

ASYMPTOTIC BEHAVIOUR OF COOPERATIVE SYSTEMS: AN APPLICATION TO MALARIA CONTROL

FELIPE J.P. ANTUNES ^{*}, M. SOLEDAD ARONNA [†], AND CLÁUDIA T. CODEÇO [‡]

Abstract. In this work we propose a model that represents the relation between fish ponds, the mosquito population and the transmission of malaria. It has been observed that in the Amazonic region of Acre, in the North of Brazil, fish farming is correlated to the transmission of malaria when carried out in artificial ponds that become breeding sites. Evidence has been found indicating that cleaning the vegetation from the edges of the crop tanks helps to control the size of the mosquito population.

We use our model to determine the effective contribution of the fish tanks to the epidemic. The model consists of a nonlinear system of ordinary differential equations with jumps at the cleaning time, which act as *impulsive controls*. We study the asymptotic behaviour of the system in function of the intensity and periodicity of the cleaning, and the value of the parameters. In particular, we state sufficient conditions under which the mosquito population is exterminated or prevails, and under which the malaria is eradicated or becomes endemic.

Key words. example, L^AT_EX

AMS subject classifications. 92B05, 92D30, 92D25, 34C12, 34C25

1. Introduction. Malaria is a disease caused by parasites of genus *Plasmodium*, transmitted to human beings through the bite of the female *Anopheles darlingi* mosquito. This species of mosquito is highly antropophilic and is present throughout the whole Amazon river basin [6]. 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 five 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 [6]. 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 there are four counties with high incidence of the disease: Cruzeiro do Sul, Mâncio Lima, Rodrigues Alves and Tarauacá [6]. 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 [5] give evidence that fish ponds are correlated to an increase in mosquito population, with fish ponds having four times more larvae than natural water bodies. Cases of malaria also spatially and temporally correlated with the opening of fish ponds. The most significant predictor of larval incidence found in [5] was percentage of border vegetation, which *Anopheline* larvae use to hide from potential predators. Overall, increase of border covered with vegetation was correlated with 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 more infested than those for family use. However, if the

^{*}Escola de Matemática Aplicada FGV EMap, Fundação Getulio Vargas, Rio de Janeiro, Brazil (fjpantunes2@gmail.com).

[†]Escola de Matemática Aplicada FGV EMap, Fundação Getulio Vargas, Rio de Janeiro, Brazil (soledad.aronna@fgv.br, <https://sites.google.com/view/aronna>).

[‡]Programa de Computação Científica-Fundação Oswaldo Cruz, Rio de Janeiro, Brazil (codeco@fiocruz.br).

amount of border vegetation is low enough, then commercial ponds were less infested with larvae than non-commercial ponds; this is attributed to the high amount of fishes predating on the mosquito larvae. We incorporate the possibility of presence of larvae predatory fish in our model. 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.

Some simplifying assumptions are made for the model we proposed here. 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 it occurs 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 impulses that are 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.

The article is organized as follows. A detailed description of the model, its components and assumptions are given in Section 2. We derive analytical and numerical results from the model. In Section 3 we apply Theorem B.3 to the study of the asymptotic behaviour of our system, establishing sufficient conditions for the mosquito population and the disease to either assume asymptotic periodic behaviour or to be eradicated. In Section 4, we simulate the system numerically in order to illustrate 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.

1.1. Notation and preliminary definitions. In this section, we introduce some notation and definitions that will be used throughout the article.

Given any function u defined in the interval $(t, t + \epsilon_0)$ (resp., $(t - \epsilon_0, t)$), set $u(t^+) := \lim_{\epsilon \rightarrow 0^+} u(t + \epsilon)$ (resp., $u(t^-) := \lim_{\epsilon \rightarrow 0^-} u(t - \epsilon)$). For $x, y \in \mathbb{R}^n$, we write $x < y$ and $x \leq y$ if the inequalities hold component-wise. We use $x \lesssim y$ if $x \leq y$ and $x \neq y$. If x and y are matrices, then the inequalities should hold entry-wise. For $x < y$, we define $[x, y] := \{z : x \leq z \leq y\}$, $(x, y] := \{z : x < z \leq y\}$ and $(x, y) = \{z : x < z < y\}$.

Given an open set $\Omega \subseteq \mathbb{R} \times \mathbb{R}^n$, Our model will be a differential equation of the form

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

where $\mathcal{F}: \Omega \rightarrow \mathbb{R}^n$ is differentiable w.r.t. x , measurable and τ -periodic w.r.t. t . The function \mathcal{F} is called *concave* if $0 < x < y$ implies

$$D_x \mathcal{F}(t, x) \succeq D_x \mathcal{F}(t, y),$$

where $D_x \mathcal{F}(t, x)$ denotes the *Jacobian matrix* of \mathcal{F} with respect to x . The system is

called *cooperative* if

$$\frac{\partial \mathcal{F}_i}{\partial x_j}(t, x) \geq 0, \quad \text{for } i \neq j,$$

for $(t, x) \in \Omega$. This is equivalent to saying that $D_x \mathcal{F}(t, x)$ has non-negative off-diagonal terms.

Given a Cauchy problem associated to (1.1) and with initial condition $x(t_0) = x_0$, we write $\mathbf{x}(t; t_0, x_0)$ to denote the value of an associated trajectory at time t . A *Carathéodory solution* of a Cauchy problem is an absolutely continuous function $t \mapsto \mathbf{x}(t; t_0, x_0)$ defined on some interval $[t_0, t_1]$ which satisfies (1.1) almost everywhere. We may simply write $\mathbf{x}(t)$ if both t_0 and x_0 are implicit from the context.

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 (1.1) with $x(t_0) = x_0$ satisfies $x(t) \in \mathcal{K}$ for every $t > t_0$ for which the solution x is defined, then we say that \mathcal{K} is a *forward invariant set* for \mathcal{F} . We say that a trajectory \mathbf{x} is *globally asymptotic attractive* for (1.1) if, for every $(t_0, x_0) \in \Omega$, the solution x of (1.1) with initial condition $x(t_0) = x_0$ satisfies

$$(1.2) \quad \lim_{n \rightarrow \infty} \max_{t \in [n, \infty)} |\mathbf{x}(t; t_0, x_0) - x(t)| = 0.$$

An $n \times n$ -matrix A is called *cooperative* if its off-diagonal entries are non negative. 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 its determinant is the *leading principal minor*.

Given a time-dependent $n \times m$ -matrix $A: [0, \tau] \rightarrow \mathbb{R}^{n \times m}$ set, for $i = 1, \dots, n$, $j = 1, \dots, m$, $\bar{a}_{ij} := \text{ess sup}_{[0, \tau]} a_{ij}(t)$, $\underline{a}_{ij} := \text{ess inf}_{[0, \tau]} a_{ij}(t)$, and write \bar{A} and \underline{A} for the $n \times m$ -matrices with entries $\bar{a}_{i,j}$ and $\underline{a}_{i,j}$, respectively.

2. The Model. In this section we introduce the model. More precisely, in subsection 2.1, we present a model for the interaction between the spread of malaria and the mosquito population dynamics. Subsection 2.2 is dedicated to the model for border vegetation growth and human action, that consists in border cleaning. Finally, subsection 2.3 joins both models in order to asses cleaning border vegetation as a control method for malaria.

2.1. Malaria Model. A rough malaria model will be introduced, joining ideas *e.g.* from [11] and the classical model by Ross [14]. In the Amazonian region, the prevalent malaria is due to *Plasmodium vivax*, which has negligible mortality and a high rate of reinfection [5, 6]. We therefore disregard the possibility of gaining immunity to the disease (that is, we discard the inclusion of a *recovered* compartment R in our malaria *SIS* model).

We combine an *SIS* model for the disease with a two-stage aquatic-adult population model for the mosquitoes. Both the human and adult mosquito populations are divided in two compartments, namely susceptible and infected. The proportion of susceptible humans is denoted by S , and the proportion of infected by I . In regard to mosquito population, we consider an aquatic stage L gathering eggs, larvae and pupae, which is subjected to resource competition; and two adult stages, the susceptible adults M_S and the infected adults M_I .

