y(t))$ is inside the compact K where g and g^\dagger are

defined to be equal. The function $\hat{x}(\cdot)$ is, therefore, a solution to (2.9) defined on a strictly larger interval $[t_0, t^* + \delta]$, contradicting the maximality of t^* and proving the theorem. \square

Remark. The statement of Theorem 2.6 implies a trichotomy. Solutions for Cauchy problems are either

- defined on the time interval $[t_0, +\infty)$,
- unbounded in some finite time interval $[t_0, t_1)$, or
- reach the boundary $\partial\Omega$ of the set Ω on which the right-hand side function is defined (This boundary can be in time or in the state space).

2.2.1 Well-Definedness and Differentiability of Poincaré Map

Recall the definition of the Poincaré map for a differential equation given in (2.3)

$$T : \mathbb{R}^n \mapsto \mathbb{R}^n, \quad T(x_0) := \mathbf{x}(\tau, t_0, x_0).$$

For the mapping T to be well-defined, we require

- that the underlying Cauchy problem have a solution *at time* τ , i.e. given x_0 there exists $T(x_0)$.
- that the solution is unique, i.e. given x_0 , $T(x_0)$ is unique.

Corollary 2.6.1 below uses the theorems of this section to prove that there exists an operator T with the desired properties.

Corollary 2.6.1 (Existence and continuity of Poincaré map). *Under the hypothesis of Theorem 2.3, assume that the differential equation $\dot{x} = g(t, x)$ admits a compact forward invariant set $\mathcal{K} \subset \mathbb{R}^n$. Then, the mapping T is well-defined and continuous.*

Proof. For a given x_0 , let $t^* > t_0$ be a given time such that (2.9) has a solution $x(\cdot)$ defined on $[t_0, t^*]$, guaranteed to exist due to statement 1. of Theorem 2.3. From condition (B), there exists some constant C such that $g(t, x) \leq C$ for every $(t, x) \in [t_0, t^*] \times \mathcal{K}$. From Theorem 2.4, $|x(t)|$ is bounded for every $t \in [t_0, t^*]$. From the compactness of $[t_0, t^*] \times \mathcal{K}$, there exists an ϵ such that $d([t_0, t^*] \times \mathcal{K}, \partial\Omega) > \epsilon$. Therefore, it follows from Theorem 2.6 that the solution $x(\cdot)$ can be extended to $t^* = \infty$. Moreover, from Theorem 2.5, the solution is unique.

Continuity with respect to x_0 follows from a similar argument to that of statement 2. of Theorem 2.3, using compactness of $[t_0, t^*] \times \mathcal{K}$ for bounded t^* and condition (B).

Therefore, for any given $\tau > t_0$, $x_0 \in \mathcal{K}$, the solution $x(\cdot)$ is unique, and the mapping $(g, t_0, x_0) \mapsto x(\cdot)$ is continuous w.r.t. x_0 , from which continuity of T follows.

□

Our next step is proving the differentiability w.r.t. the initial conditions. In order to do this, we look at the changes in the solution of the Cauchy problem under changes of the initial condition x_0 , which is the subject of the following Theorem.

Theorem 2.7 (Differentiability of the Poincaré Map). *Let $g : \Omega \rightarrow \mathbb{R}^n$ be a function satisfying both (A) and (B). Assume further that g is continuously differentiable with respect to x . Let $\mathbf{x}(t, t_0, x_0)$ be the solution to the Cauchy problem (2.9). Then, for all $t \in [t_0, t_1]$, the map $x_0 \mapsto T_t x_0 := \mathbf{x}(t, t_0, x_0)$ is continuously differentiable with respect to x_0 . Its Jacobian matrix is*

$$D_{x_0} T_t = M(t, t_0), \quad (2.37)$$

Where $M(\cdot, \cdot)$ is the fundamental matrix solution³ to the linear problem

$$\dot{v}(t) = \partial_x g(t, \mathbf{x}(t, t_0, x_0)) \cdot v(t). \quad (2.38)$$

³The *fundamental matrix* solution to a linear differential equation is a family of matrices $M(t, s)$ such that, for any ξ , the Cauchy problem

$$\dot{x} = A(t)x \quad x(s) = \xi$$

has solution $x(t) = M(t, s)\xi$

In other words, given $v_0 \in \mathbb{R}^n$ with $\|v_0\| = 1$, the limit

$$\lim_{\epsilon \rightarrow 0^+} \left| \frac{T(x_0 + \epsilon v_0) - T(x_0) - \epsilon M(t, t_0)v_0}{\epsilon} \right| \quad (2.39)$$

exists and is equal to 0.

Proof. Setting $\mathbf{x}_\epsilon(t) := \mathbf{x}(t, t_0, x_0 + \epsilon v_0)$, $\mathbf{y}_\epsilon(t) := \mathbf{x}(t, t_0, x_0) + \epsilon M(t, t_0)v_0$. Our objective is then to show that

$$\lim_{\epsilon \rightarrow 0^+} \left| \frac{\mathbf{x}_\epsilon(t) - \mathbf{y}_\epsilon(t)}{\epsilon} \right| = 0. \quad (2.40)$$

Note that $\mathbf{x}_\epsilon(\cdot)$ is the fixed point for the mapping $w \mapsto \psi(x_0 + \epsilon v_0, w)$ given by:

$$\psi(x_0 + \epsilon v_0, w(\cdot))(t) = x_0 + \epsilon v_0 + \int_{t_0}^t g(s, w(s))ds. \quad (2.41)$$

From the proof of Theorem 2.3, we know that ψ is contractive in the continuous function space with norm $\|\cdot\|_{\dagger}$. From the Contraction Mapping Theorem, it follows that

$$\frac{1}{\epsilon} \|\mathbf{x}_\epsilon - \mathbf{y}_\epsilon\|_{\dagger} \leq \frac{2}{\epsilon} \|\psi(x_0 + \epsilon v_0, \mathbf{y}_\epsilon) - \mathbf{y}_\epsilon\|_{\dagger}, \quad (2.42)$$

so it suffices to show that

$$\lim_{\epsilon \rightarrow 0^+} \sup_{t_0 \leq t \leq T} \left| \frac{1}{\epsilon} \left(x_0 + \epsilon v_0 + \int_{t_0}^t g(s, \mathbf{y}_\epsilon(s))ds - \mathbf{y}_\epsilon(t) \right) \right|, \quad (2.43)$$

As g is differentiable in x , we can write

$$g(s, \mathbf{y}_\epsilon(s)) = g(s, \mathbf{x}(s, t_0, x_0)) + \int_0^1 \partial_x g(s, \mathbf{x}(s, t_0, x_0) + \sigma \epsilon M(s, t_0)v_0) \epsilon M(s, t_0)v_0 d\sigma. \quad (2.44)$$

Remind that

$$\mathbf{x}(t, t_0, x_0) = x_0 + \int_{t_0}^t g(s, \mathbf{x}(s, t_0, x_0))ds, \quad (2.45)$$

and

$$\epsilon M(t, t_0)v_0 = \epsilon v_0 + \int_{t_0}^t \partial_x g(s, \mathbf{x}(s, t_0, x_0)) \epsilon M(s, t_0)v_0 ds, \quad (2.46)$$

giving

$$\mathbf{y}_\epsilon(t) = x_0 + \epsilon v_0 + \int_{t_0}^t g(s, \mathbf{x}(s, t_0, x_0)) ds + \int_{t_0}^t \partial_x g(s, \mathbf{x}(s, t_0, x_0)) \epsilon M(s, t_0) v_0 ds. \quad (2.47)$$

Finally, cancelling equal terms, we can write the term in (2.43) as

$$\begin{aligned} & \frac{1}{\epsilon} \left| \int_{t_0}^t \int_0^1 [\partial_x g(s, \mathbf{x}(s, t_0, x_0) + \sigma \epsilon M(s, t_0) v_0) - \sigma \partial_x g(s, \mathbf{x}(s, t_0, x_0))] \cdot \epsilon M(s, t_0) v_0 d\sigma ds \right| \\ & \leq \int_{t_0}^t \int_0^1 \|\partial_x g(s, \mathbf{x}(s, t_0, x_0) + \sigma \epsilon M(s, t_0) v_0) - \sigma \partial_x g(s, \mathbf{x}(s, t_0, x_0))\| \cdot |M(s, t_0) v_0| d\sigma ds. \end{aligned} \quad (2.48)$$

Let $K \subset \Omega$ be a compact set containing a neighborhood of the graph of \mathbf{x} , and L_K as in (B). Then $|M(s, t_0) v_0|$ is bounded by $e^{L_K(s-t_0)} v_0$. As g is in C^1 over x , the last term in the r.h.s. of (2.48) converges to zero uniformly in $[t_0, t_1]$, which shows that the limit (2.39) is 0. This completes the proof. \square

Corollary 2.6.1 and Theorem 2.7 guarantee that the operator T is continuous and differentiable, which are the regularity conditions we need for the analysis of iterated applications of the operator.

2.3 Asymptotic Behaviour

This section is concerned with the analysis of the behaviour of cooperative, concave, periodic systems when time t goes to ∞ . We are interested in determining conditions for the system to assume the following behaviour: divergence to ∞ , convergence to 0, or to some periodic solution. Theorem 2.14 will provide conditions for these situations, and show that those are the only possibilities. In order to arrive at these results, we will analyze in Subsection 2.3.1 the behaviour of iterated applications of the class of monotone, concave operators, and arrive at Theorem 2.8. Then, in Subsection 2.3.2 we will show that the Poincaré map for cooperative, concave, periodic systems belongs to this class of operators, so we can use the results of Subsection 2.3.1 to analyze our desired class of systems. Subsection 2.3.3 finishes our analysis, providing

sufficient conditions involving the principal minors for determining the asymptotic behaviour of solutions.

2.3.1 Asymptotic Behaviour of Operators

This section follows through with analysis of infinitely iterated applications of an operator $U : \mathbb{R}_+^n \mapsto \mathbb{R}_+^n$, which is monotone, concave and differentiable. The analysis will show that the limit of $U^n(x)$ as n goes to ∞ is determined by the spectral radius of $DU(0)$ (the derivative of U at 0) as stated in Theorem 2.8.

Theorem 2.8 (Discrete Dynamics Behaviour). *Let $U : \mathbb{R}_+^n \rightarrow \mathbb{R}_+^n$ be continuously differentiable in \mathbb{R}_+^n , and suppose $DU(0) = \lim_{x \rightarrow 0, x > 0} DU(x)$ exists. Assume also that:*

$$DU(0) > 0 \quad \text{and} \quad DU(x) \geq 0 \quad \text{if } x > 0 \quad (M_0)$$

and

$$DU(y) \leq DU(x) \quad \text{if } 0 < x < y. \quad (C)$$

If $U(0) = 0$, let $\lambda = \rho(DU(0))$. If $\lambda \leq 1$, then for $x \geq 0$, $U^n(x) \rightarrow 0$ as $n \rightarrow +\infty$. If $\lambda > 1$, then either $U^n(x) \rightarrow \infty$ as $n \rightarrow \infty$ for every $x \gneq 0$, or U has a unique nonzero fixed point $q > 0$, and $U^n(x) \rightarrow q$ as $n \rightarrow +\infty$, for $x \gneq 0$.

If $U(0) \neq 0$, then either $U^n(x) \rightarrow \infty$ as $n \rightarrow \infty$, or U has a unique fixed point $q > 0$, and $U^n(x) \rightarrow q$ as $n \rightarrow +\infty$ for $x \geq 0$.

Remark: For $U : [0, p] \mapsto [0, p]$, $p \in \mathbb{R}_+^n$, Theorem 2.8 would be valid, without the possibility of divergence of $U^n(x)$ to ∞ .

In order to prove Theorem 2.8, we will begin by proving four lemmas. Lemma 2.9 shows that the class of operators is order preserving over \mathbb{R}_+^n , while Lemmas 2.10 and 2.11 concern some useful inequalities. Lemmas 2.12 and 2.13 concern limiting behaviour as n goes to ∞ , and make use of Perron-Frobenius Theory. In all of them, consider $x, y \in \mathbb{R}_+^n$, and assume (M_0) and (C) are satisfied.

Lemma 2.9. *The following statements hold:*

1. *If $0 < x \preceq y$, then $U(x) \leq U(y)$.*
2. *If $0 \leq x \leq y$, then $U(x) \leq U(y)$.*

Proof. From the Fundamental Theorem of Calculus, we can write

$$U(y) - U(x) = \left[\int_0^1 DU((1-s)x + sy) ds \right] (y - x). \quad (2.49)$$

As $(1-s)x + sy > 0$, (M₀) implies that $DU((1-s)x + sy) \geq 0$ for $s \in (0, 1)$. From the latter equation, $U(y) - U(x) \geq 0$, which proves Statement 1. Statement 2. follows from Statement 1. by continuity of the operator U .

□

Lemma 2.10. *If $x > 0$, then $DU(0) \succeq DU(x)$.*

Proof. For $0 < s < \frac{1}{2}$, (C) implies that $DU(sx) \succeq DU\left(\frac{1}{2}x\right) \succeq DU(x)$. Setting $s \rightarrow 0$, the statement follows.

□

Lemma 2.11. *If $x \succeq 0$, then $U^n(x) > 0$ for $n \geq 1$.*

Proof. From Lemma 2.9, $\epsilon \rightarrow 0^+$:

$$U(x) \geq U(\epsilon x) = U(0) + \epsilon[DU(0)x + O(\epsilon)], \quad (2.50)$$

As $U(0) \in \mathbb{R}_+^n$,

$$U(x) \geq \epsilon[DU(0)x + O(\epsilon)]. \quad (2.51)$$

From (M₀) and Lemma 2.9, we have $DU(0) > 0$, so $U(x) > 0$. This implies that there exists some $\epsilon > 0$ such that $U(x) \geq \epsilon x$, so $U^2(x) \geq U(\epsilon x) > 0$. An argument by induction finishes the proof of the statement.

□

Remark. Lemma 2.11 implies that U has no non-zero fixed points on the boundary of \mathbb{R}_+^n , as for any fixed point q , we have $q = U(q) > 0$.

Lemma 2.12. *Let $q \geq 0$, $U(q) = q$, and $\rho(DU(q)) \leq 1$. Then for all $x \geq q$, $U^n(x) \rightarrow q$ as $n \rightarrow \infty$.*

Proof. As q is a fixed point, by Lemma 2.11, either $q = 0$ or $q > 0$. From (M_0) , we can assume $DU(q) \geq 0$. The proof consists on analyzing the behaviour of U on the line between q and $q + \epsilon v$, where v is an eigenvector of $DU(q)$ such that $DU(q)v = \rho(DU(q))v$ and $\epsilon > 0$. We can write

$$U(q + \epsilon v) = q + \left[\int_0^1 DU(s(q + \epsilon v) + (1-s)q) ds \right] \epsilon v. \quad (2.52)$$

From (C) , it follows that

$$U(q + \epsilon v) \preceq q + \epsilon DU(q)v = q + \epsilon \rho(DU(q))v \leq q + \epsilon v, \quad (2.53)$$

so

$$q + \epsilon v \succeq U(q + \epsilon v) \geq U^2(q + \epsilon v) \geq \dots \geq U^n(q + \epsilon v) \geq \dots \geq q. \quad (2.54)$$

It follows that $\lim_{n \rightarrow \infty} U^n(q + \epsilon v) = p_\epsilon \geq q$ exists, and $U(p_\epsilon) = p_\epsilon$ by continuity of U . We have 2 cases: $p_\epsilon = q$ or $p_\epsilon \succ q$, in which case $p_\epsilon = U(p_\epsilon) > U(q) = q$, by Lemma 2.9. We can write

$$p_\epsilon - q = \left[\int_0^1 DU(sp_\epsilon + (1-s)q) ds \right] (p_\epsilon - q). \quad (2.55)$$

Let A be the matrix inside brackets in the latter equation. Then $\rho(A) \geq 1$. But $A \not\leq DU(q)$, so Perron-Frobenius Theorem 2.1 implies $\rho(A) < \rho(DU(q)) \leq 1$. But that means $1 \leq \rho(A) < 1$, which is a contradiction. This rules out $p_\epsilon \geq q$, so $p_\epsilon = q$.

Finally, if $x \geq q$, then $x \leq q + \epsilon e$ for some ϵ , so

$$q \leq U^n(x) \leq U^n(q + \epsilon e), \quad (2.56)$$

for $n \in \mathbb{N}$, so $U^n(x) \rightarrow q$ as $n \rightarrow \infty$.

□

Remark. Lemma 2.12 implies there can only be an unique fixed point q with $\rho(DU(q)) \leq 1$. For, suppose both $q_1 < q_2$ are fixed points with $\rho(DU(q_1)) \leq 1$ and $\rho(DU(q_2)) \leq 1$. Then $U^n(q_2) \rightarrow q_1$, but $U^n(q_2) = q_2$, so $q_1 = q_2$.

