Analysis of the Basic Ross-Macdonald Malaria Model Parameters

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Abstract

We consider a basic finite dimensional Ross-Macdonald malaria mathematical model on interaction of the infected humans and the infected mosquitoes. We study this system for consistence of the equations to the real biomedical situation that they model. Local and global well-posedness of the system is proven and the analysis of the equilibrium points is carried out. Numerical analysis show that mathematical analysis is very powerful for understanding such systems.

Keywords: Ross-Macdonald model, Well-posedness, Basic reproduction number, Malaria, Equilibrium points

Mathematics Subject Classification (2000): MSC 00A0, MSC 00A69, MSC 00A70

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1 Introduction

In this paper, we study a simple system of two equations modelling the interaction between the infected proportions of the human host population and the mosquito vector population,

proposed by Sir Ronald Ross [1] in the 1890s.

$$\begin{cases} \dfrac{dx}{dt} = abmy(1-x) - rx \\ \\ \dfrac{dy}{dt} = acx(1-y) - \mu y, \end{cases} \tag{1}$$

where $x(t)$, $y(t)$ denote the unknown proportions of infected humans and mosquitoes at time t, respectively. The constant parameters hold the following biological significance:

$a =$ the rate of biting on humans by a single mosquitoes
$b =$ the proportion of infected bites on humans that produce an infection
$c =$ the transmission efficiency from human to mosquito
$m =$ ratio of number of female mosquitoes to that of humans
(number of female mosquitoes per human host)
$r =$ average recovery rate of humans
$\mu =$ average mortality rate of mosquitoes.

Now, let

$$\begin{cases} \mathbf{x} & = (x,y)^\top \qquad\qquad \text{so that } \dot{\mathbf{x}} = \left(\frac{dx}{dt}, \frac{dy}{dt}\right)^\top, \\ \\ \mathbf{A} & = \begin{pmatrix} -r & 0 \\ 0 & -\mu \end{pmatrix}, \\ \\ \mathbf{F}(\mathbf{x}) & = \begin{pmatrix} abmy - abmxy \\ acx - acxy \end{pmatrix}. \end{cases} \tag{2}$$

Then (1) can be compactly rewritten as

$$\dot{\mathbf{x}} = \mathbf{A}\mathbf{x} + \mathbf{F}(\mathbf{x}). \tag{3}$$

Malaria is caused by four species of protozoan parasites: *Plasmodium vivax*, *P. falciparum*, *P. malariae*, and *P. ovale*. Infection occurs through the bite of an infected mosquito or by contact with blood products from an infected individual. A mosquito carrier bites a human host and injects the sporozoites, which reside and multiply in the parenchymal cells of the liver. After a maturation period averaging 2 to 4 weeks, merozoites are released and invade the erythrocytes. The infected erythrocytes rupture and release merozoites, pyrogens, and toxins, which cause hemolysis, sluggish blood flow in the capillaries, and adherence of infected erythrocytes to venous walls, obstructing blood flow, increasing the permeability of the capillaries, and causing tissue extravasation, particularly in the brain and gastrointestinal system, see [2] among others.

In (1), the total population of humans and mosquitoes is assumed to be constant, so that the proportion infected of each population (x and y) are the variables. New infections in humans are acquired at a rate that depends on the number of mosquito bites per person per unit time, am, on the probabilities that the biting mosquito is infected, y, and that a bitten human is uninfected, $1-x$, and on the chance that an uninfected person thus bitten will actually develop a patent infection. Infections in humans are lost when infected humans become uninfected at a net recovery rate rx. New infection in mosquitoes depends on the number of bites per mosquito per time unit, a, on the probabilities that the biting mosquito is uninfected, $1-y$, and that the bitten human is infected, x, and on the chance that an uninfected mosquito acquired an infection from biting an infectious human, c. Since mosquitoes do not appear to recover from malarial infection, infection in mosquitoes is lost through death, μy. We refer the reader to other reference sources for more detailed models [2, 3, 4].

We stress here that this finite dimensional Ross-Macdonald malaria mathematical model is the simplest formulation. It is however still the basis for much malarial epidemiological modelling. More complicated extensions of the Ross-Macdonald model have been made. Among which we will mention a few. Aron and May [5] included the consideration of age structure in the human population (see also [3, 6]), and the element of acquired immunity. Gu et al. [7] considered individual-based models, while Ruan et al. [2] included the element of time delays in the Ross Macdonald model by taking explicit account of the incubation periods of parasites within the human and the mosquito. More in depth study of this model and similar numerical simulations can be found in [8, 9, 10, 11].