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:

$$\begin{aligned}
 \dot{S} &= -\beta_{vh}SM_I + \kappa I, \\
 \dot{I} &= \beta_{vh}SM_I - \kappa I, \\
 \dot{M}_S &= \nu L - \beta_{hv}IM_S - \mu_M M_S, \\
 \dot{M}_I &= \beta_{hv}IM_S - \mu_M M_I, \\
 \dot{L} &= \alpha(M_I + M_S) \left(1 - \frac{L}{K}\right) - (\nu + \mu_L)L,
 \end{aligned}
 \tag{2.1}$$

where the meaning of the involved parameters is given in Table 1.

Parameter	Biological Meaning
K_p, K_w	Aquatic stage carrying capacity of fish ponds with/without predatory fish, respectively, as a function of border vegetation.
τ	Period of vegetation cleaning in days.
α	Intrinsic reproduction rate
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.
γ	Proportion of vegetation removed as a function of time.

TABLE 1

Biological meaning of the parameters for systems (2.1) and (2.3).

2.2. Dynamics of Vegetation. Next we present a model for the growth of the border vegetation of the fish tanks, which is supposed to be affected by periodic cleaning. Previous studies in the Alto Juruá region [5, 6] established a correlation between lack of cleaning and presence of *Anopheles* larvae in fish farming ponds. We model this in such a way that the carrying capacity of larvae is a function of the proportion of ponds' border covered by vegetation. We assume that the percentage of border vegetation $V : \mathbb{R}_+ \mapsto [0, 1]$ grows proportionally to available space $1 - V$, and that *some* cleaning occurs every τ days, in which a part γ of border vegetation is removed. Hence $\gamma : \mathbb{R}_+ \mapsto [0, 1]$ is the fraction of vegetation cleaned as function of time. More precisely, at day $n\tau$, the proportion of vegetation removed is $\gamma(n\tau)$. We propose the following system of impulsive ordinary differential equations to model the described situation:

$$\begin{aligned}
 \frac{dV(t)}{dt} &= r(1 - V(t)), \quad \text{for } t \neq \tau n, \\
 V(n\tau^+) &= V(n\tau) - \gamma(n\tau)V(n\tau), \quad \text{for } n \in \mathbb{N} \setminus \{0\}, \\
 V(0) &= V_0,
 \end{aligned}
 \tag{2.2}$$

where $r > 0$ is the vegetation growth rate (see Table 1).

PROPOSITION 2.1. *Given any initial condition $V_0 \in [0, 1]$, there exists a unique solution of (2.2), it is defined in $[0, +\infty)$, it is left-continuous and takes values in $[0, 1]$.*

Proof. The proof follows by induction on n . For $n = 1$, let us consider the interval $[0, \tau)$. It is straightforward that $V(t) = 1 - (1 - V_0)e^{rt}$ is a solution of (2.2) in $[0, \tau]$. Moreover, it is unique, it is continuous and takes values in $[0, 1]$. Suppose now that there exists a unique solution V_n defined on $[0, n\tau]$ that is left-continuous and takes values in $[0, 1]$. Set $V_n^+ := (1 - \gamma(n\tau))V_n(n\tau^-)$. Since $V_n(n\tau^-) \in [0, 1]$ and $1 - \gamma(n\tau) \in [0, 1]$, we have that $V_n^+ \in [0, 1]$. Consider the initial value problem on $[n\tau, (n+1)\tau]$:

$$\dot{V}(t) = r(1 - V(t)), \quad V(n\tau^+) = V_n^+.$$

It follows easily that $V(t) = 1 - (1 - V_n^+)e^{rt}$ is its unique solution. Set now

$$V_{n+1}(t) := \begin{cases} V_n(t), & \text{for } t \in [0, n\tau] \\ 1 - (1 - V_n^+)e^{rt}, & \text{for } t \in (n\tau, (n+1)\tau]. \end{cases}$$

The function V_{n+1} is the unique solution of (2.2) in $[0, (n+1)\tau]$ and satisfies the desired properties. This concludes the inductive step and the proof. \square

2.3. The Complete Model. We conclude the construction of our model by putting together (2.1) and (2.2), and adding a new feature that consists in assuming two different types of ponds, namely *with predatory fish* and *without predatory fish*. This difference induces a splitting in the aquatic stage L into L_p and L_w , corresponding to larvae in ponds with and without predatory fish, respectively. Border vegetation on fish ponds affects the dynamics through two effects. First, both carrying capacities K_p and K_w are given, and they are strictly increasing continuous functions of border vegetation that assume strictly positive values. Second, vegetation protects larvae from predation in ponds with predatory fish by offering hiding places for larvae [5], a feature that we model by adding the extra mortality rate $\mu_p(1 - V)$ to L_p , which decreases predation as vegetation increases. The following system describes the joint dynamics of malaria, aquatic-stage and adult mosquitoes, and vegetation:

(2.3)

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

where the biological meaning of the parameters is given in Table 1. The compartmental diagram for system (2.3) is shown in Figure 1.

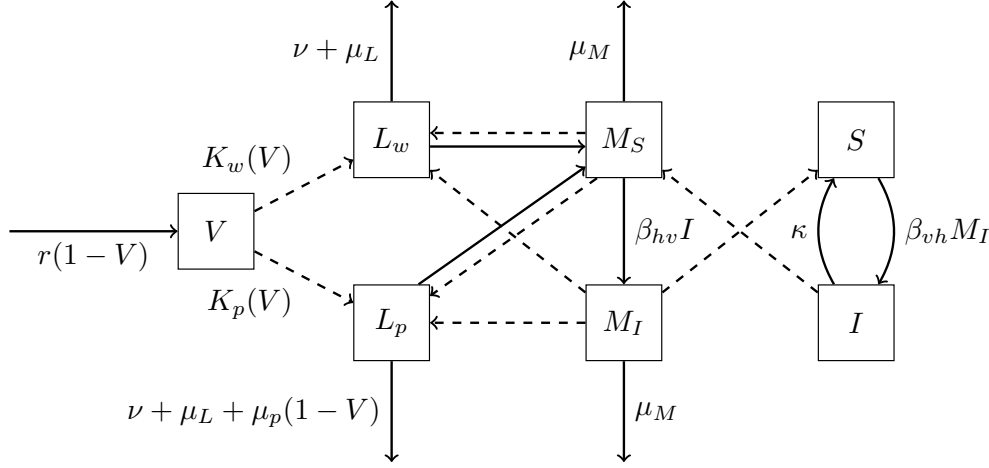


FIG. 1. *Compartmental diagram for the dynamics described in system (2.3).*

We now state and prove results concerning properties of solutions to initial value problems for system (2.3). Consider the compact set

$$(2.4) \quad \mathcal{K} := \left\{ (V, M_S, M_I, L_p, L_w, S, I) \in \mathbb{R}_+^7 : V \leq 1, S + I \leq 1, \right. \\ \left. M_S + M_I \leq (\nu/\mu_M)(L_p + L_w), L_p \leq \max_{V \in [0,1]} K_p(V), L_w \leq \max_{V \in [0,1]} K_w(V) \right\}.$$

PROPOSITION 2.2. *Given an initial condition x_0 belonging to \mathcal{K} , there exists a unique Carathéodory solution of (2.3) with value x_0 at $t = 0$, it is defined in $[0, \infty)$ and remains in \mathcal{K} . The last assertion states that \mathcal{K} is positively invariant under (2.3).*

Proof. The equation for the vegetation can be solved independently of the rest of the system, and gives a solution V that is left-continuous and bounded (thanks to Proposition 2.1). Inserting this solution in the equations for M_S, M_I, L_p, L_w, S, I yields a system that satisfies the conditions of Theorem A.1 in the Appendix A, which guarantees local existence.

Proof of positive invariance of \mathcal{K} follows easily by checking that, when a trajectory issuing from \mathcal{K} hits the boundary of \mathcal{K} , the dynamics pushes the trajectory inwards the set.

The existence of a global solution is a consequence of Theorems A.1-A.3 in the Appendix A. \square

3. Asymptotic behaviour. In this section we study the asymptotic behaviour of system (2.3). We split this analysis in three parts. In subsection 3.1 our focus is the vegetation system (2.2). We prove, in Proposition 3.1, that if cleaning at times $t = n\tau$ tends to a constant value then border vegetation approaches a τ -periodic solution. Subsection 3.2 is dedicated to the study of the behaviour of mosquito population when border vegetation is periodic, and 3.3 investigates malaria incidence under periodic vegetation cleaning. We derive sufficient conditions for the trajectories of (2.3) to asymptotically approach either a positive solution or the origin.