Lemma 2.13. *Let $q > 0$, $U(q) = q$ and $U^n(p) \rightarrow q$ as $n \rightarrow \infty$ for some $p < q$. Then $\rho(DU(q)) \leq 1$.*

Proof. Our hypotheses, together with Lemma 2.9 imply that $U^n(x) \rightarrow q$ as $n \rightarrow \infty$ for every $x \in [p, q]$. Suppose $\rho(DU(q)) > 1$, and v an corresponding non-negative eigenvector (guaranteed to exist by Perron-Frobenius Theory): $DU(q)v = \rho(DU(q))v$. For $\epsilon \rightarrow 0_+$ and (C), we have:

$$\begin{aligned} U(q - \epsilon v) &= q - \epsilon DU(q)v + o(\epsilon) \\ &= q - \epsilon \rho(DU(q))v + o(\epsilon) \\ &= q - \epsilon v - \epsilon[(\rho(DU(q)) - 1)v] + o(\epsilon). \end{aligned} \quad (2.57)$$

As $\epsilon[(\rho(DU(q)) - 1)v] \geq 0$, it follows that $U(q - \epsilon v) \leq q - \epsilon v$ for some $\epsilon > 0$. This implies that $U^n(q - \epsilon v) \leq q - \epsilon v$ for $n = 1, 2, \dots$, which contradicts that $U^n(q - \epsilon v) \rightarrow q$ as $n \rightarrow \infty$. By contradiction, we conclude that necessarily $\rho(DU(q)) \leq 1$. □

Now, we can proceed to prove Theorem 2.8

Proof. 1. Lets begin with the case $U(0) = 0$. If $\rho(DU(0)) \leq 1$, Lemma 2.12 yields the result.

For $\rho(DU(0)) > 1$, let $\lambda = \rho(DU(0))$, and v an corresponding eigenvector. For small enough ϵ ,

$$U(\epsilon v) = U(0) + \epsilon DU(0)v + o(\epsilon) = \epsilon \lambda v + o(\epsilon) > \epsilon v. \quad (2.58)$$

Iterations of Lemma 2.9 lead us to

$$\epsilon v < U(\epsilon v) < U^2(\epsilon v) < \dots < U^n(\epsilon v) < \dots \quad (2.59)$$

This implies that either $\lim_{n \rightarrow \infty} U^n(\epsilon v) = \infty$ or $\lim_{n \rightarrow \infty} U^n(\epsilon v) = q_\epsilon$, with $q_\epsilon > 0$ and $U(q_\epsilon) = q_\epsilon$.

In the case $\lim_{n \rightarrow \infty} U^n(\epsilon v) = \infty$, for $x \gtrsim 0$ we have $U(x) > 0$ by Lemma 2.11. For sufficiently small ϵ we have $U(x) > \epsilon v$, which implies $\lim_{n \rightarrow \infty} U^n(x) = \infty$, as $U^n(x) > U^{n-1}(\epsilon v)$.

In the case $\lim_{n \rightarrow \infty} U^n(\epsilon v) = q_\epsilon$, by (2.59) and Lemma 2.13, we have $\rho(DU(q_\epsilon)) \leq 1$. As previously noted, from Lemma 2.12 there can only be an unique fixed point q with $\rho(DU(q)) \leq 1$. We can henceforth drop the subscript. Additionally, $\lim_{n \rightarrow \infty} U^n(x) = q$ for $x \geq q$, again by Lemma 2.12.

For $x \in [0, q] - \{0\}$ there exist ϵ with $\epsilon v < x$. Together with Lemma 2.9 this inequality implies $\lim_{n \rightarrow \infty} U^n(x) = q$.

For $x \notin [0, q] \cup [q, \infty) - \{0\}$, as $x \in \mathbb{R}_+$ we have $x \gtrsim 0$. Lemma 2.11 guarantees that $U(x) > 0$, so there exist $u \in [0, q]$, $w \geq q$ such that $u < U(x) < w$. Applying U^n and taking the limit as $n \rightarrow \infty$ shows that $\lim_{n \rightarrow \infty} U^n(x) = q$.

2. Now, if $U(0) \gtrsim 0$, by Lemma 2.9, we have

$$0 \lesssim U(0) \leq U^2(0) \dots \leq U^n(0) \leq \dots \quad (2.60)$$

Either $\lim_{n \rightarrow \infty} U^n(0) = \infty$ or $\lim_{n \rightarrow \infty} U^n(0) = q > 0$. In the first case, applying U^n on the inequality $0 \leq x$ and taking the limit as $n \rightarrow \infty$ shows that $\lim_{n \rightarrow \infty} U^n(x) = \infty$ for $x \geq 0$.

As for the second case, applying U^n to the inequality $0 \leq x \leq q$ and taking the limit as $n \rightarrow \infty$ shows that $\lim_{n \rightarrow \infty} U^n(0) = q$ for $x \in [0, q]$ and that $\rho(DU(q)) \leq 1$, by Lemma 2.13. Lemma 2.12 proves convergence to q for $x \in [q, \infty]$. The argument for all $x \geq 0$ goes exactly as the latter argument for situation 1.

□

2.3.2 Asymptotic Behaviour of Differential Equations

We now turn to the asymptotic behaviour of solutions to differential equations. Recalling equation (2.2), we are concerned with *concave, cooperative, irreducible* systems such as

$$\dot{x} = F(t, x), \quad (3.2)$$

where $F: \Omega \rightarrow \mathbb{R}^n$ is continuous w.r.t. x , measurable and τ -periodic w.r.t. the variable t . Let

$$\dot{z} = \partial_x F(t, 0)z, \quad (2.61)$$

be the variational equation of (2.2) about $x = 0$. Let λ denote the Floquet multiplier [Kra68] of maximum modulus of (2.61). Theorem 2.14 will provide conditions for the convergence of solutions to a periodic solution, for convergence to 0 or for divergence of solutions.

Theorem 2.14 (Periodic Solutions). *Let $F: \mathbb{R} \times \mathbb{R}_+^n \rightarrow \mathbb{R}_+^n$, satisfying (A) and (B), τ -periodic in t for fixed x . Assume that*

- $\partial_x F(t, x)$ exists and is continuous over x ,
- if $x \geq 0$ with $x_i = 0$, then $F_i(t, x) \geq 0$, $1 \leq i \leq n$, $t \in \mathbb{R}$,
- $\partial_x F(t, x)$ exists and is continuous over x ,

- $\partial_x F(t, 0)$ is irreducible for any $t \in \mathbb{R}$,

Assume as well that the system is cooperative:

$$\frac{\partial F_i}{\partial x_j} \geq 0, i \neq j, (t, x) \in \mathbb{R} \times \mathbb{R}_+^n, \quad (M_1)$$

and concave:

$$\text{if } 0 < x < y, \text{ then } \partial_x F(t, x) \succeq \partial_x F(t, y). \quad (C)$$

Then every solution of (2.2) with $x(t_0) \geq 0$ can be extended to $[t_0, \infty)$. Let $\lambda = \rho(\partial_x F(t, 0))$.

The following assertions hold

1. If $F(t, 0) = 0$ and $\lambda \leq 1$, then $\lim_{t \rightarrow \infty} x(t) = 0$, for all solutions to (2.2) with $x(t_0) \geq 0$.
2. If $F(t, 0) = 0$ and $\lambda > 1$, then
 - either every solution of (2.2) with $x(t_0) \succeq 0$ satisfies $\lim_{t \rightarrow \infty} x(t) = \infty$,
 - or there is a unique non-zero τ -periodic solution $q(t)$, $q(t) > 0$ for all t and $\lim_{t \rightarrow \infty} (x(t) - q(t)) = 0$ for all solutions of (2.2) with $x(t_0) \succeq 0$.
3. If $F(t, 0) \neq 0$, then
 - either every solution of (2.2) with $x(t_0) \geq 0$ satisfies $\lim_{t \rightarrow \infty} x(t) = \infty$,
 - or there is a unique non-zero τ -periodic solution $q(t)$, $q(t) > 0$ for all t and $\lim_{t \rightarrow \infty} (x(t) - q(t)) = 0$ for all solutions of (2.2) with $x(t_0) \geq 0$.

Remark. We can prove an analogous result for systems bounded in an interval $[0, p]$ with $p \in \mathbb{R}^n$, as in Theorem 2.8, discarding the possibility of divergence to ∞ .

The proof consists in verifying that the Poincaré map $T : \mathbb{R}_+^n \mapsto \mathbb{R}_+^n$ such that $T(x_0) = \mathbf{x}(\tau + t_0, t_0, x_0)$, and \mathbf{x} is a Carathéodory solution for (2.2), satisfies the hypotheses for Theorem 2.8.

The proof will be broken down into four lemmas, for which the hypothesis of Theorem 2.14 are assumed:

Lemma 2.15. *If $x(t)$ is a solution to (2.2) with $x(t_0) \geq 0$, then $x(t)$ is extendable to $[t_0, \infty)$ and $x(t) \geq 0$, for $t \geq t_0$.*

Proof. We can write

$$F(t, x) = F(t, 0) + \left(\int_0^1 \partial_x F(t, sx) ds \right) x. \quad (2.62)$$

From (C), we have that $\partial_x F(t, x) \leq \partial_x F(t, 0)$, from which follows that

$$F(t, x) \leq F(t, 0) + \partial_x F(t, 0)x. \quad (2.63)$$

Let $y(t)$ be the solution to $\dot{y} = F(t, 0) + \partial_x F(t, 0)y$, with $y(t_0) = x(t_0)$. From Theorem 2.2, it follows that $x(t) \leq y(t)$ on the maximal interval of existence $[t_0, \omega)$. As $y(t)$ is extendable to $[t_0, \infty)$, then $x(t)$ also is.

□

Lemma 2.16. *If $x(t)$ and $y(t)$ are solutions to (2.2) with $0 \leq y(t_0) < x(t_0)$, then $y(t) < x(t)$ for $t > t_0$.*

This result is straightforward from (M_1) and Kamke's Theorem. This implies \mathbb{R}_+^n is *positively invariant*.

Let $\mathbf{x}(t, t_0, x)$ be the solution to (2.2) which satisfies $\mathbf{x}(t_0, t_0, x) = x$. From Theorems 2.3 and 2.7, the Poincaré map

$$T(x) = \mathbf{x}(\tau, 0, x), \quad (2.64)$$

is a well defined C^1 mapping $T : \mathbb{R}_+^n \rightarrow \mathbb{R}_+^n$. In order to apply Theorem (2.8), it is necessary to prove that

$$DT(x) = \partial_x \mathbf{x}(\tau, 0, x), \quad (2.65)$$

satisfies both (M_0) and (C) . From Theorem 2.7, we have that

$$DT(x) = M(\tau, 0, x), \quad (2.66)$$

where $M(\cdot, \cdot, x)$ is the fundamental matrix solution to the linear problem

$$\dot{X}(t) = \partial_x F(t, \mathbf{x}(t, 0, x)) \cdot X(t), \quad (2.67)$$

and I is the $n \times n$ identity matrix.

Lemma 2.17. *If $x > 0$, then $M(t, 0, x) \geq 0$ for $t > 0$. In addition, if $F(t, 0) = 0$ then $M(t, 0, x) > 0$ for $t > 0$.*

Proof. Fix $x > 0$. As $\partial_x F(t, \mathbf{x}(t, 0, x))$ is cooperative, it follows from [Hir85] that $M(t, 0, x) \geq 0$ for $t > 0$. If $F(t, 0) = 0$, then $\mathbf{x}(t, 0, 0) = 0$ and $M(t, 0, 0)$ is the solution to

$$\dot{X}(t) = \partial_x F(t, 0) \cdot X(t), \quad X(0) = I. \quad (2.68)$$

By (M_1) , $\partial_x F(t, 0)$ is cooperative and irreducible. From [Hir85], we conclude that $M(t, 0, 0) > 0$ for $t > 0$. □

We only need now to verify (C) .

Lemma 2.18. *If $0 < x < y$ then $DT(x) \gneq DT(y)$.*

Proof. If $0 < x < y$ then $\mathbf{x}(t, 0, x) < \mathbf{x}(t, 0, y)$ for $t > 0$, so, from (C) of Theorem 2.14 we have that $\partial_x F(t, \mathbf{x}(t, 0, x)) \gneq \partial_x F(t, \mathbf{x}(t, 0, y))$. Setting $A(t, z) := \partial_x F(t, \mathbf{x}(t, 0, z))$, we have that

$$\dot{M}(t, 0, x) = A(t, x)M(t, 0, x), \quad \dot{M}(t, 0, y) = A(t, y)M(t, 0, y). \quad (2.69)$$

As $M(0, 0, x) = M(0, 0, y) = I$, we can apply Kamke's Theorem, and conclude that $M(t, 0, x) \geq M(t, 0, y)$. Setting $Y(t) := M(t, 0, x) - M(t, 0, y)$, we have that satisfies Y the following differential equation

$$\dot{Y}(t) = A(t, x)Y(t) + [A(t, x) - A(t, y)]M(t, 0, y), \quad Y(0) = 0. \quad (2.70)$$

Rearranging the terms, and multiplying by an integrating term $H(t)$:

$$H(t)\dot{Y}(t) - H(t)A(t, x)Y(t) = H(t)[A(t, x) - A(t, y)]M(t, 0, y). \quad (2.71)$$

We want $H(t)$ to be such that $\dot{H}(t) = -H(t)A(t, x)$. Note that $M(0, t, x)$ satisfies this differential equation. Setting $H(t) = M(0, t, x)$ and using the formula for the derivative of the product, we get

$$\frac{d}{dt}(M(0, t, x)Y(t)) = M(0, t, x)[A(t, x) - A(t, y)]M(t, 0, y). \quad (2.72)$$

the latter expression can be integrated from 0 to τ and manipulated to yield

$$Y(\tau) = \int_0^\tau M(\tau, 0, x)M(0, s, x)[A(s, x) - A(s, y)]M(s, 0, y)ds. \quad (2.73)$$

Note that $M(\tau, 0, x)M(0, s, x) = M(\tau, s, x) \gneq 0$, also that both $[A(s, x) - A(s, y)] \gneq 0$ and $M(s, 0, y) \geq 0$ for $0 < s \leq \tau$. This implies $Y(\tau) \geq 0$.

Suppose that $Y(\tau) = 0$. From the continuity and non-negativity of each term in the integral, we conclude that $M(\tau, 0, x)M(0, s, x)[A(s, x) - A(s, y)]M(s, y) = 0$ for all $0 \leq s \leq \tau$. But, as all M matrices are invertible, this implies that $A(t, x) - A(s, x) = 0$, which is a contradiction. We conclude that $Y(\tau) \gneq 0$, that is, $DT(x) \gneq DT(y)$.

□

Theorem 2.14 follows from Theorem 2.8 because $\lambda = \rho(DT(0)) = \rho(M(\tau, 0, 0))$ is the Floquet multiplier of maximum modulus of equation (2.61).

2.3.3 Algebraic Criteria for Periodic Behaviour

Finally, we establish a criteria involving the principal minors of the Jacobian matrix for the right-hand side function of a differential equation which determines the asymptotic behaviour of solutions for the equation. We begin by stating Theorem 2.19.

Theorem 2.19. *Suppose A is cooperative. Then $s(A) > 0$ if and only if there exists a principal minor $\det A(i_1 \ i_2 \ \dots \ i_k)$ such that $(-1)^k \det A(i_1 \ i_2 \ \dots \ i_k) < 0$.*

Proof. See Theorem 5.1 in [Jif90].

□

Theorem 2.20. *Let $X = \mathbb{R}_+^n$ or $[0, p]$. Suppose $T : X \rightarrow \mathbb{R}^n$ satisfy (A) and (B). Assume $T(0) = 0$, and there is a bounded orbit $\{T^n(x)\}_{n \geq 0}$ for $x \gneq 0$. Then*

1. *If all principal minors of $I - DT(0)$ are nonnegative, then $\lim_{n \rightarrow \infty} T^n(x) = 0$ for each $x \in X$.*
2. *If at least one principal minor of $I - DT(0)$ is negative, then there exists a unique positive fixed point q of T such that $\lim_{n \rightarrow \infty} T^n(x) = q$ for each $x \in X - 0$.*

Proof. From our assumptions, all orbits $\{T^n x\}_{n \geq 0}$ are bounded. By Theorems 2.3 and 2.8, we only have to prove that $\rho(DT(0)) \leq 1$ under the condition for (1), and that $\rho(DT(0)) > 1$

under the condition for (2) If all principal minors of $A = I - DT(0)$ are non-negative, we have, for all principal minors of $-A$:

$$(-1)^k \det -A(i_1, i_2, \dots, i_k) = (-1)^{2k} \det A(i_1, i_2, \dots, i_k) > 0. \quad (2.74)$$

From Theorem 2.19, we have that $s(-A) = s(DT(0) - I) \leq 0$ From (2.1), it follows that

$$\rho(DT(0)) = s(DT(0)) = s(DT(0) - I) + 1 \leq 1. \quad (2.75)$$

If, conversely, there is at least one negative principal minor, we can follow the same argument, and from Theorem 2.19, we have that $s(DT(0) - I) > 0$. A similar calculation yields $\rho(DT(0)) > 1$ in this case.