While most of the above mentioned studies analysed the model based on the basic reproduction number, none of them, to the best of the authors' knowledge, have given a rigorous analysis of the local and global well-posedness of the model. We will include these analyses, to some extend in this paper.

This paper is organised as follows. In Section 2, we study the local well-posedness of the system of ordinary differential equations (1), and for completeness, we provide an analysis of the stability properties of the steady state solutions. More precisely, we will identify the steady state solutions of (1), and then, via linearization of the vector field about these fixed points, we calculate the eigenvalues, and analyse their sign, so as to classify the nature of these steady state solutions. In Section 3, we study, directly from the system of equations, the global asymptotic dynamics. In Section 4, we present numerical validation of the theoretical results.

2 Local Well-posedness and Analysis of the Steady states

In what follows, we will write $\|\cdot\|_2$ to denote the euclidean norm of $\mathbb{R}^2$.

Theorem 1. *Let $\Phi = \{\mathbf{u} \in \mathbb{R}^2 : \|\mathbf{u}\|_2 \leq \rho\}$, where $0 < \rho < 1$ is an adequately chosen real number. If $\mathbf{x}_0 \in \Phi$ are given initial conditions, then the system of nonlinear ordinary differential equations (1) has a unique solution that is continuous in time with values in Φ, and it is of the form*

$$\mathbf{x}(t, \mathbf{x}_0) = e^{\mathbf{A}t}\mathbf{x}_0 + \int_0^t e^{\mathbf{A}(t-s)}\mathbf{F}(\mathbf{x}(s))\, ds, \tag{4}$$

where

$$e^{\mathbf{A}t} = diag\left(e^{-rt}, e^{-\mu t}\right), \tag{5}$$

and is such that it is continuously differentiable on $(0,T)$.

Furthermore, for all $t \in (0,T)$, $\mathbf{x}(t) \in \Phi$, the system of ordinary differential equations (1) is satisfied, with $\mathbf{x}(0) = \mathbf{x}_0$.

Proof. Let $\mathbf{x}_1 = (x_1, y_1)^\top$ and $\mathbf{x}_2 = (x_1, y_2)^\top$, and for simplicity, we denote $\beta = abm$, $\gamma = ac$. Then we have that

$$\mathbf{F}(\mathbf{x}_1) - \mathbf{F}(\mathbf{x}_2) = \begin{pmatrix} \beta y_1 - \beta x_1 y_1 - \beta y_2 + \beta x_1 y_2 \\ \gamma x_1 - \gamma x_1 y_1 - \gamma x_2 + \gamma x_1 y_2 \end{pmatrix}. \tag{6}$$

If we take the euclidean norm of $\mathbb{R}^2$ and estimate from above, we get,

$$
\begin{aligned}
\|\mathbf{F}(\mathbf{x}_1)-\mathbf{F}(\mathbf{x}_2)\|_2^2 &= \beta^2|y_1-x_1y_1-y_2+x_2y_2|^2+\gamma^2|x_1-x_1y_1-x_2+x_2y_2|^2\\
&\leq \beta^2\left(|y_1-y_2|^2+|x_1y_1-x_1y_2|^2+|x_1y_2-x_2y_2|^2\right)+\\
&\quad+\gamma^2\left(|x_1-x_2|^2+|x_1y_1-x_2y_1|^2+|x_2y_1-x_2y_2|^2\right)\\
&\leq \beta^2\left(|y_1-y_2|^2+|x_1|^2|y_1-y_2|^2+|y_2|^2|x_1-x_2|^2\right)+\\
&\quad+\gamma^2\left(|x_1-x_2|^2+|y_1|^2|x_1-x_2|^2+|x_2|^2|y_1-y_2|^2\right)\\
&\leq \beta^2(1-\rho^2)|y_1-y_2|^2+\beta^2\rho^2|x_1-x_2|^2+\\
&\qquad+\gamma^2(1-\rho^2)|x_1-x_2|^2+\gamma^2\rho^2|y_1-y_2|^2\\
&= (\gamma^2-\gamma^2\rho^2+\beta^2\rho^2)|x_1-x_2|^2+(\beta^2-\beta^2\rho^2+\gamma^2\rho^2)|y_1-y_2|^2\\
&\leq \max\{(\gamma^2-\gamma^2\rho^2+\beta^2\rho^2),(\beta^2-\beta^2\rho^2+\gamma^2\rho^2)\}\times\\
&\qquad\times\left(|x_1-x_2|^2+|y_1-y_2|^2\right)\\
&= \max\{(\gamma^2-\gamma^2\rho^2+\beta^2\rho^2),(\beta^2-\beta^2\rho^2+\gamma^2\rho^2)\}\|\mathbf{x}_1-\mathbf{x}_2\|_2^2.
\end{aligned}
$$