3.1. Asymptotic behaviour of vegetation. We focus now on the vegetation model (2.2). We aim to prove that if cleaning is done every τ days and approaches a constant value, then the vegetation converges to a periodic solution that is discontinuous at the cleaning times. We get the following result.

PROPOSITION 3.1 (Periodic solutions for vegetation).

Let $\gamma^* \in [0, 1]$, and assume that $\gamma: [0, \infty) \rightarrow [0, 1]$ is such that $\lim_{t \rightarrow \infty} \gamma(t) = \gamma^*$. Then any trajectory V of (2.2) with initial condition in $[0, 1]$ converges to the periodic solution

$$(3.1) \quad V_{\text{per}}(t) := 1 - \frac{\gamma^* e^{-r(t-n\tau)}}{1 - (1 - \gamma^*)e^{-r\tau}}, \quad \text{for } t \in [n\tau, (n+1)\tau),$$

in the following sense:

$$(3.2) \quad \max_{t \in [n\tau, (n+1)\tau)} |V(t) - V_{\text{per}}(t)| \rightarrow 0, \quad \text{as } n \rightarrow \infty.$$

Proposition 3.1 follows from a direct application of Lemma C.1 in the Appendix C by setting $\gamma_n := \gamma(n\tau)$. We conclude that, under periodic cleaning, the border vegetation approaches a periodic behaviour. Figure 2 illustrates Proposition 3.1, by showing the solutions to the impulsive initial value problem (2.2) for a range of initial values in $[0, 1]$ and for values of γ sampled at each $n\tau$ from an uniform distribution over the interval $[0.65 * (1 - \frac{5}{n\tau}), (0.65 + (1 - 0.65) \frac{5}{n\tau})]$, so that the values of γ at $n\tau$ converge to 0.65. Note that at each point of discontinuity, the trajectories come closer together, and asymptotically approach V_{per} .

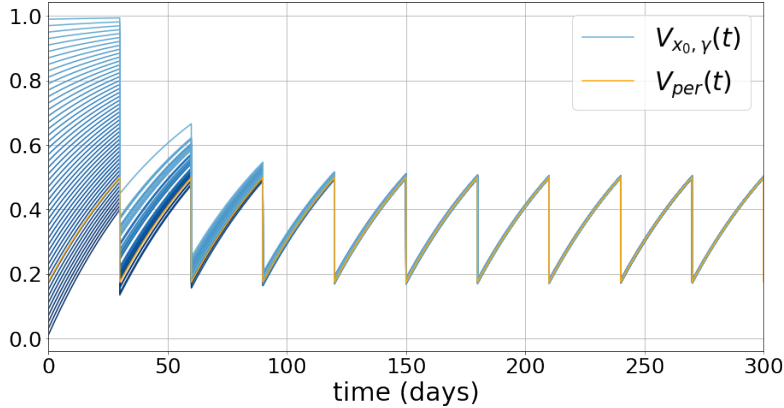


FIG. 2. Impulsive behaviour of System (2.2), for different initial values. V_{per} is shown in orange.

3.2. Asymptotic behaviour of mosquito population. We now turn to the analysis of the asymptotic behaviour of the mosquito population, assuming that border vegetation is periodic equal to V_{per} . 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 with positive values.

Recalling system (2.3), there are two aspects to consider. First, that vegetation behaviour impacts the system through the aquatic compartments L_w and L_p , then

both carrying capacities $K_w(V_{\text{per}})$ and $K_p(V_{\text{per}})$ are also periodic. Second, by setting $M := M_S + M_I$, we can isolate mosquito population dynamics in the following subsystem:

$$(3.3) \quad \begin{aligned} \dot{L}_p &= \alpha \frac{K_p(V_{\text{per}})}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} M \left(1 - \frac{L_p}{K_p(V_{\text{per}})} \right) - (\nu + \mu_L + \mu_p(1 - V_{\text{per}})) L_p, \\ \dot{L}_w &= \alpha \frac{K_w(V_{\text{per}})}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} M \left(1 - \frac{L_w}{K_w(V_{\text{per}})} \right) - (\nu + \mu_L) L_w, \\ \dot{M} &= \nu(L_p + L_w) - \mu_M M. \end{aligned}$$

Let us write the system in the compact form $\dot{X}(t) = F(t, X(t))$ for $X := (L_p, L_w, M)^\top$, F being the function on the r.h.s. of (3.3), and let us consider initial conditions on the set

$$(3.4) \quad \mathcal{K}_X := \left\{ (t, L_p, L_w, M) \in \mathbb{R}_+^4 : \right. \\ \left. M \leq \frac{\nu}{\mu_M} (L_p + L_w), L_p \leq K_p(V_{\text{per}}(t)), L_w \leq K_w(V_{\text{per}}(t)) \right\}.$$

Due to the discontinuities and periodicity of V_{per} , the function F itself is piecewise-continuous and τ -periodic both w.r.t. the time variable t . We next apply Theorem B.3 of Appendix B to get the results on the asymptotic behaviour of (3.3) stated in Theorem 3.2 below.

Let us first recall the formula for the *basic offspring number*

$$\mathcal{N} := \frac{\alpha \nu}{\mu_M (\nu + \mu_L)},$$

that represents the *average number of offspring that an individual produces during its lifespan* [19, 7], and is considered a measure of the growth of a population.

THEOREM 3.2 (Asymptotic behaviour of the mosquito population). *The following assertions hold.*

(i) *If both conditions*

$$\begin{aligned} \frac{\left(\max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}}) \dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right) \right) \min_{t \in [0, \tau]} (K_p(V_{\text{per}}) + K_w(V_{\text{per}}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{\text{per}})} &\geq \mathcal{N}, \\ \frac{\left(\max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}}) \dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) \min_{t \in [0, \tau]} (K_p(V_{\text{per}}) + K_w(V_{\text{per}}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_w(V_{\text{per}})} &\geq \mathcal{N}, \end{aligned}$$

are satisfied, then the trajectories of (3.3) asymptotically approach the origin for any initial condition in \mathcal{K}_X .

(ii) *If one of the conditions*

$$\begin{aligned} \frac{\left(\min_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}}) \dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \max_{t \in [0, \tau]} V_{\text{per}} \right) \right) \max_{t \in [0, \tau]} (K_p(V_{\text{per}}) + K_w(V_{\text{per}}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{\text{per}})} &< \mathcal{N}, \\ \frac{\left(\min_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}}) \dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) \max_{t \in [0, \tau]} (K_p(V_{\text{per}}) + K_w(V_{\text{per}}))}{(\nu + \mu_L) \min_{t \in [0, \tau]} K_w(V_{\text{per}})} &< \mathcal{N}, \end{aligned}$$

is satisfied, then there exists a strictly positive periodic solution of (3.3) which attracts all initial conditions in $\mathcal{K}_X \setminus \{0\}$.

Proof. The difficulty in dealing with system (3.3) is that the set \mathcal{K}_X (see (3.4)) where it is monotone is time-dependent, and then the results of Theorem B.3 are not directly applicable. For this reason, we perform a change of variables. Let us set

$$\tilde{L}_p(t) := \frac{L_p(t)}{K_p(V_{\text{per}}(t))}, \quad \tilde{L}_w(t) := \frac{L_w(t)}{K_w(V_{\text{per}}(t))}, \quad \text{for } t \in [0, \tau].$$

Then, on $[0, \tau]$, these functions are derivable and, in the variables $\tilde{L}_p, \tilde{L}_w, M$, system (3.3) becomes

$$\begin{aligned} \dot{\tilde{L}}_p &= \frac{\alpha}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} M (1 - \tilde{L}_p) - \left(\frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p(1 - V_{\text{per}}) \right) \tilde{L}_p, \\ \dot{\tilde{L}}_w &= \frac{\alpha}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} M (1 - \tilde{L}_w) - \left(\frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) \tilde{L}_w, \\ \dot{M} &= \nu (K_p(V_{\text{per}})\tilde{L}_p + K_w(V_{\text{per}})\tilde{L}_w) - \mu_M M. \end{aligned}$$

Extending the latter system to $t \in \mathbb{R}$ by the periodicity of V_{per} , we obtain a system that is cooperative in the time-independent set $[0, 1] \times [0, 1] \times [0, M_{\text{max}}]$, where $M_{\text{max}} := \frac{\nu}{\mu_M} \max_{t \in [0, \tau]} (K_p(V_{\text{per}}) + K_w(V_{\text{per}}))$, and that satisfies the conditions of Theorem B.3.