□

Consider the following system of differential equations

$$\dot{x} = A(t)x, \quad (2.76)$$

where $A(t)$ is measurable and bounded in every compact $K \subset \mathbb{R}$, τ -periodic in t . Set

$$\bar{a}_{ij} := \max_{0 \leq t \leq \tau} a_{ij}(t), \quad (2.77)$$

$$\underline{a}_{ij} := \min_{0 \leq t \leq \tau} a_{ij}(t), \quad (2.78)$$

$$\bar{A} := (\bar{a}_{i,j}), \quad (2.79)$$

$$\underline{A} := (\underline{a}_{i,j}). \quad (2.80)$$

Then

$$\underline{A} \leq A(t) \leq \bar{A}, \text{ for } 0 \leq t \leq \tau. \quad (2.81)$$

Proposition 2.1. *Let $A(t)$ be a continuous cooperative matrix, τ -periodic, and λ be the Floquet multiplier with maximum modulus of (2.76). Then*

$$\exp(\tau s(\underline{A})) \leq \lambda \leq \exp(\tau s(\bar{A})). \quad (2.82)$$

Proof. Consider the 2 linear systems

$$\dot{X} = \underline{A}X, \quad X(0) = I, \quad (2.83)$$

and

$$\dot{Y} = \bar{A}Y, \quad Y(0) = I. \quad (2.84)$$

Let $\Phi(t)$ denote the fundamental matrix solution to (2.76), with $\Phi(0) = I$. It follows from (2.81) and Kamke's Theorem that

$$\exp(\underline{A}t) \leq \Phi(t) \leq \exp(\bar{A}t), \quad \text{for } t > 0. \quad (2.85)$$

This implies that

$$\exp(\tau \underline{A}) \leq \Phi(\tau) \leq \exp(\tau \bar{A}). \quad (2.86)$$

Using (2.1), we get

$$\rho(\exp(\tau \underline{A})) \leq \rho(\Phi(\tau)) \leq \rho(\exp(\tau \bar{A})), \quad (2.87)$$

and using (2.1) again, we have that $\rho(\exp(\tau \underline{A})) = \exp(\tau s(\underline{A}))$ and $\rho(\exp(\tau \bar{A})) = \exp(\tau s(\bar{A}))$, which proves the proposition. □

Theorem 2.21. *Let $X = \mathbb{R}^n$ or $[0, p]$, and $F : \mathbb{R} \times X \mapsto X$, satisfying the hypothesis of Theorem 2.14. Assume also that $F(t, 0) = 0$ and all solutions to (2.2) are bounded. Then, setting $A(t) := \partial_x F(t, 0)$, we have*

1. *If all principal minors of $-\bar{A}$ are non-negative, then $\lim_{t \rightarrow \infty} x(t) = 0$ for all solutions of (2.2).*
2. *If $-\underline{A}$ has at least one negative principal minor, then (2.2) has a unique τ -periodic solution which attracts all initial conditions in $X - \{0\}$.*

Proof. The result follows from proposition 2.1, and Theorems 2.14, 2.19. □

2.4 Conclusion

In order to close the chapter, we rewrite Theorem 2.21 in a format which can be applied to System (\mathcal{S}_3), in the way it is used in Chapter 3.

Theorem 2.22 (Conditions for Periodic Solutions). *Let $F : \mathbb{R} \times \mathbb{R}_+^n \rightarrow \mathbb{R}_+^n$ be a function, measurable over \mathbb{R} for each fixed $x \in \mathbb{R}_+^n$, and continuous over \mathbb{R}_+^n for each fixed $t \in \mathbb{R}$, τ -periodic in t for a fixed x , and assume its Jacobian $\partial_x F(t, x)$ exists and is continuous on the whole domain. If the following conditions are met:*

- *All solutions to $\dot{x} = F(t, x)$ are bounded,*
- *$F(t, 0) = 0$,*
- *All non-diagonal terms of $\partial_x F(t, x)$ are non-negative,*

- $\partial_x F(t, 0)$ is irreducible for any $t \in \mathbb{R}_+$,
- if $0 < x < y$ then $\partial_x F(t, x) > \partial_x F(t, y)$.

Setting $A(t) := \partial_x F(t, 0)$, it follows that

1. If all principal minors of $-\bar{A}$ are non-negative, then $\lim_{t \rightarrow \infty} x(t) = 0$ for every solution of $\dot{x} = F(t, x)$ in $[0, 1]^n$
2. If $-\underline{A}$ has at least one negative principal minor, then $\dot{x} = F(t, x)$ possesses a unique τ -periodic solution which attracts all initial conditions in $[0, 1]^n$.

Chapter 3

Malaria and Fish Pond Cleaning: Model Description and Analysis

3.1 Problem Description

In this chapter, we propose a mathematical model relating the dynamics of malaria, of the *Anopheles* mosquitoes and of the environmental carrying capacity, the latter depending on border vegetation which is modified by cleaning from external agents. The proposed model consists in a system of differential equations.

Through this model, we argue that it is possible to reduce the mosquito population, and therefore reduce the incidence of malaria, through cleaning of border vegetation in fish farming tanks. Removal of border vegetation reduces the carrying capacity of larvae, and subsequently, this reduction propagates to the mosquito population and the incidence of malaria.

Some simplifying assumptions are made for the model. The system dynamics is considered spatially independent, and homogeneous for each compartment. We assume that vegetation cleaning is synchronized, happens periodically, and its time frame is small when compared to the time frame of the mosquito population and disease dynamics (i.e. cleaning is an event that happens in a few hours, and after a number of days happens again; while larvae maturation,

mosquito lifespan and the spread of malaria through mosquito bites are phenomena that have a daily timescale). Therefore, we model vegetation cleaning as impulse that is applied to the vegetation variable, this is, at the cleaning instants we apply a jump to the vegetation with the magnitude of the proportion of vegetation cleaned at that time. A detailed description of the model, its components and assumptions are given in Section 3.3.

Beyond structuring the model, we derive analytical and numerical results from it. In Section 3.4 we apply the theoretical results developed in Chapter 2, specially Theorem 2.22, to the study of the asymptotic behaviour of our system of differential equations. In Section 3.5, we simulate the system numerically in order to show its different possible asymptotic behaviours. We also simulate different values for cleaning periodicity, in order to show the effect of increased cleaning frequency on the incidence of malaria.

3.2 Malaria in Acre

Malaria is a disease caused by parasites of genus *Plasmodium*, transmitted to human beings through the bite of the female *Anopheles darlingi* mosquito (known locally as *Carapanã*). This species of mosquito is highly antropophilic, and is present throughout the whole Brazilian Amazon river basin [RHB⁺15]. At least 33 other species of *Anopheles* inhabit the Amazon basin, and several of them are also possible malaria vectors. Symptoms of malaria range from fever, tiredness, shivers, vomits and headaches in mild cases to coma or even death in severe cases. It is specially dangerous to pregnant women and small children. Of the 5 species of *Plasmodium*, *Plasmodium falciparum* causes the most virulent malaria, and *Plasmodium vivax* is the most frequent cause of recurrent malaria.

In Brazil, 99.9% of cases of malaria are found in the Amazon region, with an annual mean of 310,390 cases between 2000 and 2014. Even inside the Amazon region, incidence of the disease is concentrated: 37 out of 808 counties have 80% of all cases in 2013. In the state of Acre, shown in Figure 3.1, there are 4 counties with high incidence of the disease: Cruzeiro do Sul, Mâncio Lima, Rodrigues Alves and Tarauacá [RHB⁺15].

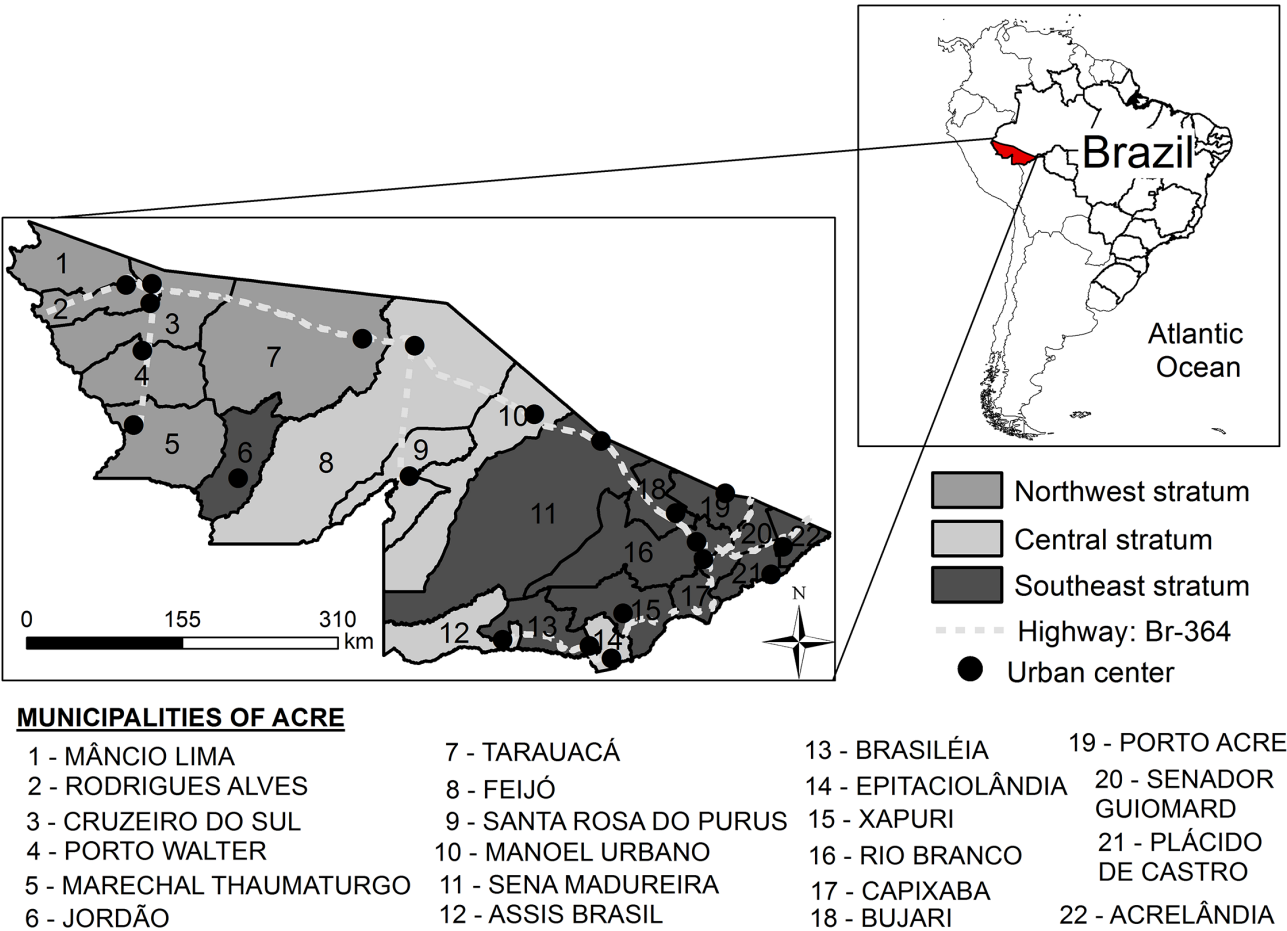


Figure 3.1: Counties of Acre, Brazil, obtained from [RHB+15].

In this region, fish farming was stimulated as a sustainable way to develop the local economy, as part of the Brazilian Federal Government's poverty alleviation program. However, works such as [dRCD+15] give evidence that fish ponds are correlated to an increase in mosquito population, with fish ponds having 4 times more larvae than natural water bodies. Cases of malaria are also spatially and temporally correlated with the opening of fish ponds. The most significant predictor of larval incidence found in [dRCD+15] was percentage of border vegetation, which *Anopheline* larvae use to hide from potential predators. Overall, 10% increase of border covered with vegetation caused a 10% increase in larval abundance. A difference in infestation levels has been observed between commercial and non-commercial ponds. In average, fishponds that contained fish intended for sale were 1.7 times more infested than those for family use. However, if less than 65 % of the border had vegetation, then commercial ponds were less infested with larvae than non-commercial ponds; this is attributed to the high amount of fishes predating on



Figure 3.2: Pictures of Acre: (a) An operational fish farming pond; (b) Measurement of mosquito larvae; (c) Interview with a fish farmer; (d) Education event organized by Oswaldo Cruz Foundation.

the mosquito larvae.

Reduction of border vegetation depends crucially on maintenance of fish ponds. Fish farmers keep ponds clean of vegetation due to concerns regarding production, presence of snakes and other animals. While there is government incentive for the construction of ponds, there is no incentive for maintenance, neither for landfilling of ponds that are no longer in use. Due to the impact border vegetation has on larval abundance, cleaning of border vegetation can be used as a measure of malaria control. Fish farmers were interviewed for information regarding the cost of border cleaning and the speed of vegetation growth, during an educational event organized by Oswaldo Cruz Foundation (see picture in Figure 3.2(d)).

3.2.1 Parameters Survey

Mancio Lima, Acre, is an important malaria hotspot. There, malaria is strongly associated with fish farming ([dRCD⁺15, RHB⁺15]). In a survey with 55 fish farmers, 25 said that cleaning the

border of the ponds was important to prevent mosquitoes (as well as snakes and other animals). The frequency of cleaning varied from once a month to once a year, with median equal to 2 months. Those cleaning once a month were the ones most aware of the relation between pond cleaning and malaria.

In this area, there are ponds with commercial fishes and ponds with natural fishes, and natural water bodies (creeks, swamps). Aquaculture ponds had 4.4 more larvae than natural water bodies. In fishponds, larval abundance increased proportionally to the amount of vegetation border. The average size of ponds was 110m (perimeter), with an average of 80% of the border with vegetation.

3.3 The Model

In this section, we describe the system of differential equations used to model the biological situation at the Alto Juruá region. In subsection 3.3.1, we present a mathematical model for the interaction between the spread of malaria and the mosquito population dynamics. Subsection 3.3.2 introduces the model for border vegetation growth and human action, that consists in border cleaning. Finally, subsection 3.3.3 joins both models in order to study cleaning border vegetation as a control method for malaria.

3.3.1 Malaria Model

Before studying the impact of vegetation cleaning on mosquito population and Malaria, we will introduce a rough mosquito and malaria model, joining ideas from [MSS11]. In the area of Alto Juruá, the prevalent malaria is due to *Plasmodium vivax*, which has negligible mortality and a high rate of reinfection [dRCD⁺15, RHB⁺15]. We therefore disregard the possibility of gaining immunity to the disease (that is, we disconsider the inclusion of a *recovered* R compartment and the use of an SIR model). The model for malaria coincides with the Ross-McDonald model [Ros11]. As *Plasmodium vivax* mortality rate is negligible, we consider a constant human

population normalized to 1.

We will combine an SIS-SI model for the disease with a two-stage population model for the mosquitoes. This means that both the human and adult mosquito populations are divided in two compartments, namely susceptibles and infected. The proportion of susceptible humans is denoted by S , and the proportion of infected is denoted by I . For the adult mosquitoes, we let M_S and M_I denote the susceptibles and infected mosquitoes, respectively. In regards to mosquito population, two main stages are considered: an aquatic stage $L : \mathbb{R}_+ \mapsto \mathbb{R}_+$ (egg, larvae and pupae), and two adult stages, M_S and M_I . Mosquitoes enter the adult stage in the $M_S : \mathbb{R}_+ \mapsto \mathbb{R}_+$ compartment, not infected but susceptible to become vectors of the disease. After biting an infected individual $I : \mathbb{R}_+ \mapsto [0, 1]$, they become infected mosquitoes $M_I : \mathbb{R}_+ \mapsto \mathbb{R}_+$, which infect susceptible humans $S : \mathbb{R}_+ \mapsto [0, 1]$.