It then follows that $\mathbf{F}(\mathbf{x})$ is locally Lipschitz continuous. The existence and uniqueness of solutions will then follow from the general results for non-linear ordinary differential equations in, among others, [12, 13]. In particular, the form of the solution follows from Theorem 1 in [13]. □

In what follows, we will study the dynamical properties of the fixed points (the steady state solutions / equilibrium points) of the system of equations (1). It is a simple exercise to show that these equilibrium points are

$$
\begin{cases}
(x^*,y^*) &= (0,0)\\
\textit{and/or}\quad (x^*,y^*) &= \left(\frac{a^2bcm-r\mu}{a^2bcm+acr},\frac{a^2bcm-r\mu}{a^2bcm+abm\mu}\right)=\left(\frac{R_0-1}{R_0+\frac{ac}{\mu}},\frac{R_0-1}{R_0+\frac{abm}{r}}\right),
\end{cases}
$$

where $R_0=\frac{a^2bcm}{r\mu}>0$ is the basic reproduction number [3, 2]. The basic reproduction number is the average total number of secondary infection cases, calculated as the product of the total number of mosquitoes infected by the primary human case ($\frac{amc}{r}$) and the total number of infectious bites ($\frac{ab}{\mu}$). We note that when $R_0\leq 1$, we only have one fixed point at $(0,0)$.

For the discussion of the nature of the fixed points, we will use the following notations:

$$
\begin{cases}
\mathbf{x} &= (x,y)^\top \quad \text{so that } \dot{\mathbf{x}}=\left(\frac{dx}{dt},\frac{dy}{dt}\right)^\top,\\
\tilde{\mathbf{F}}(\mathbf{x}) &= \begin{pmatrix} -rx+abmy-abmxy\\ acx-\mu y-acxy\end{pmatrix},
\end{cases}
\tag{7}
$$

so that (1) becomes

$$\dot{\mathbf{x}} = \tilde{\mathbf{F}}(\mathbf{x}). \tag{8}$$

We will then use the classic method based on the analysis of the signs of the eigenvalues of the linearised vector field of the system of equations (1). To this end, we have the following lemma.

Lemma 2. *Consider the system of equations (1) and assume that all the constants are positive. Then we have the following:*

- *If $R_0 < 1$, then the system of equations (1) only has the trivial fixed point $(x^*, y^*) = (0,0)$, and it is a stable node.*
- *If $R_0 > 1$, then the system of equations (1) has two fixed points $(x^*, y^*) = (0,0)$, which is saddle point, and $(x^*, y^*) = \left(\frac{a^2bcm - r\mu}{a^2bcm + acr}, \frac{a^2bcm - r\mu}{a^2bcm + abm\mu}\right)$, which is a stable node.*

Proof. We consider the vector field $\tilde{\mathbf{F}}(\mathbf{x})$ of the system of equations (1) as defined in (7). The Jacobian matrix for $\tilde{\mathbf{F}}(\mathbf{x})$ is calculated as

$$D\tilde{\mathbf{F}}(\mathbf{x}) = \begin{pmatrix} -r - abmy & abm - abmx \\ ac - acy & -\mu - acx \end{pmatrix}. \tag{9}$$

Evaluating the Jacobian Matrix at the fixed point $(x^*, y^*) = (0,0)$, followed by calculating its characteristic equation, we get that

$$\begin{aligned} |D\tilde{\mathbf{F}}(0,0) - \lambda I_2| = 0 &\Rightarrow (-r - \lambda)(-\mu - \lambda) - a^2bcm = 0 \\ &\Rightarrow \lambda^2 + (r + \mu)\lambda + r\mu - a^2bcm = 0. \end{aligned}$$

Solving this quadratic equation gives us the following eigenvalues:

$$\lambda_1 = \frac{-(r+\mu) - \sqrt{(r-\mu)^2 + 4a^2bcm}}{2},$$

$$\textit{and} \quad \lambda_2 = \frac{-(r+\mu) + \sqrt{(r-\mu)^2 + 4a^2bcm}}{2},$$

and they are both real. Now, we observe that $\lambda_1 < 0$. With regard to λ_2, we have that if $R_0 < 1$, then $\lambda_2 < 0$, and thus the fixed point $(x^*, y^*) = (0,0)$ is a stable node (sink). On the other hand, if $R_0 > 1$, then $\lambda_2 > 0$, and thus the fixed point $(x^*, y^*) = (0,0)$ is a saddle point.