Next, we compute the matrix $A(t) := D_x F(t, 0)$, and find conditions for all principal minors of $-\bar{A}$ to be non-negative, and conditions for at least one of the principal minor of $-\bar{A}$ to be negative (see definition of \bar{A} and \bar{A} in (B.4)-(B.5)). We have

$$-A(t) = \begin{bmatrix} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p(1 - V_{\text{per}}) & 0 & -\frac{\alpha}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} \\ 0 & \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L & -\frac{\alpha}{K_w(V_{\text{per}}) + K_p(V_{\text{per}})} \\ -\nu K_p(V_{\text{per}}) & -\nu K_w(V_{\text{per}}) & \mu_M \end{bmatrix}.$$

The seven principal minors of $-\bar{A}$ are:

$$\begin{aligned} \bar{p}_1 &:= \left(\max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right) \right) \left(\max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) \mu_M \\ &\quad - \frac{\alpha \nu \max_{t \in [0, \tau]} K_p(V_{\text{per}})}{\min_{t \in [0, \tau]} (K_w(V_{\text{per}}) + K_p(V_{\text{per}}))} \left(\max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) \\ &\quad - \frac{\alpha \nu \max_{t \in [0, \tau]} K_w(V_{\text{per}})}{\min_{t \in [0, \tau]} (K_w(V_{\text{per}}) + K_p(V_{\text{per}}))} \left(\max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right) \right), \\ \bar{p}_2 &:= \mu_M \left(\max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right) - \frac{\alpha \nu \max_{t \in [0, \tau]} K_w(V_{\text{per}})}{\min_{t \in [0, \tau]} (K_w(V_{\text{per}}) + K_p(V_{\text{per}}))}, \\ \bar{p}_3 &:= \mu_M \left(\max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right) \right) - \frac{\alpha \nu \max_{t \in [0, \tau]} K_p(V_{\text{per}})}{\min_{t \in [0, \tau]} (K_w(V_{\text{per}}) + K_p(V_{\text{per}}))}, \\ \bar{p}_4 &:= \left(\max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right) \right) \left(\max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L \right), \\ \bar{p}_5 &:= \max_{t \in [0, \tau]} \frac{K'_p(V_{\text{per}})\dot{V}_{\text{per}}}{K_p(V_{\text{per}})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{\text{per}} \right), \quad \bar{p}_6 := \max_{t \in [0, \tau]} \frac{K'_w(V_{\text{per}})\dot{V}_{\text{per}}}{K_w(V_{\text{per}})} + \nu + \mu_L, \\ \bar{p}_7 &:= \mu_M. \end{aligned}$$

Principal minors $\bar{p}_4, \bar{p}_5, \bar{p}_6$ and \bar{p}_7 are trivially non-negative. We want conditions that ensure that $p_1 \geq 0, p_2 \geq 0$ and $p_3 \geq 0$. Recalling that $\bar{a}_{ij} := \text{ess sup}_{[0, \tau]} a_{ij}(t)$, we find that

$$\bar{p}_1 = \bar{a}_{1,1}\bar{p}_2 - \bar{a}_{3,1}\bar{a}_{2,2}\bar{a}_{1,3} = \bar{a}_{2,2}\bar{p}_3 - \bar{a}_{3,2}\bar{a}_{1,1}\bar{a}_{2,3}.$$

From latter equation, we have that $\bar{p}_1 \geq \bar{a}_{1,1}\bar{p}_2$, from which follows that $\bar{p}_2 \geq 0 \Rightarrow \bar{p}_1 \geq 0$. Analogously, $\bar{p}_3 \geq 0 \Rightarrow \bar{p}_1 \geq 0$. Therefore we only need to impose $\bar{p}_2 \geq 0$ and $\bar{p}_3 \geq 0$. This gives

$$\begin{aligned} \mu_M \left(\max_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{per} \right) \right) &\geq \frac{\alpha \nu \max_{t \in [0, \tau]} K_p(V_{per})}{\min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}, \quad \text{and} \\ \mu_M \left(\max_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L \right) &\geq \frac{\alpha \nu \max_{t \in [0, \tau]} K_w(V_{per})}{\min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}. \end{aligned}$$

If both inequalities above are satisfied, then all principal minors of $-\bar{A}$ are non-negative. Putting the basic offspring number \mathcal{N} in evidence gives us

$$\begin{aligned} \frac{\left(\max_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p \left(1 - \min_{t \in [0, \tau]} V_{per} \right) \right) \min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{per})} &\geq \mathcal{N}, \quad \text{and} \\ \frac{\left(\max_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L \right) \min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_w(V_{per})} &\geq \mathcal{N}, \end{aligned}$$

which yields item (i) (in view of Theorem B.3).

The principal minors of $-\underline{A}$ are the principal minors of $-\bar{A}$ with all maxima exchanged for minima, and vice-versa. Let us use $\underline{p}_1, \underline{p}_2, \dots, \underline{p}_7$ to denote them. Again, principal minors $\underline{p}_4, \underline{p}_5, \underline{p}_6$ and \underline{p}_7 are trivially non-negative. The same reasoning used before shows us that $\underline{p}_1 \geq \underline{a}_{1,1}\underline{p}_2$, from which it follows that $\underline{p}_1 < 0 \rightarrow \underline{p}_2 < 0$ and, conversely, $\underline{p}_1 < 0 \rightarrow \underline{p}_3 < 0$. These conditions means that if $\underline{p}_1 < 0$ then both $\underline{p}_2 < 0$ and $\underline{p}_3 < 0$. Therefore the weakest condition for a negative principal minor is \underline{p}_2 or \underline{p}_3 . We arrive at the following conditions:

$$\begin{aligned} \mu_M \left(\min_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p \left(1 - \max_{t \in [0, \tau]} V_{per} \right) \right) &< \frac{\alpha \nu \min_{t \in [0, \tau]} K_p(V_{per})}{\max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}, \quad \text{or} \\ \mu_M \left(\min_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L \right) &< \frac{\alpha \nu \min_{t \in [0, \tau]} K_w(V_{per})}{\max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}. \end{aligned}$$

If **either** of the inequalities above is satisfied, then at least one principal minor of $-\underline{A}$ is negative and there exists a strictly positive periodic solution which attracts all non-zero initial conditions. Again, putting the basic offspring number \mathcal{N} in evidence gives us

$$\begin{aligned} \frac{\left(\min_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p \left(1 - \max_{t \in [0, \tau]} V_{per} \right) \right) \max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{per})} &< \mathcal{N}, \\ \frac{\left(\min_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L \right) \max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{\min_{t \in [0, \tau]} K_w(V_{per})} &< \mathcal{N}. \end{aligned}$$

as stated in the theorem. \square

3.3. Asymptotic behaviour of malaria. 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} be the periodic solution for the mosquito population. We get that the infected components (M_I, I) follow the dynamics:

$$(3.5) \quad \begin{aligned} \dot{M}_I &= \beta_{hv}I(M_{\text{per}} - M_I) - \mu_M M_I; \\ \dot{I} &= \beta_{vh}(1 - I)M_I - \kappa I. \end{aligned}$$

Note that system (3.5) is cooperative in the time-dependent domain

$$\mathcal{K}_Y = \{(t, M_I, I) \in \mathbb{R}_+^3 : M_I \leq M_{\text{per}}(t), I \leq 1\}.$$

We can apply Theorem B.3 to arrive at the following result:

THEOREM 3.3 (Limit Behaviour of Disease).

If

$$\frac{\beta_{vh}\beta_{hv} \max_{t \in [0, \tau]} M_{\text{per}}(t)}{\kappa \left(\mu_M - \min_{t \in [0, \tau]} \frac{\dot{M}_{\text{per}}(t)}{M_{\text{per}}(t)} \right)} \leq 1,$$

then the trajectories (M_I, I) of (3.5) verify $\lim_{t \rightarrow +\infty} (M_I, I)(t) = 0$ for all initial conditions in \mathcal{K}_Y .

If

$$\frac{\beta_{vh}\beta_{hv} \min_{t \in [0, \tau]} M_{\text{per}}(t)}{\kappa \left(\mu_M - \max_{t \in [0, \tau]} \frac{\dot{M}_{\text{per}}(t)}{M_{\text{per}}(t)} \right)} > 1,$$

then there exists a strictly positive periodic solution of (3.5) which attracts all initial conditions in $\mathcal{K}_Y \setminus \{0\}$.