Assuming initially that the carrying capacity for the larvae in the environment is a positive constant K , the evolution of the state variables is given by the following system of differential equations:

$$\begin{cases} \dot{S} &= -\beta_{vh}SM_I + \kappa I, \\ \dot{I} &= \beta_{vh}SM_I - \kappa I, \\ \dot{M}_S &= \nu L - \beta_{hv}IM_S - \mu_M M_S, \\ \dot{M}_I &= \beta_{hv}IM_S - \mu_M M_I, \\ \dot{L} &= \alpha(M_I + M_S) \left(1 - \frac{L}{K}\right) - (\nu + \mu_L)L, \end{cases} \quad (S_1)$$

where the meaning of the parameters is given in Table 1.1. We next prove existence and uniqueness results for the system (S_1) using the theoretical backbone from Chapter 2. We also prove that the system is well-posed and biologically reasonable, in the sense that the trajectories have nonnegative components, whenever they start from nonnegative values.

Proposition 3.1. *Given a vector of initial values at time t_0 , there exists a unique C^1 solution for the Cauchy problem associated with system (S_1) , defined on the time interval $[t_0, \infty)$.*

Furthermore, the compact set

$$\mathcal{K} := \{(S, I, M_S, M_I, L) \in \mathbb{R}_+^5 : S + I \leq 1; M_S + M_I \leq (\nu/\mu_M)L; L \leq K\} \quad (3.1)$$

is positively invariant under system (S_1) .

Proof. Writing the system as $\dot{x} = F(x)$, we notice that F is a second degree polynomial, therefore, on every compact set K it is Lipschitz continuous with some Lipschitz constant L_K . We conclude that F satisfies both Conditions (A) and (B). Therefore, Theorem 2.3 guarantees that there is an $\epsilon > 0$ such that a Carathéodory solution defined for $[t_0, t_0 + \epsilon]$ exists. As the right-hand side function is continuous, the solution is C^1 .

For any state variable $X \in \{S, I, M_S, M_I, L\}$, if $X(t) = 0$ then $\dot{X}(t) \geq 0$. This means the flow cannot cross the coordinate hyperplanes from the positive side, so trajectories issuing from initial conditions in \mathbb{R}_+^5 stay in \mathbb{R}_+^5 . By the same token, and from $S + I = 1$, we have

- $\dot{L} < 0$ for $L = K$
- $\dot{I} \leq 0$ for $I = 1$
- $\dot{S} \leq 0$ for $S = 1$
- $\dot{M}_S + \dot{M}_I \leq 0$ for $M_S + M_I \geq (\nu/\mu_M)L$.

The four conditions above guarantee that the flow at the boundary of \mathcal{K} never points outwards, which means the set is positively invariant.

We already know that a solution exists on an interval $[t_0, t_0 + \epsilon]$, and that trajectories are bounded in the compact set \mathcal{K} . As $\mathcal{K} \cap \partial\mathbb{R}^5 = \emptyset$, we can conclude from Theorem 2.6 that the time interval over which the solution is defined can be extended to $[t_0, \infty)$, and from Theorem 2.5 can deduce that the solution is unique.

□

3.3.2 Dynamics of Vegetation

In this section, we present a model for the growth of the border vegetation of the fish tanks and the associated cleaning effects in the form of an impulsive differential equation. Field work in the Alto Juruá region [dRCD⁺15, RHB⁺15] established a correlation between lack of cleaning and an increase in the number of *Anopheles* larvae on fish farming ponds. We model this in such a way that the carrying capacity of larvae is a function of the proportion of borders covered by vegetation, and hence this proportion impacts mosquito population and malaria cases. Figure 3.3 shows some examples of ponds, with low and with high amounts of border vegetation.



Figure 3.3: Pictures of fish farming ponds: Row (a) shows ponds with low levels of border vegetation. Row (b) shows ponds with high levels of border vegetation.

We assume that the proportion of border vegetation $V : \mathbb{R}_+ \mapsto [0, 1]$ grows in proportion to available space $1 - V$, and that *some* cleaning occurs every τ days, in which a part of border vegetation is removed. The function $H : \mathbb{R}_+ \mapsto [0, 1]$ is the fraction of the human population engaging in vegetation cleaning at a given day, and $\gamma : [0, 1] \mapsto [0, 1)$ is the fraction of vegetation cleaned as function of H . Therefore, at day $n\tau$, the proportion of vegetation

removed is $\gamma(H(n\tau))$. We consider a model consisting of an ODE with jumps at given times $n\tau$, with $n \in \mathbb{N}$. It seems reasonable to adopt this "discrete time" cleaning behaviour since the time required for cleaning is small compared to the time frame of border vegetation growth, while the interval between episodes of cleaning is comparable, ranging between every 15 days and two months. The model will assume the following form

$$\begin{cases} \frac{dV(t)}{dt} = r(1 - V(t)), & t \in \bigcup_{n \in \mathbb{N}} (\tau n, \tau(n+1)), \\ \Delta V(n\tau) = -\gamma(H(n\tau))V(n\tau), & n \in \mathbb{N} - \{0\}, \end{cases} \quad (S_2)$$

where $r > 0$ is the vegetation growth rate, and the starting day of periodic vegetation cleaning is set to 0.

Proposition 3.2. *Given any initial condition $V_0 \in [0, 1]$ at time 0, there exists a unique solution for system (S_2) , defined on $\bigcup_{n \in \mathbb{N}} (\tau n, \tau(n+1))$, taking values in $[0, 1]$.*

Proof. Our proof will follow by induction in n .

First, let's consider the interval $[0, \tau)$. It is straightforward to show by separation of variables that

$$V(t) = 1 - (1 - V_0)e^{rt}$$

is a solution for $\dot{V} = r(1 - V(t))$ in $[0, \tau)$. Moreover, the solution is unique and takes values in $[0, 1]$.

Now, suppose there exists a unique solution $\mathbf{V}_k(\cdot)$ defined on $\bigcup_{i < k} (\tau i, \tau(i+1))$ taking values in $[0, 1]$. Define

$$V_{k+} := \left(1 - \gamma(H(n\tau))\right) \lim_{t \rightarrow k\tau-} \mathbf{V}_k(t).$$

As $\mathbf{V}_k(t)$ takes values in $[0, 1]$, we have $\lim_{t \rightarrow k\tau-} \mathbf{V}_k(t) \in [0, 1]$. Moreover, $1 - \gamma(H(n\tau)) \in [0, 1]$, so $V_{k+} \in [0, 1]$. Consider the initial value problem

$$\dot{V}(t) = r(1 - V(t)), \text{ for } t \in (k\tau, (k+1)\tau), \quad V(k\tau) = V_{k+}.$$

Separation of variables show, again, that $V(t) = 1 - (1 - V_{k+})e^{rt}$ is the unique solution for the

latter IVP. Lets define

$$\mathbf{V}_{\mathbf{k}+1}(t) := \begin{cases} \mathbf{V}_{\mathbf{k}}(t), & \text{if } t \in \bigcup_{i < k} (\tau i, \tau(i+1)) \\ 1 - (1 - V_{k+})e^{rt}, & \text{if } t \in (k\tau, (k+1)\tau). \end{cases} \quad (3.2)$$

The function $\mathbf{V}_{\mathbf{k}+1}$ satisfies the impulsive differential equation and the requirements of the proposition. Besides, it is defined on $\bigcup_{i < k+1} (\tau i, \tau(i+1))$, which concludes the inductive step. \square

3.3.3 Complete Model

We finish our construction of the model by putting together (S_1) and (S_2) . When doing this, we take into account the different nature of the fish in the ponds, we split the aquatic stage L into L_p and L_w , namely the aquatic stage population in ponds with predatory fish and without predatory fish, respectively. Border vegetation on fish ponds affects the complete model (S_3) below through two effects. First, both carrying capacities $K_p : [0, 1] \mapsto \mathbb{R}_+$ and $K_w : [0, 1] \mapsto \mathbb{R}_+$ are functions of border vegetation. Secondly, vegetation protects larvae from predation on ponds with predatory fish by offering hiding places for larvae [dRCD⁺15], which leads us to add a term $\mu_p(1 - V)$ which decreases predation as vegetation increases. Both K_w and K_p are strictly increasing function over $[0, 1]$. The system of differential equations (S_3) describes the joint dynamics of malaria, adult mosquitoes, larvae and vegetation:

$$\left\{ \begin{array}{l} \dot{V}(t) = r(1 - V(t)); \text{ for } t \neq n\tau \\ \Delta V(t) = -\gamma(H(t))V(t), \text{ for } t = n\tau, n \in \mathbb{N}; \\ \dot{M}_S = \nu(L_w + L_p) - \beta_{hv}IM_S - \mu_M M_S; \\ \dot{M}_I = \beta_{hv}IM_S - \mu_M M_I; \\ \dot{L}_p = \alpha \frac{K_p(V)}{K_w(V) + K_p(V)} (M_I + M_S) \left(1 - \frac{L_p}{K_p(V)}\right) - (\nu + \mu_L + \mu_p(1 - V))L_p; \\ \dot{L}_w = \alpha \frac{K_w(V)}{K_w(V) + K_p(V)} (M_I + M_S) \left(1 - \frac{L_w}{K_w(V)}\right) - (\nu + \mu_L)L_w; \\ \dot{S} = -\beta_{vh}SM_I + \kappa I; \\ \dot{I} = \beta_{vh}SM_I - \kappa I. \end{array} \right. \quad (S_3)$$

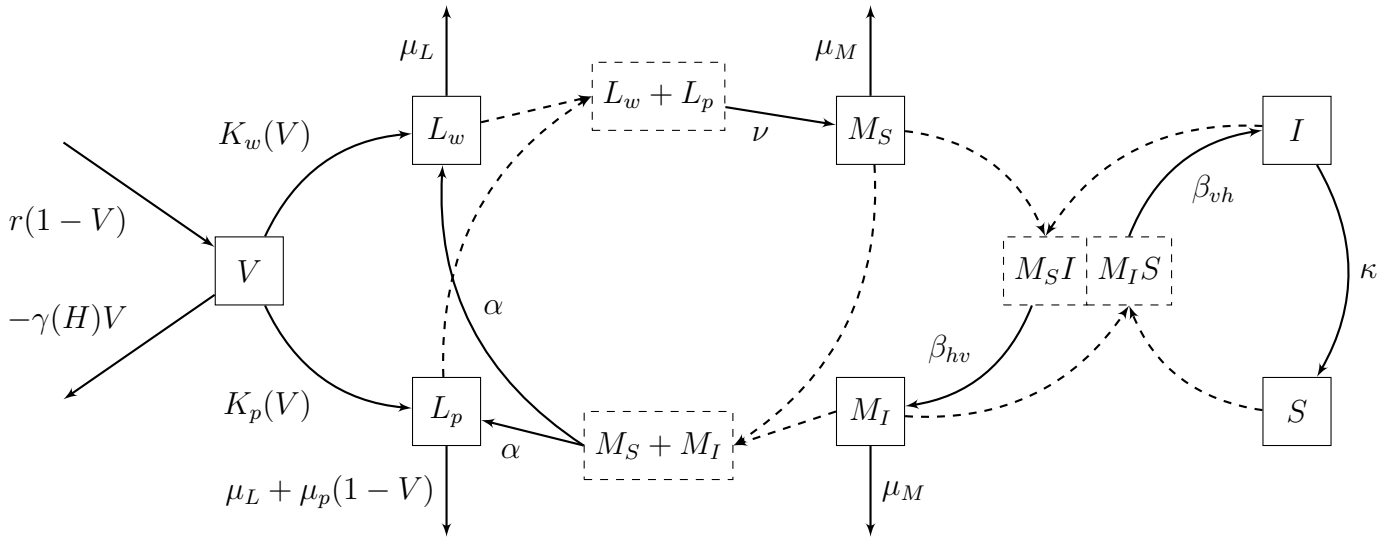


Figure 3.4: Compartmental diagram for the dynamics described in System (S_3) .

where the biological meaning of the parameters is given in Table 3.1. The compartmental diagram for system (S_3) is shown in Figure 3.4. The functions K_p and K_w are fixed, so if the only difference between p and w ponds are the predatory fish, we can take the fractions $K_p/(K_p + K_w)$ and $K_w/(K_p + K_w)$ as constants that are the proportions of pond border with predatory fish and without predatory fish, respectively. This may lead to some simplifications. However, we can think that the presence of predatory fish actually prevents mosquitoes to lay their eggs on those ponds and, in that case, it is appropriate to consider different function laws for K_w and K_p . In either case, the functions $K_p(V)$ and $K_w(V)$ remain in the denominator of the r.h.s, and there is no simplification for that.

We now state and prove propositions concerning *existence and uniqueness* of solutions to initial value problems for system (S_3) , and a *forwardly invariant set* for the system.

Proposition 3.3. *Given a vector of initial conditions at time 0, there exists a unique Carathéodory solution for system (S_3) , defined on $\bigcup_{n \in \mathbb{N}} (n\tau, (n+1)\tau)$. Furthermore, the compact set*

$$\mathcal{K}_2 := \{(V, S, I, M_S, M_I, L_p, L_w) \in \mathbb{R}_+^7 : V \leq 1; S + I \leq 1; M_S + M_I \leq (\nu/\mu_M)(L_p + L_w); \\ L_p \leq \max_{V \in [0,1]} K_p(V), L_w \leq \max_{V \in [0,1]} K_w(V)\} \quad (3.3)$$

is positively invariant under System (S_3) .

Proof. Writing system (S_3) as $\dot{x} = F(t, x)$ for $t \in (0, \tau)$, we have that $t \mapsto F(t, x)$ is piecewise continuous for every fixed x . Moreover, $K_p(V) + K_w(V) > 0$ for $V \in (0, 1]$. Therefore, $t \mapsto F(t, x)$ is measurable for every fixed x and $x \mapsto F(t, x)$ is continuous for almost every t . Therefore F satisfies conditions (A) for $t \in (0, \tau)$. As for condition (B), the Jacobian matrix DF of (S_3) is continuous over \mathbb{R}_+^7 , for $t \in (0, \tau)$. This implies that the norm of DF is bounded in every compact set K . We can write

$$|F(y) - F(x)| = \left| \int_0^1 DF(sy + (1-s)x)ds \cdot (y - x) \right| < M_K |y - x| \quad (3.4)$$

where M_K is a strict bound on DF for the compact set K . This shows that F satisfies (B). We can then apply Theorem 2.3 to prove that there exists an interval $[0, \epsilon]$ on which a solution for the initial value problem for system (S_3) exists.

Proof of compactness and positive invariance of \mathcal{K}_2 is analogous to the proof in Proposition 3.1, so we omit it.

We already know that a solution exists on an interval $[0, \epsilon]$, and that trajectories are bounded in the compact set \mathcal{K}_2 given in (3.3). As $\mathcal{K}_2 \cap \partial\mathbb{R}^7 = \emptyset$, we can conclude from Theorem 2.6 that the time interval over which the solution is defined can be extended to $[0, \tau)$. As we did in Proposition 3.2, at $n\tau, n \in \mathbb{N}$, we update the value of V in order to obey the impulsive equation. At every interval $(n\tau, (n+1)\tau)$, our latter argument proves recursively that a solution exists. Finally, applying Theorem 2.5 on $(0, \tau)$, then on $(\tau, 2\tau)$ and so on, we conclude that the solution is unique. \square

Solutions for system (S_3) are discontinuous at the points $n\tau$, due to the jump behaviour in the vegetation. In fact, only the vegetation variable is undefined at these points, while the trajectories of the other variables will be continuous, but not differentiable. Proposition 3.3 guarantees important basic properties of system (S_3) . Those properties will be used to prove sufficient conditions for (S_3) to asymptotically approach periodic behaviour or to converge to 0.

Parameter	Biological Meaning
K	Aquatic stage carrying capacity of the environment.
K_p	Aquatic stage carrying capacity of fishing ponds with predatory fish, as a function of border vegetation.
K_w	Aquatic stage carrying capacity of fishing ponds without predatory fish, as a function of border vegetation.
α	Mean number of eggs per mosquito which become larvae.
ν	Aquatic to adult transition rate.
μ_L	Aquatic stage basic mortality rate.
μ_p	Added mortality due to predatory fish.
μ_M	Adult mosquito mortality rate.
κ	Recovery rate for infected individuals.
β_{vh}	Mosquito to human infection rate.
β_{hv}	Human to mosquito infection rate.
r	Rate of growth of vegetation.
H	Proportion of population cleaning the vegetation as function of time.
γ	Proportion of vegetation removed as function of H .

Table 3.1: Biological meaning of the parameters.

3.4 Asymptotic Behaviour

In this section, we study the asymptotic behaviour of system (S_3) . We split this analysis in three parts. In subsection 3.4.1, our focus is the vegetation system (S_2) . We prove in Proposition 3.4 that, under τ -periodic cleaning, border vegetation approaches a τ -periodic solution. Subsection 3.4.2 studies the behaviour of mosquito population when border vegetation is periodic, and 3.4.3 studies malaria incidence under periodic border vegetation. We derive sufficient conditions for (S_3) to converge to a periodic solution.