Proof. Following the same reasoning as in the proof of Theorem 3.2, we can define $\bar{M}_I = M_I/M_{\text{per}}$, which gives us the system

$$(3.6) \quad \begin{aligned} \dot{\bar{M}}_I &= \beta_{hv}I(1 - \bar{M}_I) - \left(\mu_M + \frac{\dot{M}_{\text{per}}}{M_{\text{per}}} \right) \bar{M}_I; \\ \dot{I} &= \beta_{vh}M_{\text{per}}(1 - I)\bar{M}_I - \kappa I. \end{aligned}$$

from which we calculate $-A$ to be

$$(3.7) \quad -A = \begin{pmatrix} \mu_M - \frac{\dot{M}_{\text{per}}}{M_{\text{per}}} & -\beta_{hv} \\ -\beta_{vh}M_{\text{per}} & \kappa \end{pmatrix}.$$

The principal minors of $-A$ are

$$(3.8) \quad \begin{aligned} \bar{p}_1 &= \kappa \left(\mu_M - \min_{t \in [0, \tau]} \frac{\dot{M}_{\text{per}}(t)}{M_{\text{per}}(t)} \right) - \beta_{vh}\beta_{hv} \max_{t \in [0, \tau]} M_{\text{per}}(t); \\ \bar{p}_2 &= \beta_{hv}; \\ \bar{p}_3 &= \beta_{vh} \max_{t \in [0, \tau]} M_{\text{per}} \end{aligned}$$

Both \bar{p}_2 and \bar{p}_3 are always non-negative. We will therefore focus on the condition that $\bar{p}_1 \geq 0$, from which we get

$$(3.9) \quad \frac{\beta_{vh}\beta_{hv} \max_{t \in [0, \tau]} M_{\text{per}}(t)}{\kappa \left(\mu_M - \min_{t \in [0, \tau]} \frac{\dot{M}_{\text{per}}(t)}{M_{\text{per}}(t)} \right)} \leq 1.$$

If the inequality is satisfied, then trajectories of solutions to (3.5) converge to 0 for all initial conditions. However, if we consider the principal minors of $-\underline{A}$, we arrive at

$$(3.10) \quad \frac{\beta_{vh}\beta_{hv} \min_{t \in [0, \tau]} M_{per}(t)}{\kappa \left(\mu_M - \max_{t \in [0, \tau]} \frac{M_{per}(t)}{M_{per}(t)} \right)} > 1.$$

If the inequality is satisfied, then there exists a strictly positive periodic solution of (3.5) which attracts all feasible initial conditions, as stated. \square

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

$$(3.11) \quad \mathcal{R}_0 := \frac{\beta_{hv}\beta_{vh}M}{\kappa\mu_M}.$$

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. [17]), 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 state variables converging to zero. If we defined a *time dependent* reproduction number by

$$(3.12) \quad \mathcal{R}(t) := \frac{\beta_{hv}\beta_{vh}M_{per}(t)}{\kappa\mu_M},$$

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.

4. Numerical simulations. In this last section we present simulations to illustrate our model and results. In Table 2 we expose ranges of realistic values for the parameters involved in system (2.3). In Subsection 4.2, we present some scenarios for the possible asymptotic behaviours of the system, as predicted by Theorems 3.2 and 3.3. Subsection 4.3 explores the conditions from Theorems 3.2 and 3.3, analyzing the effect of the system's parameters on its asymptotic behaviour.

4.1. Parameters and Survey. The locality of Mancio Lima, in the state of Acre in northwestern Brazil, is an important malaria hotspot. There, malaria is strongly associated with fish farming [5, 6]. In this area, there are ponds with commercial fishes and ponds with natural fishes, and natural water bodies (creeks, swamps). In Table 2 we gathered realistic parameters for the situation in Mancio Lima. Some data was gathered in a visit to the region in 2018.

Comments about Table 2:

1. From interviews with the fish farmers, it was inferred that it takes two months for the vegetation to completely cover the fish tanks borders and border

Parameter	Value/ Range	Note/ Ref.	Scenario 1	Scenario 2	Scenario 3
r	0.01666 day ⁻¹	1	0.01666	0.01666	0.01666
τ	30 – 60 days	1	30	30	30
$\gamma(t)$	0.5 – 1 dimensionless	1, [6, 5]	0.65	0.65	0.65
α	8.75 – 43.66 day ⁻¹	[16, 13]	43.66	43.66	8.75
ν	1/(15.6 ± 2.86) day ⁻¹	[16]	0.0641	0.0641	0.0541
μ_L	0.51 – 0.79 day ⁻¹	[18]	0.62	0.62	0.99
μ_p	0.11 – 0.39 day ⁻¹	2	0.31	0.31	0.31
μ_M	0.089 – 0.476 day ⁻¹	[2]	0.089	0.16	0.8
κ	0.024 – 0.16 day ⁻¹	3	0.05	0.05	0.05
β_{vh}	0.02 – 0.25 day ⁻¹	[11]	0.2	0.1	0.2
β_{hv}	0.05 – 0.25 day ⁻¹	[11]	0.2	0.1	0.2

TABLE 2

Biologically feasible parameter ranges.

cleaning is done between 30 to 60 days. Moreover, at each cleaning episode more than half of the border vegetation is removed, which makes the cleaned proportion $\gamma(t)$ greater than 0.5.

2. Pond vegetation interferes with the feeding behavior of the fish, and indirectly protects the larvae from their predators [9]. Without vegetation, larvivorous fishes can reduce the amount of larvae in 90%.
3. The range of values for κ is calculated from [1]. Adherence to treatment directly affects the recovery rate [12]. We choose a value of κ for the simulation corresponding roughly to 14 days of treatment and a week until symptoms onset.

4.2. Numerical Validation of Theorems. We aim at illustrating Theorems 3.2 and 3.3 with numerical simulations. The following scenarios will be simulated.

Scenario 1: Positive periodic mosquito and infected human populations.

Scenario 2: Positive periodic mosquito population, and infected population converging to 0.

Scenario 3: Mosquito population and infected population converging to 0.

The numerical values used for the simulations are given in Table 2. For $K_w(V)$ and $K_p(V)$, we choose the following arbitrary functions:

$$(4.1) \quad K_p(V) := \frac{0.8}{1 + e^{-5(V-0.5)}}, \quad K_w(V) := 4V + 0.5.$$

The equation for $K_w(V)$ was interpolated by taking $K_w(0.2) = 1.3$ thousand larvae and $K_w(0.8) = 3.7$ thousand larvae [6, 5]. K_p is chose to be a sigmoid function with arbitrary parameters such that $K_p(0.5) = 0.4$ thousand larvae. We chose two different kinds of functions so as not to simplify the conditions on Theorem 3.2. We consider that the vegetation has assumed periodic behaviour as described in Proposition 3.1, with the asymptotic value $\gamma^* = 0.65$. The values for μ_M and μ_L in Scenario 3 were chosen outside of the biological feasible range in order to force the differential equation system to assume the desired asymptotic behaviour. System (2.3) was integrated numerically for each scenario fixing the initial conditions

$$(V, S, I, M_S, M_I, L_p, L_w)(0) = (0.7, 0.9, 0.1, 0.5, 0, 2, 0.2).$$

The values for the conditional expressions of both Theorem 3.2 and 3.3 are given in

Expression	1	2	3
\mathcal{N}	45.967	25.569	0.567
$\frac{\left(\max_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p(1 - \min_{t \in [0, \tau]} V_{per})\right) \min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{per})}$	48.001	48.001	61.405
$\frac{\left(\max_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L\right) \min_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_w(V_{per})}$	1.601	1.601	2.394
$\frac{\left(\min_{t \in [0, \tau]} \frac{K'_p(V_{per})\dot{V}_{per}}{K_p(V_{per})} + \nu + \mu_L + \mu_p(1 - \max_{t \in [0, \tau]} V_{per})\right) \max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \max_{t \in [0, \tau]} K_p(V_{per})}$	5.194	5.194	7.317
$\frac{\left(\min_{t \in [0, \tau]} \frac{K'_w(V_{per})\dot{V}_{per}}{K_w(V_{per})} + \nu + \mu_L\right) \max_{t \in [0, \tau]} (K_p(V_{per}) + K_w(V_{per}))}{(\nu + \mu_L) \min_{t \in [0, \tau]} K_w(V_{per})}$	0.365	0.365	0.553
$\frac{\beta_{vh}\beta_{hv} \max_{t \in [0, \tau]} M_{per}(t)}{\kappa(\mu_M - \min_{t \in [0, \tau]} \frac{M_{per}(t)}{M_{per}(t)})}$	10.073	0.684	0.000
$\frac{\beta_{vh}\beta_{hv} \min_{t \in [0, \tau]} M_{per}(t)}{\kappa(\mu_M - \max_{t \in [0, \tau]} \frac{M_{per}(t)}{M_{per}(t)})}$	7.225	0.569	0.000

TABLE 3
Calculated values for the conditional expression.

Table 3. The simulations are shown in Figure 3. We could then validate numerically the results predicted by Theorems 3.2 and 3.3.

4.3. Analysis. Using Table 2, we can calculate the range of biologically feasible values for the basic offspring number \mathcal{N} , that gives $[0.953, 55.126]$. It is possible to observe that elimination of the mosquito population through border vegetation removal is unfeasible if \mathcal{N} is in the range of biologically feasible parameters. That is the reason why, in order to simulate a situation like the one of Scenario 3, we chose values for μ_M and μ_L that are outside the range observed in nature [2, 18].

Now, consider Theorem 3.3. In situation 1 of that theorem, 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.

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 2 allows us to calculate the biologically feasible range for it, giving $[0.013, 29.260]$.

The biological meaning of the parameters in the conditions of Theorem 3.3 are the transmission rates, the recovery rate, the mosquito mortality and the size of the 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 issue is to have a grasp on the relative effects of each factor on

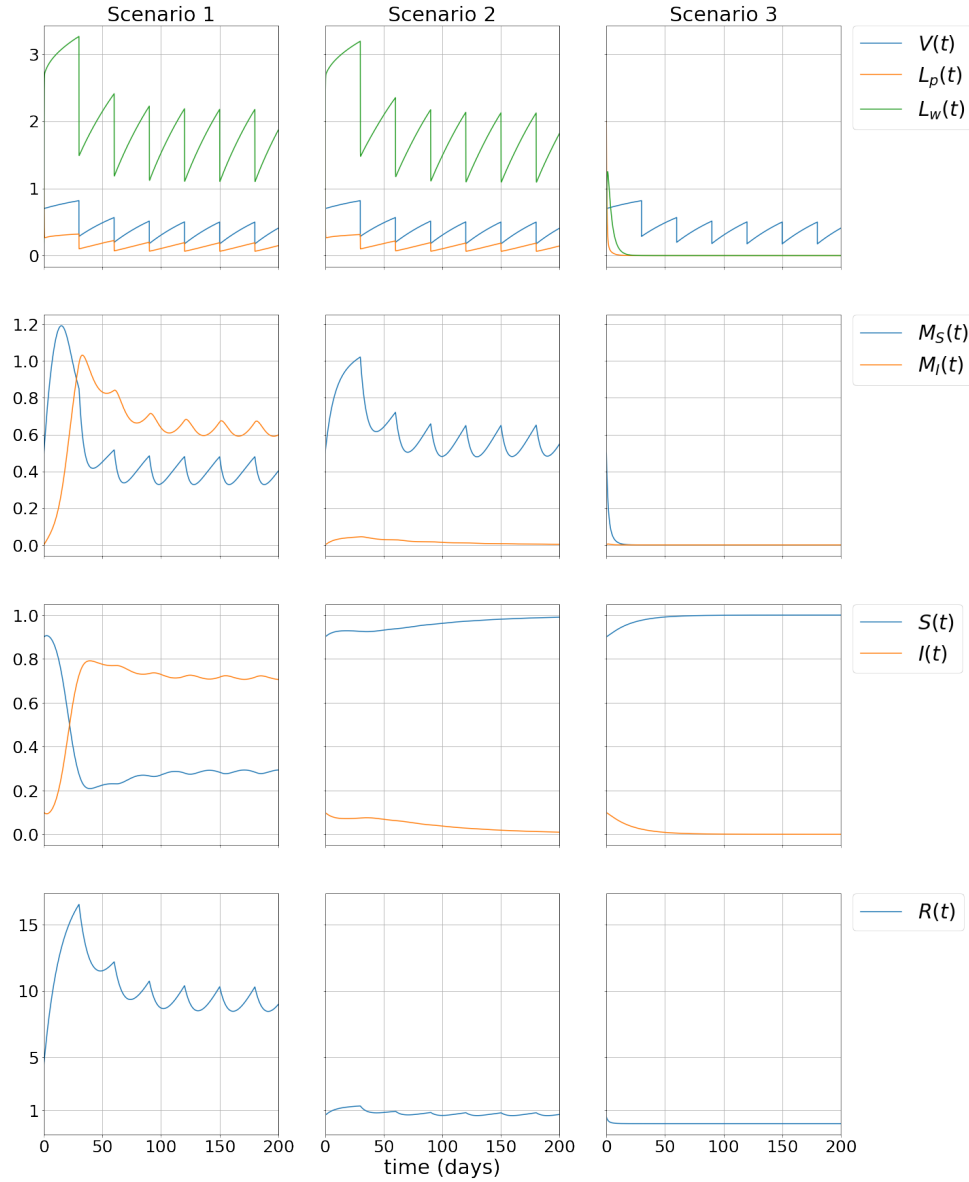


FIG. 3. Behaviour of the system under each scenario. Both mosquitoes and larvae are in the scale of thousands.

malaria transmission [11].

We simulate the effect of an increase in the frequency of cleaning, using the set of parameters described in Table 4. The values for τ range from 70 to 5 days. In Figure 4, we represent the maximum and minimum value of both $\mathcal{R}(t)$ (as defined in (3.12)) 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

Parameter	Values
r	0.01666
τ	varying
γ	0.65
α	26.2
ν	0.0641
μ_L	0.62
μ_p	0.31
μ_M	0.16
κ	0.05
β_{vh}	0.2
β_{hv}	0.2

TABLE 4

Value of parameters for the simulation of the effect of cleaning frequency change. Biological meaning of parameters is given in Table 1

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

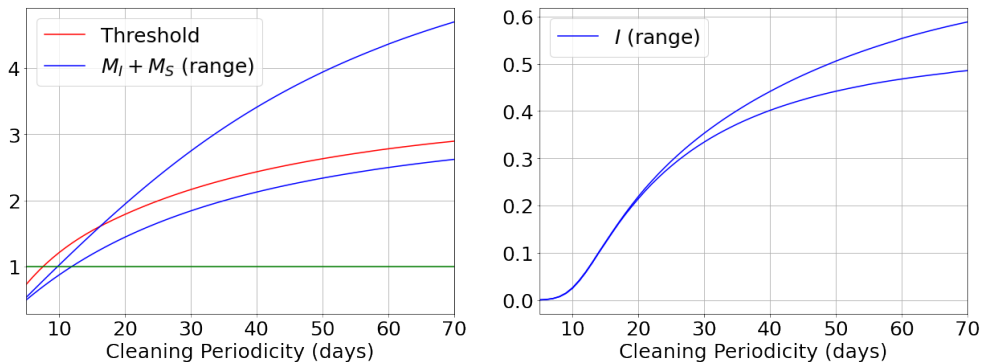


FIG. 4. Behaviour of the disease under increasing cleaning frequency. It is possible to observe that, as the threshold value for Theorem 3.3 becomes smaller than 1, the proportion of infected goes to 0.

5. Summary and Conclusion. In this paper, we use field observations and data about malaria in Acre, state in the Northwest of Brazil, to propose a system of differential equations to model the interaction between the border vegetation of fish ponds, the life cycle of *Anopheles darlingi* and the transmission of malaria. The model considers the differences observed in commercially active and inactive ponds, and the impact of maintenance on *Anopheles* larvae density. As far as we know, this is the first model linking malaria and fish farming.

In our model, we assumed that fish pond cleaning happened periodically and disregarded spatial effects on the dynamics. The model could potentially be improved by dropping these assumptions. Another important development is the collection of data to assess the validity of the model.

Through Theorems 3.2 and 3.3, we established conditions for determining the asymptotic behaviour of the mosquito population and the incidence of disease. Nu-

merical simulations of our model have shown that an increase in cleaning frequency can reduce the mosquito population, which in turn reduces incidence of malaria. Our results suggests that incentives for fish pond maintenance are potential public health measures in the state of Acre.