3.4.1 Asymptotic Behaviour of Vegetation

This subsection is focused on the vegetation model (S_2) . We aim to prove that, under periodic cleaning, the vegetation converges to a periodic solution of the differential equation. This

periodic solution is discontinuous at the cleaning time, as cleaning is modelled as an impulse. The main result of the current subsection is the following:

Proposition 3.4 (Periodic Solutions for Vegetation). *If $\lim_{t \rightarrow \infty} H(t) = H^*$, for some constant value H^* , the system (S_2) admits the periodic solution:*

$$V_{per}(t) := 1 - \frac{\gamma(H^*)e^{-r(t-n\tau)}}{1 - (1 - \gamma(H^*))e^{-r\tau}} \quad \text{for } t \in [n\tau, (n+1)\tau), \quad (3.5)$$

and, for every solution V of (S_2) with non-zero initial value, one has

$$\max_{t \in [n\tau, (n+1)\tau)} |V(t) - V_{per}(t)| \rightarrow 0 \text{ as } n \rightarrow \infty, \quad (3.6)$$

Proposition 3.4 is a direct application of the following lemma:

Lemma 3.1. *Let $(\gamma_n)_{n \in \mathbb{N}}$ be a sequence such that $0 < \gamma_n < 1$ for all $n \in \mathbb{N}$, and $\gamma_n \rightarrow \gamma > 0$. Consider the following initial value problem for $u_0 > 0$*

$$\begin{cases} \frac{du}{dt} = r(1 - u(t)), & \text{for } t \in (n\tau, (n+1)\tau) \\ \Delta u(n\tau) = -\gamma_n u(n\tau), & n \in \mathbb{N}, \\ u(0) = u_0. \end{cases} \quad (3.7)$$

Then there exists a periodic solution u_{per} given by

$$u_{per}(t) := 1 - \frac{\gamma e^{-r(t-n\tau)}}{1 - (1 - \gamma)e^{-r\tau}} \quad \text{for } t \in [n\tau, (n+1)\tau). \quad (3.8)$$

and for any solution u of (3.7), we have

$$\max_{t \in [n\tau, (n+1)\tau)} |u(t) - u_{per}(t)| \rightarrow 0 \text{ as } n \rightarrow \infty. \quad (3.9)$$

Proof. Let us begin by taking a constant sequence $\gamma_n = \gamma$ with $0 < \gamma < 1$. The proof consists in considering the recurrent sequence formed by the points of discontinuity, and studying its

convergence. We shall use the notation:

$$\begin{aligned} u(t+) &:= \lim_{\epsilon \rightarrow 0^+} u(t + \epsilon), \\ u(t-) &:= \lim_{\epsilon \rightarrow 0^-} u(t + \epsilon). \end{aligned}$$

For $n \in \mathbb{N}$, the initial value problem

$$\begin{cases} \dot{u}(t) = r(1 - u(t)), & \text{for } t \in [n\tau, (n+1)\tau), \\ u(n\tau) = u(n\tau+), \end{cases} \quad (3.10)$$

has a unique solution that is given by

$$u(t) := 1 - [1 - u(n\tau+)]e^{-r(t-n\tau)}, \quad \text{for } t \in [n\tau, (n+1)\tau). \quad (3.11)$$

Taking the limit as $t \rightarrow (n+1)\tau-$, it follows that

$$u((n+1)\tau-) = 1 - [1 - u(n\tau+)]e^{-r\tau}. \quad (3.12)$$

We can write the periodic impulse as

$$-\gamma u((n+1)\tau-) = \Delta u((n+1)\tau) = u((n+1)\tau+) - u((n+1)\tau-), \quad (3.13)$$

or, more compactly,

$$u((n+1)\tau+) = (1 - \gamma)u((n+1)\tau-). \quad (3.14)$$

Using (3.12) in the latter equation yields

$$u((n+1)\tau+) = (1 - \gamma) \left(1 - (1 - u(n\tau+))e^{-r\tau} \right). \quad (3.15)$$

Equation (3.15) gives the $(n+1)$ -th term in the sequence $(u(n\tau+))_{n \in \mathbb{N}}$ as a function of the n -th

term, defining a recurrence relation. Consider the function $f : [0, 1] \mapsto [(1-\gamma)(1-e^{-r\tau}), (1-\gamma)]$:

$$f(x) := (1-\gamma)\left(1 - (1-x)e^{-r\tau}\right). \quad (3.16)$$

In general, the recurrence can be written as

$$u((n+1)\tau+) = f(u(n\tau+)), \text{ for } n \in \mathbb{N}. \quad (3.17)$$

The following two conditions hold:

- f is a contraction: $|f'(x)| = |(1-\gamma)e^{-r\tau}| \leq |1-\gamma| < 1$,
- $f([0, 1]) \subseteq [0, 1]$, by definition.

Hence, by Banach's Fixed Point Theorem, the sequence of points $(u(n\tau+))_{n \in \mathbb{N}}$ converges to some u^* that satisfies:

$$u^* = (1-\gamma)\{1 - [1 - u^*]e^{-r\tau}\}, \quad (3.18)$$

or, explicitly,

$$u^* = \frac{(1-\gamma)(1 - e^{-r\tau})}{[1 - (1-\gamma)e^{-r\tau}]}. \quad (3.19)$$

This means any solution u converges to u_{per} given by:

$$u_{per}(t) = 1 - [1 - u^*]e^{-r(t-n\tau)} = 1 - \frac{\gamma e^{-r(t+n\tau)}}{1 - (1-\gamma)e^{-r\tau}}, \quad t \in [n\tau, (n+1)\tau); \quad n \in \mathbb{N}. \quad (3.20)$$

Finally, we notice that the proof also holds for a generic sequence $(\gamma_n)_{n \in \mathbb{N}}$ with $\gamma_n \rightarrow \gamma > 0$ as $n \rightarrow \infty$ and $0 < \gamma_n < 1$ for every $n \in \mathbb{N}$, as the recurrence relation will still be a contraction. Thus the proposition has been proven. □

Proposition 3.4 follows from Lemma 3.1 by setting $\gamma_n := \gamma(H(n\tau))$. We conclude that, under periodic cleaning, the border vegetation will eventually be arbitrarily close to periodic.

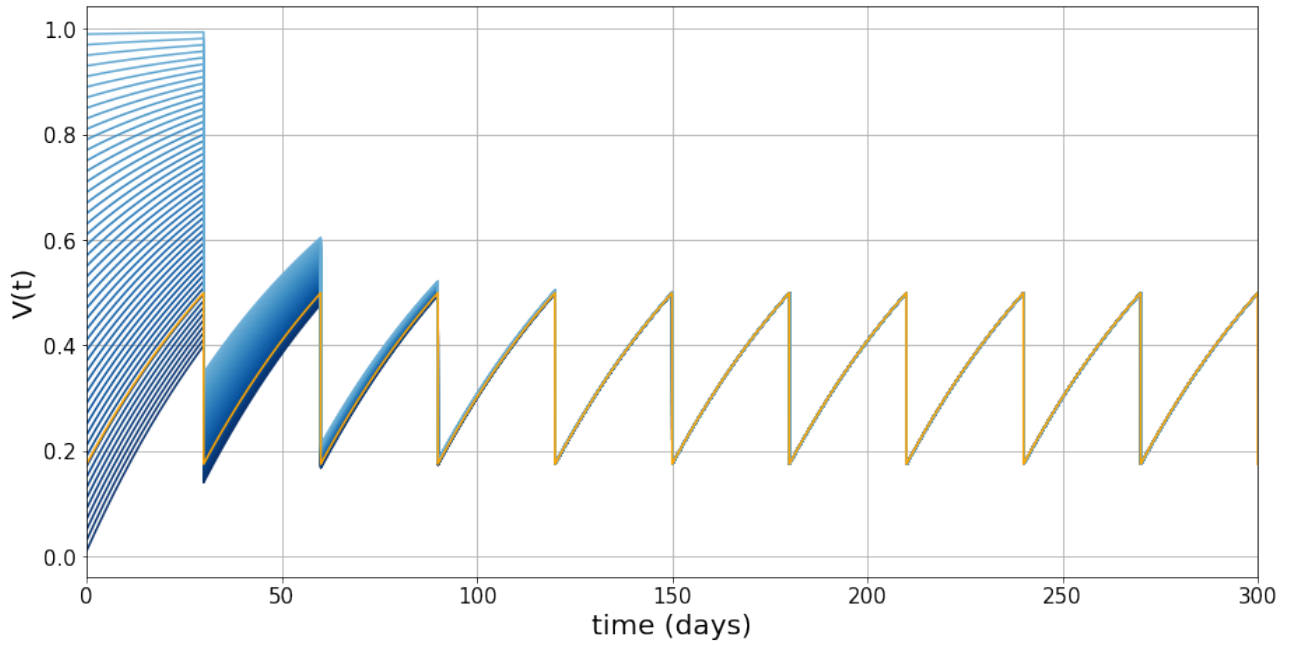


Figure 3.5: Behaviour of the IVP associated with System (S_2) , for different initial values. V_{per} is shown in orange.

Figure 3.5 illustrates Proposition 3.4, by showing the solution to the impulsive initial value problem for a range of initial values in $[0, 1]$. Note that at each point of discontinuity, the trajectories come closer together, and approach asymptotically one same function that is V_{per} .

As $K_w(V(t))$ and $K_p(V(t))$ are compositions of a strictly increasing functions with the function V , both will also assume asymptotic periodic behaviour. In the following subsections, we will consider the response of system (S_3) under periodic behaviour of border vegetation.

3.4.2 Mosquito Dynamics

We now turn to the analysis of the asymptotic behaviour of the mosquito population, *assuming that border vegetation is periodic*. Our aim is to derive sufficient conditions on the parameters of the system for the mosquito population to either converge to 0, or have asymptotic periodic behaviour.

Recalling system (S_3)

$$\left\{ \begin{array}{l} \dot{V} = r(1 - V(t)); \\ \Delta V(n\tau) = -\gamma(H(n\tau))V(n\tau), \quad n \in \mathbb{N}; \\ \dot{M}_S = \nu(L_w + L_p) - \beta_{hv}IM_S - \mu_M M_S; \\ \dot{M}_I = \beta_{hv}IM_S - \mu_M M_I; \\ \dot{L}_p = \alpha \frac{K_p(V)}{K_w(V) + K_p(V)}(M_I + M_S) \left(1 - \frac{L_p}{K_p(V)}\right) - (\nu + \mu_L + \mu_p(1 - V))L_p; \\ \dot{L}_w = \alpha \frac{K_w(V)}{K_w(V) + K_p(V)}(M_I + M_S) \left(1 - \frac{L_w}{K_w(V)}\right) - (\nu + \mu_L)L_w; \\ \dot{S} = -\beta_{vh}SM_I + \kappa I; \\ \dot{I} = \beta_{vh}SM_I - \kappa I. \end{array} \right. \quad (S_3)$$

There are two aspects to consider. First, that vegetation behaviour only impacts the system through the *larvae* compartments L_w and L_p . Let V_{per} be the periodic vegetation solution given in equation (3.5). Then both *carrying capacities* $K_w(V_{per})$ and $K_p(V_{per})$ also are periodic. Second, by setting $M := M_S + M_I$ we can isolate mosquito population dynamics in the following subsystem:

$$\left\{ \begin{array}{l} \dot{L}_p = \alpha \frac{K_p(V_{per})}{K_w(V_{per}) + K_p(V_{per})}M \left(1 - \frac{L_p}{K_p(V_{per})}\right) - (\nu + \mu_L + \mu_p(1 - V_{per}))L_p; \\ \dot{L}_w = \alpha \frac{K_w(V_{per})}{K_w(V_{per}) + K_p(V_{per})}M \left(1 - \frac{L_w}{K_w(V_{per})}\right) - (\nu + \mu_L)L_w; \\ \dot{M} = \nu(L_p + L_w) - \mu_M M. \end{array} \right. \quad (3.21)$$

The system can be written as $\dot{X}(t) = F(t, X(t))$. Due to the discontinuities and periodicity of V_{per} , the right-hand side function F is piecewise-continuous and τ -periodic. F satisfies the conditions of Theorem 2.22, so we can get Theorem 3.2. Let us first recall the formula for the basic offspring number:

$$\mathcal{N} \doteq \frac{\alpha\nu}{\mu_M(\nu + \mu_L)}.$$

The basic offspring number is well known in the literature as a value that determines the growth of a population, and it represents the average number of offspring that an individual produces

during its lifespan [YMG⁺09, FG14].

Theorem 3.2 (Limit behaviour of Mosquito Population). *For $V_{per} : [0, \infty) \mapsto [0, 1]$ given in (3.5), one has*

1. *If*

$$\mathcal{N}^{-1} \geq \left[\max_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w}(V_{per}(t)) \right) + \max_{t \in [0, \tau)} \left(\frac{K_p}{K_p + K_w}(V_{per}(t)) \right) \right], \quad (\text{Condition 1})$$

then the trajectories of (3.21) are such that $\lim_{t \rightarrow +\infty} X(t) = 0$ for all feasible initial conditions.

2. *If*

$$1 + \max_{t \in [0, \tau)} \frac{K_p}{K_w}(V_{per}) < \mathcal{N}, \quad (\text{Condition 2})$$

then there exists a strictly positive periodic solution of (3.21) which attracts all initial conditions.

Note that our conditions for convergence to 0 and convergence to periodic behaviour are both *sufficient* conditions, not *necessary* conditions.

Proof. First, note that system (3.21) satisfies the conditions of Theorem 2.22. In order to apply Theorem 2.22, we need to calculate the matrix $A(t) := \partial_x F(t, 0)$, then find conditions for all principal minors of $-\bar{A}$ to be non-negative, and conditions for at least one of the principal minors of $-\underline{A}$ to be negative.

We have

$$A(t) = \begin{bmatrix} -(\nu + \mu_L + \mu_p(1 - V_{per}(t))) & 0 & \nu \\ 0 & -(\nu + \mu_L) & \nu \\ \alpha \frac{K_p(V_{per}(t))}{K_w(V_{per}(t)) + K_p(V_{per}(t))} & \alpha \frac{K_w(V_{per}(t))}{K_w(V_{per}(t)) + K_p(V_{per}(t))} & -\mu_M \end{bmatrix} \quad (3.22)$$

1. calculating the 7 principal minors of $-\bar{A}$:

$$\begin{aligned}
& (\nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per}(t)))(\nu + \mu_L)\mu_M - \nu\alpha(\nu + \mu_L) \max_{t \in [0, \tau]} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right) \\
& - (\nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per}(t)))\nu\alpha \max_{t \in [0, \tau]} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right), \quad (M_1)
\end{aligned}$$

$$(\nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per}(t)))(\nu + \mu_L), \quad (M_2)$$

$$(\nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per}(t))\mu_M - \nu\alpha \max_{t \in [0, \tau]} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right), \quad (M_3)$$

$$(\nu + \mu_L)\mu_M - \nu\alpha \max_{t \in [0, \tau]} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right), \quad (M_4)$$

$$\nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per}(t)), \quad (M_5)$$

$$\nu + \mu_L, \quad (M_6)$$

$$\mu_M. \quad (M_7)$$

Principal minors $(M_7), (M_6), (M_5)$ and (M_2) are trivially non-negative. Principal minor (M_1) can be written as a function of (M_3) and (M_5) :

$$M_1 = (\nu + \mu_L)M_3 - \nu\alpha \max_{t \in [0, \tau]} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) M_5,$$

from which it follows that $M_1 \geq 0$ implies that $M_3 \geq 0$. We can also write (M_1) as a function of (M_4) and (M_4) :

$$M_1 = M_5M_4 - \nu\alpha(\nu + \mu_L) \max_{t \in [0, \tau]} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right),$$

from which we conclude that $M_1 \geq 0$ implies $M_4 \geq 0$. Therefore, we may restrict ourselves to the study of the inequality $M_1 \geq 0$. Writing it as

$$\begin{aligned}
& (\nu + \mu_L) \left((\nu + \mu_L) \mu_M - \nu \alpha \underbrace{\left[\max_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) + \max_{t \in [0, \tau)} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right) \right]}_u \right) + \\
& \mu_p (1 - \max_{t \in [0, \tau)} V_{per}(t)) \underbrace{\left[(\nu + \mu_L) \mu_M - \nu \alpha \max_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) \right]}_v \geq 0, \quad (3.23)
\end{aligned}$$

we can see that $u < v$, so if $u \geq 0$ then $v \geq 0$. A straightforward calculation shows that $u \geq 0$ if and only if (Condition 1) is satisfied. It follows that if (Condition 1) is satisfied, then all terms in the expression are non-negative, and $M_1 \geq 0$. From Theorem 2.22, all solutions converge to 0.