Acknowledgments. This research was funded by the Applied Research Project of Fundação Getúlio Vargas “*Modelagem, análise e estimativa da contribuição dos tanques de piscicultura na população do mosquito anopheles e o impacto na transmissão da malária no Alto Juruá, Acre*”, by the Program *Jovem Cientista do Nosso Estado* of FAPERJ, Brazil, by the STIC AmSud funding for the MOSTICAW Project (Process No. 99999.007551/2015-00) and by CNPq Grant No. 454665/2014-8. The authors particularly acknowledge the fish farmers from Mâncio Lima, Acre, Brazil, for their availability.

Appendix A. On Carathéodory solutions.

Here we recall existence and uniqueness results for Cauchy problems with right-hand side functions that are merely measurable with respect to time. In Section B.1 we employ these results to prove that the *Poincaré map* associated to this type of system is well-defined, continuous and differentiable.

Basic Assumptions. For an open set $\Omega \subset \mathbb{R} \times \mathbb{R}^n$ and a function $g: \Omega \mapsto \mathbb{R}^n$, let us consider the conditions (A) and (B) below.

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

$$(B) \quad \begin{cases} \text{For any compact set } K \subset \Omega, \text{ there exist } C_K > 0, L_K > 0 \text{ such that} \\ |g(t, x)| \leq C_K, |g(t, x) - g(t, y)| \leq L_K|x - y|, \text{ for all } (t, x), (t, y) \in K. \end{cases}$$

We begin by recalling the following result [15, 3, 4].

THEOREM A.1 (Carathéodory’s Existence Theorem). *Given $g: \Omega \rightarrow \mathbb{R}^n$ satisfying (A) and (B), and some $(t_0, x_0) \in \Omega$, consider the Cauchy problem*

$$(A.1) \quad \dot{x} = g(t, x), \quad x(t_0) = x_0.$$

The following assertions hold.

- (i) *There exists $\epsilon > 0$ such that (A.1) has a local solution defined on $[t_0, t_0 + \epsilon]$.*
- (ii) *Moreover, if $\Omega = \mathbb{R} \times \mathbb{R}^n$ and there exist constants C, L such that*

$$(A.2) \quad |g(t, x)| \leq C, |g(t, x) - g(t, y)| \leq L|x - y|, \text{ for all } (t, x), (t, y) \in \mathbb{R} \times \mathbb{R}^n,$$

then, for every $t_1 > t_0$, the initial value problem (A.1) has a unique global solution defined on $[t_0, t_1]$. Moreover, the solution depends continuously on the initial data x_0 .

THEOREM A.2 (Uniqueness of solutions). *Under the hypotheses of Theorem A.1, let x_1 and x_2 be solutions of (A.1) 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 $t \in [t_0, t']$.*

THEOREM A.3 (Maximal solutions). *Under the hypotheses of Theorem A.1, let $t^* > t_0$ be the supremum of all times t_1 for which (A.1) has a solution x defined on*

$[t_0, t_1]$. Then, either $t^* = \infty$ or

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

Appendix B. Cooperative systems with time-measurable dynamics and concave nonlinearities.

In this section we show properties of the *Poincaré map* associated to system (A.1). These properties are used to extend Jifa's result [8, Theorem 5.5] to time-measurable differential equations.

B.1. Well-Definedness and Differentiability of Poincaré Map. Let us introduce the following notation: for given (t_0, x_0) in Ω , we write $\mathbf{x}(t; t_0, x_0)$ to denote the solution of (A.1) at time t , whenever it exists. For fixed $t > t_0$, we define the *Poincaré map* T corresponding to system (A.1) as the function that to each x_0 with $(t_0, x_0) \in \Omega$, associates $\mathbf{x}(t; t_0, x_0)$, i.e. $T(x_0) := \mathbf{x}(t; t_0, x_0)$.

Naturally, for the Poincaré map to be well-defined, we require that for any given x_0 , the underlying Cauchy problem has a unique solution. In the case the system admits a forward invariant and we can define the Poincaré map on this set for any $t > t_0$, as stated in the following corollary.

COROLLARY B.1 (Well-definiteness of the Poincaré map). *Assume that the hypotheses of Theorem A.1 hold and that the differential equation $\dot{x} = g(t, x)$ admits a compact forward invariant set \mathcal{C} , with $[t_0, \infty) \times \mathcal{C} \subseteq \Omega$. Then, the associated Poincaré map is well-defined on \mathcal{C} .*

Proof. It follows straightforwardly from Theorems A.1-A.3. \square

The following Theorem proves differentiability of the Poincaré map w.r.t. the initial conditions.

THEOREM B.2 (Differentiability of the Poincaré Map). *Suppose that the hypotheses of Corollary B.1 hold, and assume further that g is continuously differentiable with respect to x . Let $t_0 \in \mathbb{R}$, $t > t_0$ and consider the Poincaré map T associated to the Cauchy problem (A.1) and time t . Then, the map $x_0 \mapsto Tx_0 := \mathbf{x}(t; t_0, x_0)$ is continuously differentiable with respect to x_0 . Its Jacobian matrix is*

$$(B.1) \quad D_{x_0}T = M(t, t_0),$$

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

$$(B.2) \quad \dot{v}(t) = D_x g(t, \mathbf{x}(t; t_0, x_0)) \cdot v(t).$$

Proof. It follows from [3, Theorem 2.10].

B.2. Asymptotic behaviour. In view of the properties of the Poincaré map stated above, we can extend [8, Theorem 5.5] to the differential equation

$$(B.3) \quad \dot{x} = \mathcal{F}(t, x), \quad (t, x) \in \mathbb{R}_+ \times [0, p],$$

where p belongs to \mathbb{R}_+^n and \mathcal{F} is measurable over t . This way we get Theorem B.3 below.

Let us introduce some notation and the hypotheses imposed in Theorem B.3. Set

$$f(t, x, p - x) := \mathcal{F}(t, x), \quad \text{for } (t, x) \in \mathbb{R} \times [0, p],$$

and consider the following condition for \mathcal{F} and f :

$$(C) \quad \begin{cases} f(t, x, y) \text{ is continuous on } \mathbb{R} \times [0, p] \times [0, p], \tau\text{-periodic in } t, \\ D_x f(t, x, y), D_y f(t, x, y) \text{ are continuous in } \mathbb{R} \times [0, p] \times [0, p], \\ f_i(t, x, p-x) \geq 0, \quad \text{if } x_i = 0, 0 \leq x \leq p, \\ f_i(t, x, p-x) < 0, \quad \text{if } x_i = p_i, 0 \leq x \leq p, \\ \frac{\partial f_i}{\partial x_j}(t, x, p-x) - \frac{\partial f_i}{\partial y_j}(t, x, p-x) \geq 0, \quad \text{if } i \neq j, \\ D_x \mathcal{F}(t, 0) \text{ is irreducible for } t \in \mathbb{R}, \\ D_x \mathcal{F}(t, x) >_{\neq} D_x \mathcal{F}(t, y), \quad \text{if } 0 < x < y < p. \end{cases}$$

Given a matrix-valued τ -periodic function $C: [0, \tau] \rightarrow \mathbb{R}^{n \times n}$, set

$$(B.4) \quad \bar{c}_{ij} := \max_{t \in [0, \tau]} c_{ij}(t), \quad \underline{c}_{ij} := \min_{t \in [0, \tau]} c_{ij}(t),$$

and consider the matrices

$$(B.5) \quad \bar{C} := (\bar{c}_{ij}), \quad C := (c_{ij}).$$

THEOREM B.3 (Conditions for Periodic Solutions). *Let $\mathcal{F}: \mathbb{R} \times [0, p] \times [0, p] \rightarrow \mathbb{R}_+^n$ be a function verifying (C), where $p \in \mathbb{R}_+^n$. Assume further that $\mathcal{F}(t, 0) \equiv 0$ and all the trajectories of (B.3) are bounded. Then, setting $A(t) := D_x \mathcal{F}(t, 0)$, the following conditions hold.*

1. *If all principal minors of $-\bar{A}$ are non-negative, then $\lim_{t \rightarrow \infty} x(t) = 0$ for every solution of (B.3) with initial condition in $[0, p]$.*
2. *If $-A$ has at least one negative principal minor, then (B.3) possesses a unique τ -periodic solution which attracts all initial conditions in $[0, p] \setminus \{0\}$.*

Appendix C. Impulsive equations.

LEMMA C.1. *For a sequence $(\gamma_n)_{n \in \mathbb{N}} \subset \mathbb{R}$ and $u_0 \in \mathbb{R}$, consider the initial value problem*

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

Then, the following assertions hold.

- (i) *If $\gamma_n = \gamma \in [0, 1]$ for all $n \in \mathbb{N}$ and $u_0 = 1 - \frac{\gamma}{1 - (1 - \gamma)e^{-r\tau}}$, then (C.1) admits the periodic solution u_{per} given by*

$$(C.2) \quad u_{\text{per}}(t) := 1 - \frac{\gamma e^{-r(t-n\tau)}}{1 - (1 - \gamma)e^{-r\tau}}, \quad \text{for } t \in [n\tau, (n+1)\tau).$$

- (ii) *Moreover, if $(\gamma_n) \subset [0, 1]$ is any sequence converging to γ , then any solution u of (C.1) for any initial condition $u_0 \in [0, 1]$ verifies*

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

Proof. Item (i) follows easily. Let us prove item (ii) assuming initially that $\gamma_n = \gamma$ for all $n \in \mathbb{N}$. The proof consists in taking the sequence formed by the points of

discontinuity and studying its convergence. We begin by calculating $u((n+1)\tau^+)$ as a function of $u(n\tau^+)$. By solving the initial value problem

$$\dot{u}(t) = r(1 - u(t)), \quad \text{for } t \in (n\tau, (n+1)\tau), \quad u(n\tau) = u(n\tau^+),$$

and taking the limit as $t \rightarrow (n+1)\tau^-$, we get:

$$(C.3) \quad u((n+1)\tau^-) = 1 - [1 - u(n\tau^+)]e^{-r\tau}.$$

On the other hand, we can write $u((n+1)\tau^+)$ as a function of $u((n+1)\tau^-)$, using the impulse at $(n+1)\tau$, as $u((n+1)\tau^+) = (1 - \gamma)u((n+1)\tau^-)$. Using latter equation and (C.3) yields

$$(C.4) \quad u((n+1)\tau^+) = (1 - \gamma)\left(1 - (1 - u(n\tau^+))e^{-r\tau}\right),$$

defining a recurrence relation for $u(n\tau^+)$ induced by the function

$$(C.5) \quad x \mapsto f(x) := (1 - \gamma)\left(1 - (1 - x)e^{-r\tau}\right).$$

As f is a contraction over $[0, 1]$, the sequence $(u(n\tau^+))_{n \in \mathbb{N}}$ converges to its fixed point

$$(C.6) \quad u^* = \frac{(1 - \gamma)(1 - e^{-r\tau})}{1 - (1 - \gamma)e^{-r\tau}}.$$

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

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

Finally, in the generic case, notice that for each γ_n , we have a corresponding f_n . We have to show that the infinite composition

$$\lim_{n \rightarrow \infty} f_n \circ \cdots \circ f_1(x)$$

converges. As $\gamma_n \rightarrow \gamma > 0$, from (C.5) we get that $f_n \rightarrow f$ uniformly on $[0, 1]$. For every $n \in \mathbb{N}$, f_n is a contraction, which implies it has a fixed point u_n^* in the form of equation (C.6). From (C.6), we can see that $u_n^* \rightarrow u^*$. These conditions guarantee us (see [10]) that the infinite composition converges to the fixed point of its limit function f . Thus the proposition has been proven. \square

REFERENCES

- [1] R. AGUAS, M. U. FERREIRA, AND M. G. GOMES, *Modeling the effects of relapse in the transmission dynamics of malaria parasites*, J Parasitol Res, 2012:921715 (2012).
- [2] F. S. M. D. BARROS, N. A. HONÓRIO, AND M. E. ARRUDA, *Survivorship of Anopheles darlingi (Diptera: Culicidae) in relation with malaria incidence in the Brazilian Amazon*, PLOS ONE, 6 (2011), pp. 1–13, <https://doi.org/10.1371/journal.pone.0022388>, <https://doi.org/10.1371/journal.pone.0022388>.
- [3] A. BRESSAN AND B. PICCOLI, *Introduction to the mathematical theory of control*, vol. 2, American Institute of Mathematical Sciences Springfield, 2007.
- [4] E. A. CODDINGTON AND N. LEVINSON, *Theory of ordinary differential equations*, Tata McGraw-Hill Education, 1955.

- [5] I. C. DOS REIS, C. T. CODECO, C. M. DEGENER, E. C. KEPPELER, M. M. MUNIZ, F. G. DE OLIVEIRA, J. J. CORTES, A. DE FREITAS MONTEIRO, C. A. DE SOUZA, F. C. RODRIGUES, G. R. MAIA, AND N. A. HONORIO, *Contribution of fish farming ponds to the production of immature Anopheles spp. in a malaria-endemic amazonian town*, Malar. J., 14:452 (2015), p. 452.
- [6] I. C. DOS REIS, N. A. HONORIO, F. S. BARROS, C. BARCELLOS, U. KITRON, D. C. CAMARA, G. R. PEREIRA, E. C. KEPPELER, M. DA SILVA-NUNES, AND C. T. CODECO, *Epidemic and endemic malaria transmission related to fish farming ponds in the amazon frontier*, PLoS ONE, 10(9): e0137521 (2015).
- [7] C. P. FERREIRA AND W. A. GODOY, *Ecological modelling applied to entomology*, Springer, 2014.
- [8] J. JIFA, *The algebraic criteria for the asymptotic behaviour of cooperative systems with concave nonlinearities*, Systems Science and Mathematical Sciences, (1993), pp. 193–208.
- [9] L. KAMAREDDINE, *The Biological Control of the Malaria Vector*, Toxins, 4 (2012), pp. 748–767.
- [10] L. LORENTZEN, *Compositions of contractions*, Journal of Computational and Applied Mathematics, 32 (1990), pp. 169–178.
- [11] S. MANDAL, R. R. SARKAR, AND S. SINHA, *Mathematical models of malaria - A review*, Malaria journal, 10:202 (2011).
- [12] E. A. PEREIRA, E. A. ISHIKAWA, AND C. J. FONTES, *Adherence to plasmodium vivax malaria treatment in the brazilian amazon region*, Malaria journal, 10 (2011), p. 355.
- [13] D. ROBERTS, W. ALECRIM, A. TAVARES, AND K. MCNEILL, *Field observations on the gonotrophic cycle of Anopheles darlingi (Diptera: Culicidae)*, Journal of Medical Entomology, 20 (1983), pp. 189–192, <https://doi.org/10.1093/jmedent/20.2.189>, <https://doi.org/10.1093/jmedent/20.2.189>, <https://arxiv.org/abs/http://oup.prod.sis.lan/jme/article-pdf/20/2/189/18176833/jmedent20-0189.pdf>.
- [14] R. ROSS, *The prevention of malaria*, John Murray; London, 1911.
- [15] W. RUDIN, *Real and complex analysis*, Tata McGraw-Hill Education, 2006.
- [16] J. M. M. SANTOS, E. P. B. CONTEL, AND W. E. KERR, *Biologia de anofelinos amazônicos. - Ciclo biológico, postura e estádios larvares de Anopheles darlingi da rodovia Manaus - Boa Vista*, Acta Amazonica, 11 (1981), pp. 789–797.
- [17] P. VAN DEN DRIESSCHE AND J. WATMOUGH, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Mathematical biosciences, 180 (2002), pp. 29–48.
- [18] C. VILLARREAL-TREVIÑO, G. M. VÁSQUEZ, V. M. LÓPEZ-SIFUENTES, K. ESCOBEDO-VARGAS, A. HUAYANAY-REPETTO, Y.-M. LINTON, C. FLORES-MENDOZA, A. G. LESCANO, AND F. M. STELL, *Establishment of a free-mating, long-standing and highly productive laboratory colony of anopheles darlingi from the peruvian amazon*, Malaria journal, 14 (2015), p. 227.
- [19] H. M. YANG, M. L. G. MACORIS, K. C. GALVANI, M. T. M. ANDRIGHETTI, AND D. M. V. WANDERLEY, *Assessing the effects of temperature on the population of Aedes aegypti, the vector of dengue*, Epidemiology & Infection, 137 (2009), pp. 1188–1202.