2. The principal minors of $-\underline{A}$ will be the principal minors of $-\bar{A}$ with all maxima exchanged for minima. Again, principal minors $(M_7), (M_6), (M_5)$ and (M_2) are trivially non-negative. We can write

$$M_1 = (\nu + \mu_L) M_3 - \nu \alpha \min_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) M_5,$$

from which we deduce that $M_3 < 0$ implies $M_1 < 0$. Conversely, from

$$M_1 = M_5 M_4 - \nu \alpha (\nu + \mu_L) \min_{t \in [0, \tau)} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right),$$

we have that $M_4 < 0$ implies $M_1 < 0$. Therefore, $M_1 < 0$ is the weaker condition, and $M_4 < 0$ or $M_3 < 0$ are other possible sufficient conditions. Recalling the inequality for M_1 :

$$\begin{aligned}
& (\nu + \mu_L) \left((\nu + \mu_L) \mu_M - \nu \alpha \underbrace{\left[\min_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) + \min_{t \in [0, \tau)} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right) \right]}_u \right) + \\
& \mu_p (1 - \min_{t \in [0, \tau)} V_{per}(t)) \underbrace{\left[(\nu + \mu_L) \mu_M - \nu \alpha \min_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) \right]}_v < 0.
\end{aligned}$$

We have $u < v$, therefore $v < 0 \implies u < 0$ and $M_1 < 0$. From $v < 0$, it follows that

$$\begin{aligned}
v < 0 &\Leftrightarrow (\nu + \mu_L)\mu_M - \nu\alpha \min_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) \\
&\Leftrightarrow \mathcal{N}^{-1} < \min_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) \\
&\Leftrightarrow \mathcal{N}^{-1} < \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right), \forall t \in [0, \tau) \\
&\Leftrightarrow 1 + \frac{K_p}{K_w} (V_{per}) < \mathcal{N}, \forall t \in [0, \tau) \\
&\Leftrightarrow 1 + \max_{t \in [0, \tau)} \frac{K_p}{K_w} (V_{per}) < \mathcal{N}.
\end{aligned} \tag{3.24}$$

It follows that if (Condition 2) is satisfied, then there exist a negative principal minor of $-\underline{A}$ and, from Theorem 2.22 there exists a strictly positive periodic solution of (3.21) which attracts all initial conditions.

□

3.4.3 Disease Behaviour

Following the discussion of the previous subsection, we now analyze the behaviour of the *infected* human and mosquito populations in the same manner. Assuming we are in situation 2 of Theorem 3.2, let $M_{per} : \mathbb{R}_+ \mapsto \mathbb{R}$ be the periodic solution for the mosquito population. So, writing the differential equations for the infected components (M_I, I) as

$$\begin{cases} \dot{M}_I &= \beta_{hw} I (M_{per} - M_I) - \mu_M M_I; \\ \dot{I} &= \beta_{vh} (1 - I) M_I - \kappa I. \end{cases} \tag{3.25}$$

We can write (3.25) above as $\dot{Y}(t) = G(t, Y(t))$ and apply Theorem 2.22 to arrive at the following result:

Theorem 3.3 (Limit Behaviour of Disease). 1. If

$$\frac{\beta_{hv}\beta_{vh} \max_{t \in [0, \tau)} M_{per}(t)}{\kappa\mu_M} \leq 1,$$

then the trajectories Y of (3.25) verify $\lim_{t \rightarrow +\infty} Y(t) = 0$ for all feasible initial conditions.

2. If

$$\frac{\beta_{hv}\beta_{vh} \min_{t \in [0, \tau)} M_{per}(t)}{\kappa\mu_M} > 1,$$

then there exists a strictly positive periodic solution of (3.25) which attracts all feasible initial conditions.

Proof. Again, note that system (3.25) satisfies the conditions on Theorem 2.22. It is straightforward to calculate $A(t) := \partial_x G(t, 0)$:

$$A(t) = \begin{bmatrix} -\mu_M & \beta_{hv}M_{per}(t) \\ \beta_{vh} & -\kappa \end{bmatrix}. \quad (3.26)$$

Let us analyze the principal minors of $-\bar{A}$. Since μ_M and κ are non-negative, if

$$\kappa\mu_M - \beta_{hv}\beta_{vh} \max_{t \in [0, \tau)} M_{per}(t) \geq 0$$

then, in view of Theorem 2.22 situation 1 holds. This is, $\lim_{t \rightarrow \infty} Y(t) = 0$ for all feasible initial conditions.

Conversely, for $-\underline{A}$, if

$$\kappa\mu_M - \beta_{hv}\beta_{vh} \min_{t \in [0, \tau)} M_{per}(t) < 0$$

then situation 2 holds, i.e. there exists a strictly positive periodic solution which attracts all initial condition. \square

Parameter	Biological Meaning	Values	Comment
r	vegetation growth rate (per month)	1/2	1.
τ	Period of pond cleaning (1/frequency)	30 – 60 days	1.
$H(t)$	Proportion of population engaging in cleaning at time t	5% (max)	2.
γ	efficacy of cleaning	0.65	3.
α	daily mean number of eggs per mosquito which become larvae	8.75 – 43.66	4.
ν	aquatic to adult transition rate (per day)	1/(15.6 \pm 2.86)	[SCK81]
μ_L	larval mortality rate on ponds	0.62 – 0.99	5.
μ_p	larval mortality due to predation by fish	-	5.
μ_M	adult mosquito mortality rate (per day)	0.089 – 0.476	6.
κ	malaria (<i>vivax</i>) recovery rate for infected humans	1/11	[AFG12]
β_{vh}	mosquito to human malaria infection rate	0.02 – 0.25	7.
β_{hv}	human to mosquito malaria infection rate	0.05 – 0.25	7.

Table 3.2: Biologically feasible parameter ranges

3.5 Analysis and Simulations

In this last section, we analyze our results so far and present simulations made to illustrate our model. Our aim is threefold: observe the behaviour predicted by the preceding analysis and results, to employ realistic parameters to simulate malaria in the Alto Jurua region, and to simulate the effect that border vegetation cleaning has in the incidence of malaria. In Table 3.2, we expose the range of realistic values for the biological parameters in System (S_3) taken from [RHB⁺15, dRCD⁺15, Kam12, DT16]. In Subsection 3.5.1, we present some scenarios used to illustrate the possible asymptotic behaviours of the system, as predicted by Theorems 3.3 and 3.2. Subsection 3.5.2 explores the conditions from the theorems, analyzing the effect of the system's parameters on its asymptotic behaviour, and Subsection 3.5.3 gives a brief analysis of the effect of awareness on cleaning periodicity.

Comments about Table 3.2:

1. From the interview with the fish farmers, border cleaning is done between 30 to 60 days, and costs as far as 300 *reais* (Brazilian currency) to hire someone to do it. Moreover, fish should not affect the growth rate of the vegetation. Since cleaning is not done very often,

it is natural to model it as a discrete variable, that represents a situation in which every τ days, a certain proportion of the population cleans border vegetation.

2. In the studied area, there is roughly one fishpond for every 20 households. This gives 5% of the population engaged in fish farming. The difference between cleaning intensity of ponds with and without fish should be a result of the economic incentives.
3. The median amount of larvae in ponds with less than 20% of vegetated border was 1300 larvae/m, while a pond with more than 80% vegetated border had 3700 larvae/m. This gives an average efficacy of 0.65 for the effect of cleaning on larval abundance. [RHB⁺15, dRCD⁺15]
4. Range calculated from the mean number of hatched eggs per oviposition (83 ± 48) [SCK81], divided by the length of the gonotrophic cycle (3 - 4 days) [RATM83].
5. Pond vegetation interferes with the feeding behavior of the fish, and indirectly protects the larvae from their predators [Kam12]. Without vegetation, larvivorous fishes can reduce the amount of larvae in 90%.
6. Values taken from [BHA11] as one minus the daily survival rate. Survivability is affected by rainfall, taking a range of values with seasonal changes in precipitation.
7. Values calculated from [MSS11] from *man biting rate*, *proportion of bites that produces infection in humans* and *proportion of bites that produce infection in mosquitoes*.
8. For $K_w(V)$ and $K_p(V)$, we choose the following arbitrary functions:

$$K_p(V) := \frac{0.8}{1 + e^{-5(V-0.5)}}, \quad K_w(V) := 4V + 0.5.$$

The equation for $K_w(V)$ was interpolated by taking $K_w(0.2) = 1300$ larvae/m and $K_w(0.8) = 3700$ larvae/m. The equation for $K_p(V)$ is a sigmoid with arbitrary parameters such that $K_p(0.5) = 0.4$ larvae/m. We chose two different kinds of functions so as not to simplify the conditions on Theorem 3.2.

3.5.1 Numerical Validation of Theorems

We aim at verifying Theorems 3.2 and 3.3 with numerical simulations, by showing that the system of differential equations behaves as predicted by the Theorems. The following Scenarios will be simulated:

- Scenario 1: Periodic mosquito and periodic infected populations,
- Scenario 2: Periodic mosquito population, and infected population converging to 0.
- Scenario 3: Mosquito population and infected population converging to 0

Parameter	Scenario 1	Scenario 2	Scenario 3	Units
r	0.01666	0.01666	0.01666	month ⁻¹
τ	30	30	30	days
H	0.05	0.05	0.05	dimensionless
γ	0.65	0.65	0.65	dimensionless
α	43.66	43.66	8.75	larvae mosquito ⁻¹ day ⁻¹
ν	0.0641	0.0641	0.0541	mosquito larvae ⁻¹ day ⁻¹
μ_L	0.62	0.62	0.99	day ⁻¹
μ_p	0.31	0.31	0.31	day ⁻¹
μ_M	0.089	0.16	0.8	day ⁻¹
$K_w(1)$	4	4	4	thousand larvae m ⁻¹
$K_p(1)$	0.4	0.4	0.4	thousand larvae m ⁻¹
κ	0.0909	0.0909	0.0909	day ⁻¹
β_{vh}	0.2	0.1	0.2	mosquito ⁻¹ day ⁻¹
β_{hv}	0.2	0.1	0.2	day ⁻¹

Table 3.3: Value of parameters for each scenario.

These scenarios cover the possible combinations of conditions in Theorem 3.2 and 3.3. The numerical values used for the simulations are given in Table 3.3.

The value for μ_M in scenario 3 was chosen outside of the biological feasible range in order to force the differential equation system to assume the desired asymptotic behaviour.

System (S_3) was integrated numerically for each scenario with initial conditions

$$(S_0, I_0, M_{S,0}, M_{I,0}, L_{p,0}, L_{w,0}) = (0.9, 0.1, 0.5, 0, 2, 0.2).$$

Expression	1	2	3
\mathcal{N}^{-1}	0.021	0.039	1.762
$\max_{t \in [0, \tau)} \left(\frac{K_w}{K_p + K_w} (V_{per}(t)) \right) + \max_{t \in [0, \tau)} \left(\frac{K_p}{K_p + K_w} (V_{per}(t)) \right)$	1.025	1.025	1.025
$\left(1 + \max_{t \in [0, \tau)} \frac{K_p}{K_w} (V_{per}) \right)^{-1}$	0.918	0.918	0.918
$\frac{\beta_{hv} \beta_{vh} \max_{t \in [0, \tau)} M_{per}(t)}{\kappa \mu_M}$	10.453	0.842	0.000
$\frac{\beta_{hv} \beta_{vh} \min_{t \in [0, \tau)} M_{per}(t)}{\kappa \mu_M}$	8.567	0.621	0.000

Table 3.4: Calculated values for the conditional expression.

The value for the conditional expressions of both Theorem 3.2 and 3.3 are given in Table 3.4. The simulations are shown in figures 3.6, 3.7 and 3.8. It is observed that the variables of the system behave as predicted by Theorems 3.2 and 3.3.

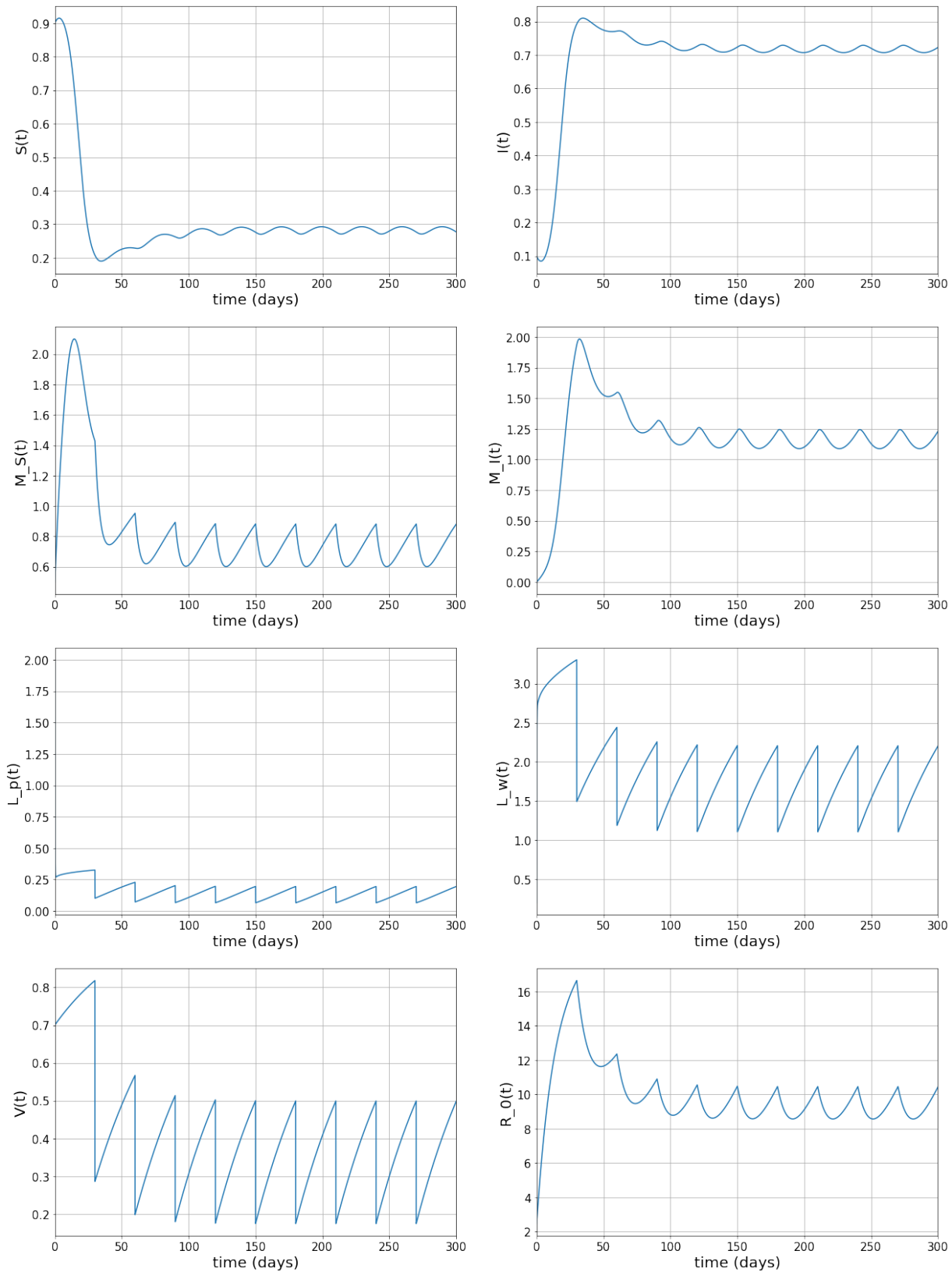


Figure 3.6: Behaviour of the system under Scenario 1

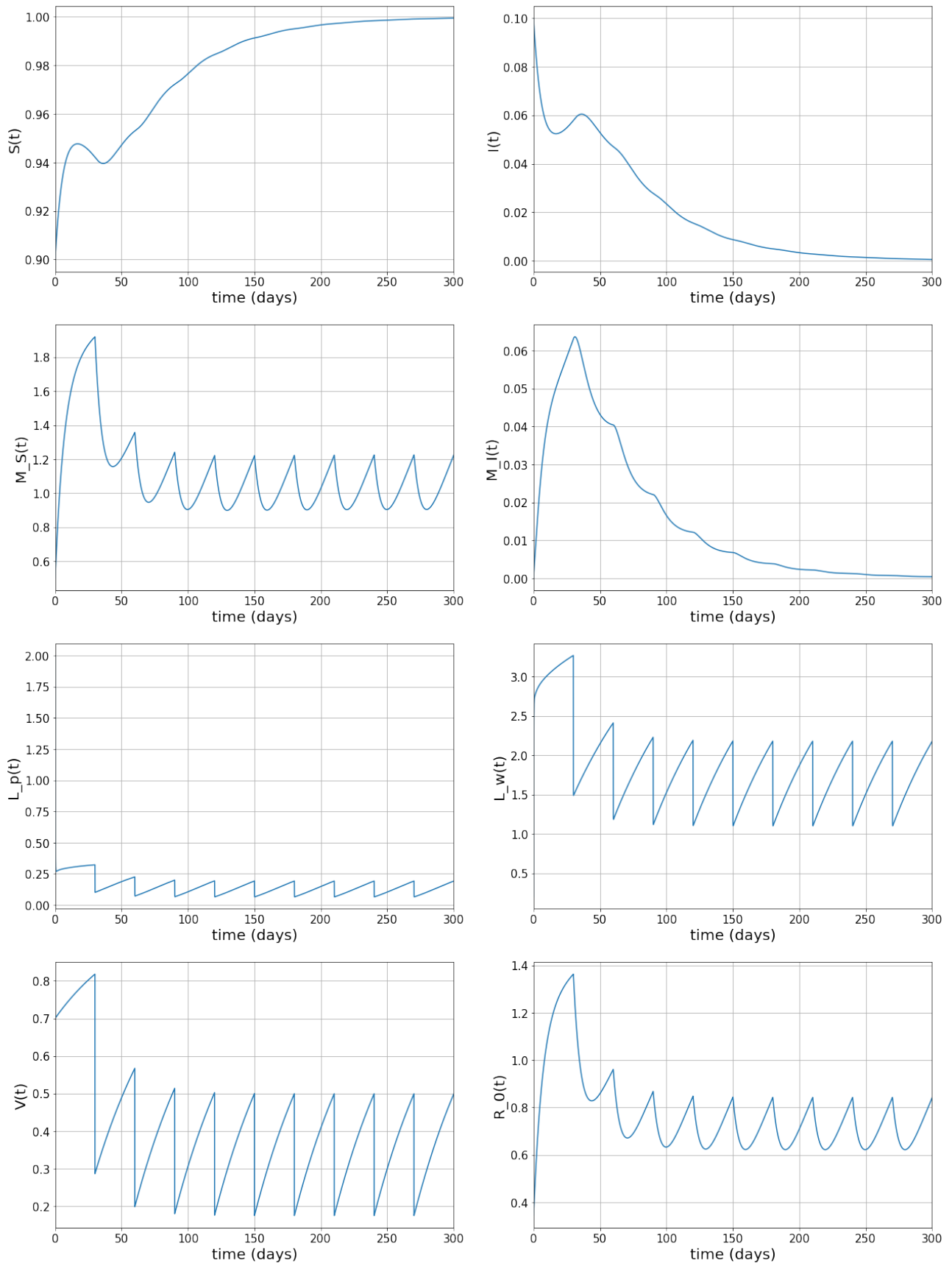


Figure 3.7: Behaviour of the system under Scenario 2

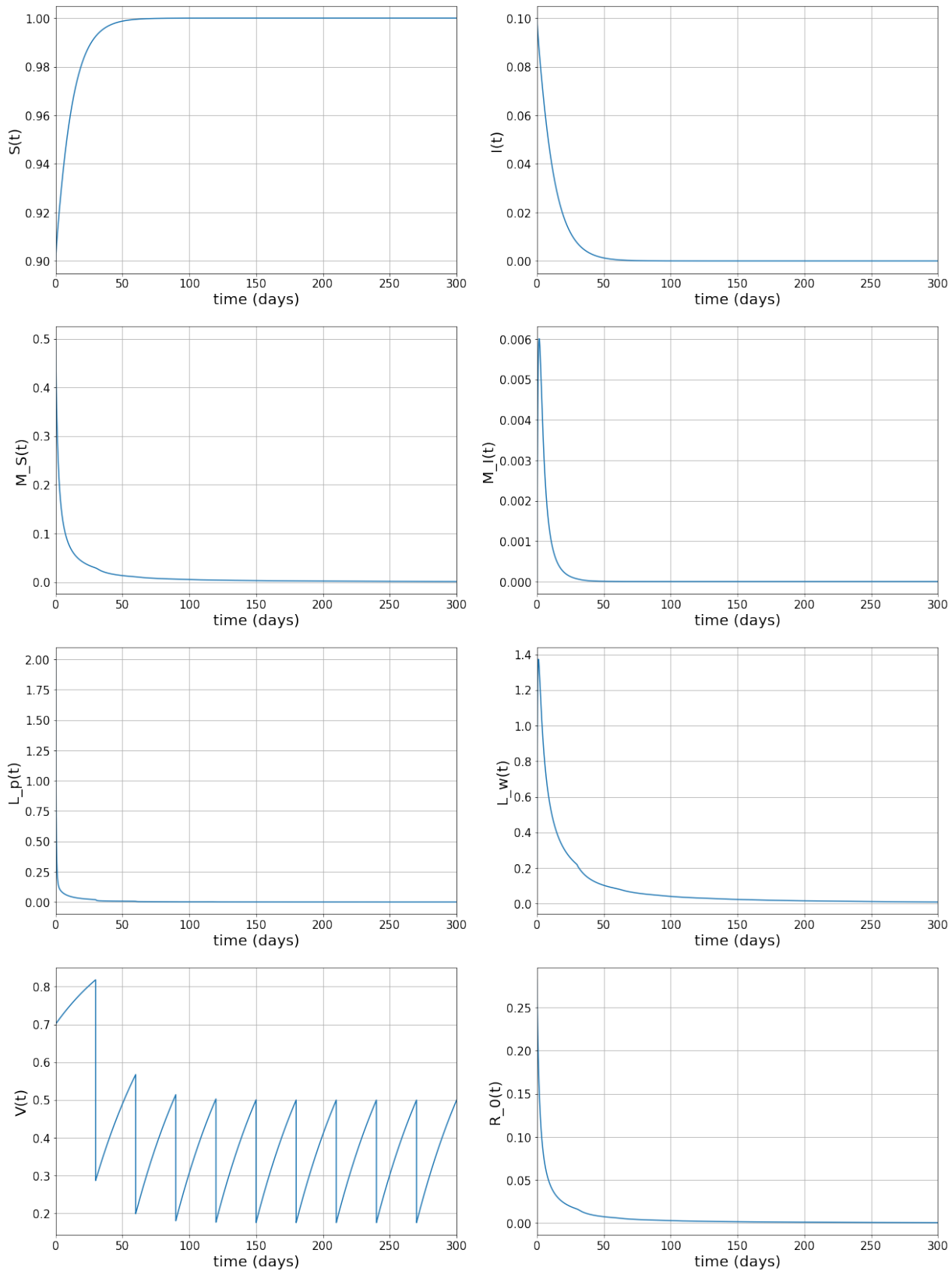


Figure 3.8: Behaviour of the system under Scenario 3

3.5.2 Analysis

First, some comments about Theorem 3.2. Both (Condition 1) and (Condition 2) depend on the basic offspring number \mathcal{N} , and they cannot be simplified further, as the maxima (or minima) of $\frac{K_w}{K_p + K_w}(V_{per})$ and of $\frac{K_p}{K_p + K_w}(V_{per})$ may not occur at the same time t . If they actually occur at the same time t , then the expressions in (Condition 1) reduces to 1.

(Condition 1) and (Condition 2) do not exhaust the possibilities for system, as \mathcal{N}^{-1} can be larger than the sum of minima in (Condition 2) and smaller than the sum of maxima in (Condition 1). Numerical simulations in the current section illustrate that in the latter case, the mosquito population assume periodic behaviour close to 0.

For the *periodic mosquito population* M_{per} , we do not have an analytical expression as we have for V_{per} in Proposition 3.4. The periodic behaviour of the population will be illustrated through numerical simulations along the current section. We are specially concerned with the effects of a reduction in the period τ , which means an increase in cleaning frequency. This reduction in period alters the value of the right-hand side in both (Condition 1) and (Condition 2), by restricting the values of *border vegetation* V_{per} to lower values (as the period τ reduces, vegetation has less time to grow between cleaning episodes). Even if the reduction in period does not change the behaviour from asymptotical periodicity to asymptotical extinction, it does reduce the average size of the mosquito population, which has measurable effects on the incidence of the disease.

Using Table 3.2, we can calculate the range of biologically feasible values for \mathcal{N} , that gives $[0.953, 55.126]$. Figure 3.9 shows the values of both (Condition 1) and (Condition 2) as a function of τ , and compares it to the feasible values of \mathcal{N}^{-1} . It is possible to observe that elimination of the mosquito population through border vegetation removal is unfeasible. However, Figure 3.9 also shows that an increase in cleaning frequency reduces the mosquito population.

We now prove the following corollary to Theorem 3.2.

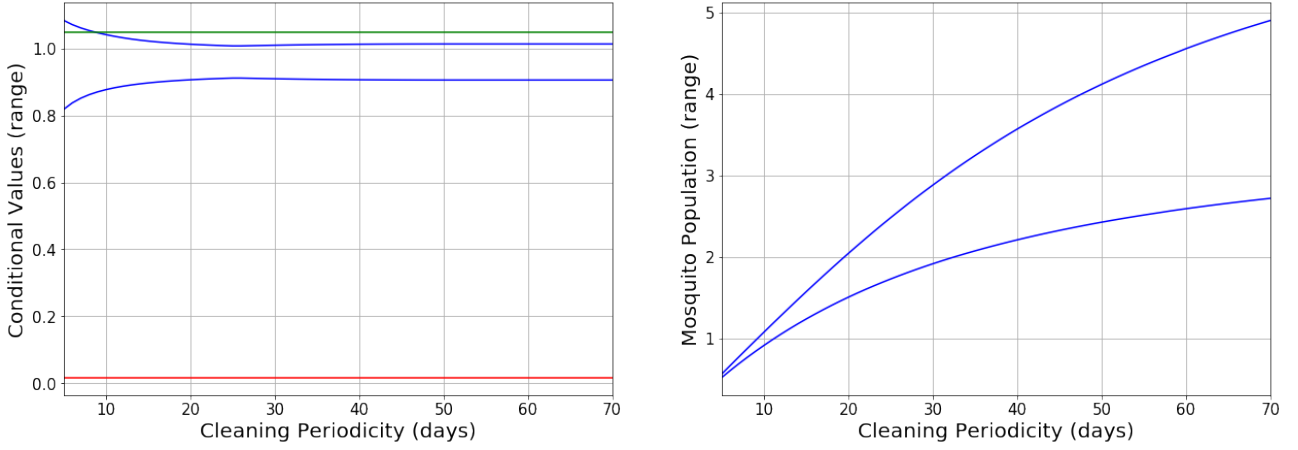


Figure 3.9: Conditional values of Theorem 3.2, as function of τ : On the left, the conditional values (in blue) are compared with the biologically feasible range of \mathcal{N}^{-1} (best value in green and worst in red). On the right, the maximum and minimum value for the mosquito population as function of τ

Corollary 3.3.1. *Assume that K_w and K_p are proportional, that is*

$$K_p/K_w \equiv \rho,$$

with ρ constant. Then the conditions for Theorem 3.2 are simplified to

1. *If $\mathcal{N} \leq 1$, then $\lim_{t \rightarrow +\infty} X(t) = 0$ for all feasible initial conditions.*
2. *If $\mathcal{N} > 1 + \rho$, then there is a strictly positive periodic solution which attracts all initial conditions.*

Proof. From the proportionality of $K_w(V)$ and $K_p(V)$, we have

$$\frac{K_w}{K_p + K_w}(V) = \frac{1}{1 + \rho}, \quad \frac{K_p}{K_p + K_w}(V) = \frac{\rho}{1 + \rho}.$$

As ρ is constant, the expression in (Condition 1) becomes

$$\mathcal{N}^{-1} \geq \frac{1}{1 + \rho} + \frac{\rho}{1 + \rho} = 1,$$

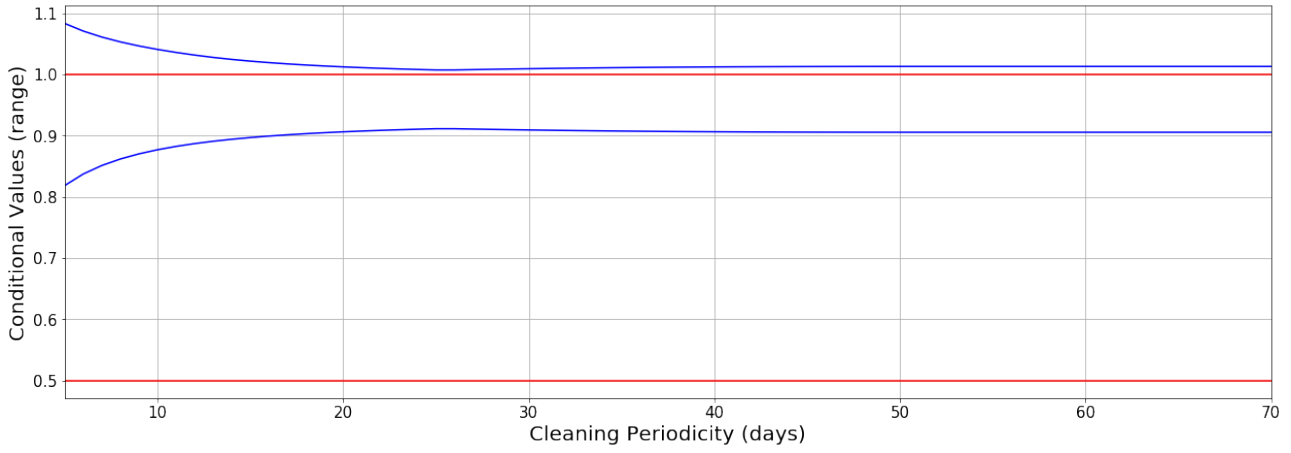


Figure 3.10: Comparison of Corollary 3.3.1: The conditional threshold values for \mathcal{N}^{-1} as function of cleaning periodicity are drawn for two situations. In blue, affine K_w and sigmoid K_p . In red, $K_w \equiv K_p$.

and the expression for (Condition 2) becomes

$$1 + \rho < \mathcal{N},$$

from which the statement of the corollary follows.

□

Corollary 3.3.1 is exemplified in Figure 3.10, where we compare the threshold values for the conditions over \mathcal{N}^{-1} in two situations:

1. when K_w is affine and K_p is sigmoid (as we did in the other simulations),
2. when $K_w \equiv K_p$, that is, $\rho = 1$.

As the corollary predicts, in situation 2. the threshold values are constant and equal to 1 and $(1 + \rho)^{-1} = 0.5$. For situation 1. the threshold values vary along with cleaning periodicity. In our simulations, we chose different functions for K_w and K_p so as not to fall into the particular case of Theorem 3.2 described in Corollary 3.3.1.

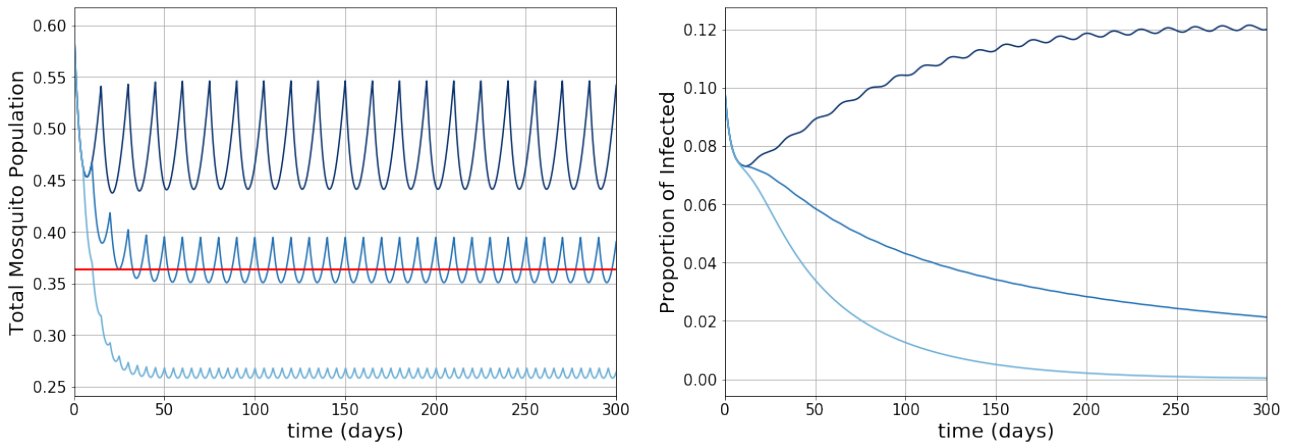


Figure 3.11: Three possible situations of Theorem 3.3: On the left, M_{per} (in shades of blue) in three situations: with minimum greater than the threshold value (in red), threshold smaller than maximum and greater than minimum, and maximum smaller than threshold. On the right, the corresponding I (in shades of blue) in the respective three situations: Asymptotic periodic, indeterminate and convergent to 0.

Now, consider Theorem 3.3. In situation 1, the disease is eradicated. In situation 2, it becomes endemic, with varying incidence levels. Again, both conditions are *sufficient* conditions, and do not exhaust the possibilities. The case where

$$\frac{\beta_{hv}\beta_{vh} \min_{t \in [0, \tau)} M_{per}(t)}{\kappa\mu_M} \leq 1 < \frac{\beta_{hv}\beta_{vh} \max_{t \in [0, \tau)} M_{per}(t)}{\kappa\mu_M},$$

was observed through numerical simulation to assume periodic behavior close to 0. Figure 3.11 shows the possible situations described in Theorem 3.3.

It is interesting to compare the formula for the conditions of Theorem 3.3 with the *basic reproduction number* \mathcal{R}_0 for the disease, defined for a constant mosquito population M , which is given by

$$\mathcal{R}_0 \doteq \frac{\beta_{hv}\beta_{vh}M}{\kappa\mu_M}.$$

This number is interpreted as the average amount of new infections an infected person causes during one infective period if introduced in a completely susceptible population. In standard compartmental models (see e.g. [VdDW02]), when $\mathcal{R}_0 > 1$, there is a locally asymptotically stable endemic equilibrium. Conversely, when $\mathcal{R}_0 < 1$ the disease goes extinct, with the infected

Parameter	Biological Meaning	Values
r	vegetation growth rate	0.01666
τ	Period of pond cleaning (1/frequency)	varying
H	Population engaging in cleaning	0.05
γ	efficacy of cleaning	0.65
α	mean number of eggs per mosquito which become larvae	26.2
ν	aquatic to adult transition rate (per day)	0.0641
μ_L	larval mortality rate on ponds without fish	0.62
μ_p	larval mortality due to predation by fish	0.31
μ_M	adult mosquito mortality rate (per day)	0.16
$K_p(1)$	carrying capacity in ponds with fish if $V = 1$	0.4
$K_w(1)$	carrying capacity in ponds without fish if $V = 1$	4
κ	malaria (vivax) recovery rate for infected humans (per month)	0.0909
β_{vh}	mosquito to human malaria infection rate	0.2
β_{hv}	human to mosquito malaria infection rate	0.2

Table 3.5: Value of parameters for the simulation of the effect of cleaning frequency change

state variables converging to zero. If we defined a *time dependent* reproduction number by

$$\mathcal{R}(t) := \frac{\beta_{hv}\beta_{vh}M_{per}(t)}{\kappa\mu_M},$$

which depends on the mosquito population at time t , our conditions would amount to

$$\max_{t \in [0, \tau)} \mathcal{R}(t) \leq 1$$

for convergence to 0 and to $1 < \min_{t \in [0, \tau)} \mathcal{R}(t)$ for the disease to be endemic, with a globally attractive strictly positive periodic solution.

From Theorem 3.3, the value

$$\frac{\kappa\mu_M}{\beta_{hv}\beta_{vh}}$$

is a threshold value for the mosquito population. If the maximum value of the mosquito population is below this threshold, the disease is eradicated. Again, Table 3.2 allows us to calculate the biologically feasible range for it, giving $[0.023, 7.724]$.

The biological meaning of the parameters in the conditions of Theorem 3.3 are the *transmission rate* (both, from vector to host and from host to vector), the *recovery rate*, the *mosquito mortality*, and the size of *mosquito population*. These give hints to the more effective ways

of fighting malaria: prevention of bites, treating infected individuals quickly, and controlling mosquito population. From the epidemiologist or the public health practitioner point of view, the most important point is to have a grasp on the relative effects of each factor on malaria transmission [MSS11].

We simulate the effect of an increase in the frequency of cleaning, using the set of parameters described in Table 3.5. The values for τ range from 70 to 5 days. In Figure 3.12, we represent the maximum and minimum value of both the $\mathcal{R}(t)$ and the size of the infected human population (after they assume periodic behaviour) as a function of τ . The green line at 1 shows the threshold value for $\mathcal{R}(t)$.

The effect of an increased frequency of cleaning is a reduction of the average mosquito population, and consequently a reduction of the average infected population. Eventually, the solution's asymptotic behaviour changes from asymptotic periodic to convergence towards 0. Even with moderate efforts, the average proportion of infected humans is significantly reduced.

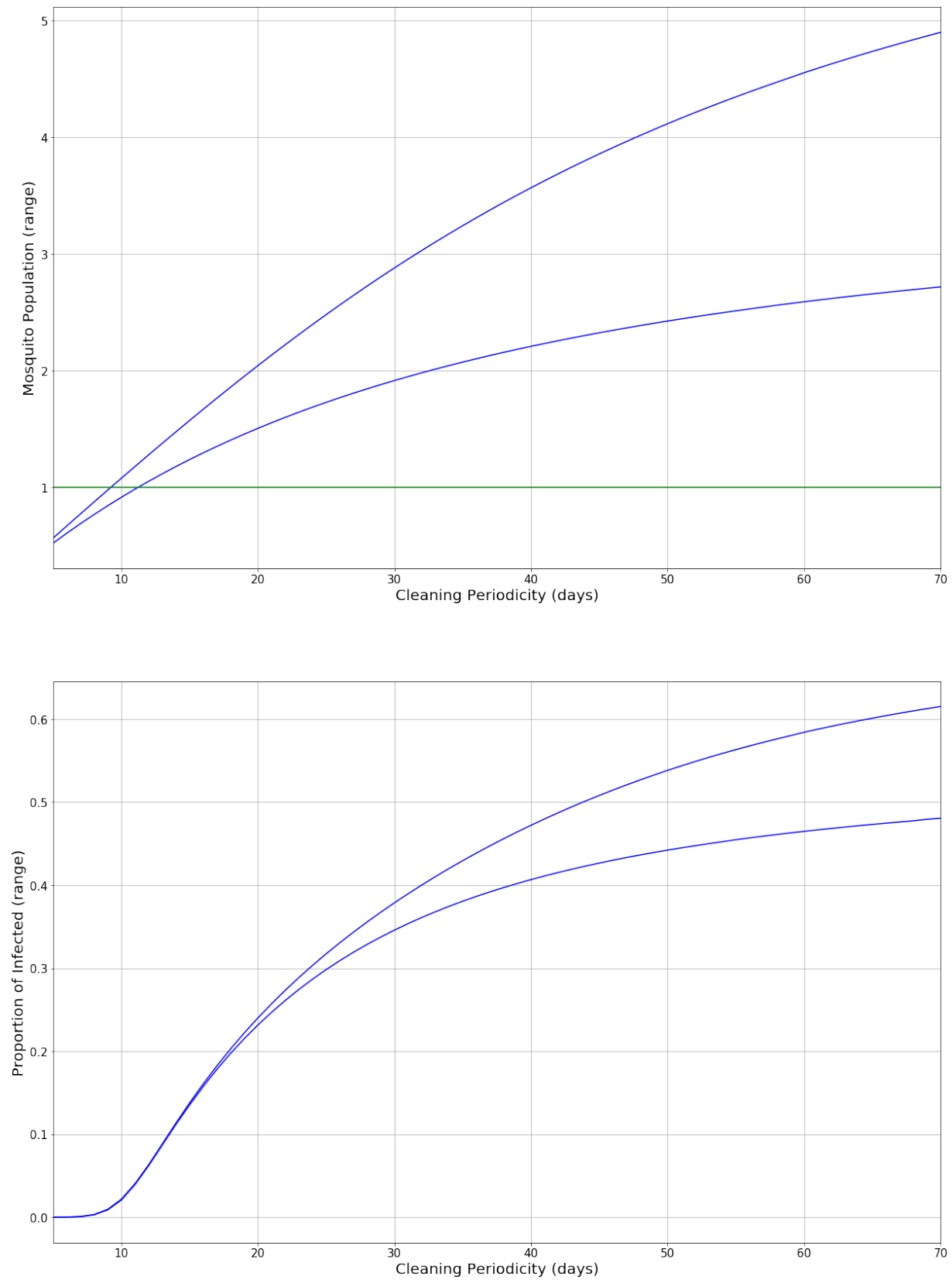


Figure 3.12: Behaviour of the disease under increasing cleaning frequency.

3.5.3 The effect of awareness in cleaning periodicity

As the cost of cleaning is 300 *reais*, we can estimate the daily averaged cost of cleaning every τ days as

$$C_{\text{clean}}(\tau) = -300/\tau.$$

Conversely, we can estimate the expected cost of getting sick as a function of τ by assuming a Bernoulli distribution for the sick state with probability equal to the asymptotic averaged proportion of infected, and calculating the monetary cost by the number of days of work lost due to the disease. Considering a minimum wage of 900 *reais* for 30 days of work, and 5 days of work lost due to the disease, we get a disease cost of 150 *reais*. Denoting the asymptotic average proportion of infected as $\bar{I}(\tau)$, the disease cost is

$$C_{\text{disease}} = -150\bar{I}(\tau).$$

Assuming that the whole population is aware of the relation between border vegetation and malaria, the period of vegetation cleaning τ will be at a value such that people are indifferent to cleaning more frequently or getting the disease, that is, the cost of cleaning as function of τ is equal to the cost of getting sick as function of τ . For a fully aware population, this would lead to $\tau \leq 20$, as shown in Figure 3.13.

Assuming that the population is fully aware is a strong hypothesis. We can include an awareness multiplier a in the disease cost, such that the *perceived* cost of the disease is given by

$$C_{\text{perceived}} = aC_{\text{disease}}.$$

For $a = 0.1$, we have $40 \leq \tau \leq 60$ as shown in Figure 3.13, a value in the observed range.

This difference in cleaning frequency argues in favor of educational campaigns explaining the relationship between malaria and border vegetation, as increased awareness would, in theory, lead to an increased frequency of vegetation border cleaning and overall lower levels of malaria incidence.

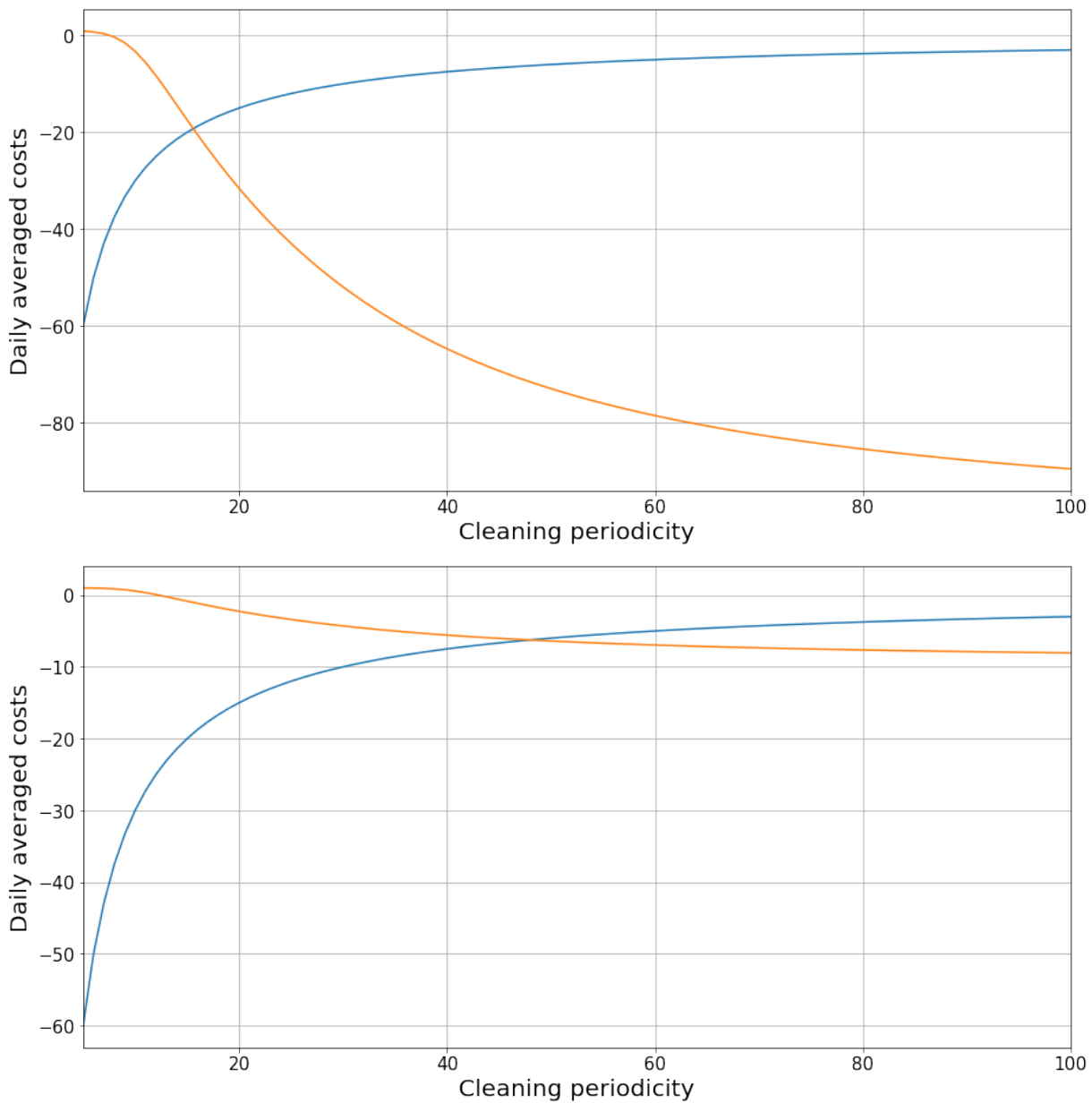


Figure 3.13: Cost comparison of cleaning and disease. Cost of cleaning as a function of τ is represented in blue, and the perceived expected daily cost of disease as a function of τ is represented in orange. In the first graph we assume the population is fully aware of the relation between cleaning and the disease. On the second graph, we assume an awareness factor $a = 0.1$.

Chapter 4

Conclusion

In this work, we achieved both theoretical and applied results. We studied the real world problem of malaria in Acre through the lens of mathematical modelling, proposing a system of differential equations as an epidemiological model. We also studied the theoretical background of concave, cooperative differential equations, going as far as extending a classical result to encompass the system of equations employed in the model.

In Chapter 2 we analyzed properties of cooperative systems of differential equations with concave non-linearities and time-measurable dynamics. We reviewed classical results, such as the Existence Theorem for Carathéodory Solutions, and the literature on the asymptotic behaviour of cooperative systems with concave non-linearities. Our main result is Theorem 2.22, which extends the theorems in [Smi86, Jif90] to time-measurable functions. This allows us to analyze the our epidemiological model with periodic impulses on border vegetation.

Throughout Chapter 3, an in-depth analysis of Malaria in Acre was made. Some historical aspects of the theory of mathematical modelling of diseases was reviewed, along with the current knowledge about malaria in Alto Juruá. We presented a model integrating malaria, mosquito population and ponds' vegetation evolution, and studied its asymptotic behaviour.

Our model aimed to analyze the relation between border vegetation cleaning and the incidence of the disease. Some simplifying assumptions were made:

- The system dynamics is considered spatially independent, and homogeneous for each compartment.
- Vegetation cleaning is assumed to be synchronized, to happen periodically, and its time frame is small when compared to the time frame of the mosquito population and disease dynamics (i.e. As would happen in a small fish farming cooperative, where cleaning is a coordinated activity).
- We disregard a recovered compartment that cannot be infected due to the high rate of reinfection of *Plasmodium vivax*.
- Conversely, we disregard human mortality and consider the population normalized to 1, due to the low mortality rate of *Plasmodium vivax*.

Through Theorems 3.2 and 3.3, we established conditions for determining the asymptotic behaviour of the system. Through analysis of these sufficient conditions we can conclude that border vegetation cleaning reduces the average mosquito population, and this in turn affects the rate at which malaria spreads through human hosts.

Numerical simulations of the model have shown that

- eliminating the mosquito population through border vegetation removal is biologically unfeasible,
- reducing the incidence of malaria through border vegetation removal is feasible,
- increasing awareness of the relation between malaria and border vegetation may affect human population behaviour and increase cleaning frequency.

Our results argue in favor of educational campaigns and incentives for fish ponds maintenance as other public health measures to control malaria in Acre.

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