Similarly, at the fixed point $(x^*, y^*) = \left(\frac{a^2bcm - r\mu}{a^2bcm + acr}, \frac{a^2bcm - r\mu}{a^2bcm + abm\mu}\right)$, we have the characteristic equation

$$|D\tilde{\mathbf{F}}\left(\frac{a^2bcm - r\mu}{a^2bcm + acr}, \frac{a^2bcm - r\mu}{a^2bcm + abm\mu}\right) - \lambda I_2| = 0.$$

This gives that

$$\lambda^2+\left(\frac{ac(abm+r)}{ac+\mu}+\frac{abm(ac+\mu)}{abm+r}\right)\lambda+a^2bcm-r\mu=0.$$

For simplicity, if we let $\phi=\frac{ac(abm+r)^2+abm(ac+\mu)^2}{(abm+r)(ac+\mu)}$ and $\psi=a^2bcm-r\mu$, then the characteristic equation becomes $\lambda^2+\phi\lambda+\psi=0$. Now, solving this characteristic equation, we get the following eigenvalues:

$$\lambda_1=\frac{-\phi-\sqrt{\phi^2-4\psi}}{2},$$
$$\textit{and}\quad \lambda_2=\frac{-\phi+\sqrt{\phi^2-4\psi}}{2},$$

Since $\phi>0$ and $\phi>\sqrt{\phi^2-4\psi}$, we observe that λ_1, $\lambda_2<0$, and thus the fixed point $(x^*,y^*)=\left(\frac{a^2bcm-r\mu}{a^2bcm+acr},\frac{a^2bcm-r\mu}{a^2bcm+abm\mu}\right)$ is a stable node (sink). □

Remark 1. *We remark that in Lemma 2, if $R_0=1$, then the system only has the trivial fixed point $(x^*,y^*)=(0,0)$, with $\lambda_2=0$, and that we have a degenerate fixed point.*

3 Global Well-posedness

In this section, we will show that the system of equations (1) is in fact globally well-posed. To this end, we have the following theorem.

Theorem 3. *Consider the system of ordinary differential equations (1) in the form (8), and assume that initial conditions $\mathbf{x}(0)=\mathbf{x}_0$ are given. If all the constant parameters are positive, then the system of equations (8) is globally well posed.*

Proof. We only need to show that $\tilde{\mathbf{F}}\in C^1(\mathbb{R}^2)$. Towards this, we calculate that the Jacobian of $\tilde{\mathbf{F}}$ is given by

$$D\tilde{\mathbf{F}}=\begin{pmatrix}-r-abmy & abm-abmx\\ ac-acy & -\mu-acx\end{pmatrix}. \tag{10}$$

Now, since $\frac{\partial\tilde{F}_i}{\partial x}$ and $\frac{\partial\tilde{F}_i}{\partial y}$, $i=1,2.$, all exist and continuous for all $(x,y)\in\mathbb{R}^2$, we conclude that $\tilde{\mathbf{F}}\in C^1(\mathbb{R}^2)$. It then follows from [13] Theorem 1, pp. 184 that the system

$$\dot{\mathbf{x}}=\frac{\tilde{\mathbf{F}}(\mathbf{x})}{1+|\tilde{\mathbf{F}}(\mathbf{x})|}, \tag{11}$$

coupled with the initial condition $\mathbf{x}(0) = \mathbf{x}_0$ has a unique solution $\mathbf{x}(t)$ defined for all $t \in \mathbb{R}$, and that (11) is topologically equivalent to (8) on $\mathbb{R}^2$, so that (8) has unique solutions defined for all $t \in \mathbb{R}$ by

$$x(t) = e^{-rt}x(0) + abm \int_0^t e^{-r(t-s)}y(s)(1-x(s))\, ds, \tag{12}$$

$$y(t) = e^{-\mu t}y(0) + ac \int_0^t e^{-\mu(t-s)}x(s)(1-y(s))\, ds. \tag{13}$$

□

4 Numerical Experiments

In this section, we will perform various numerical experiments to demonstrate agreement of the numerical results with the theoretical results derived above. The ranges of the parameter values that we will be using for our numerical experiments are from various sources, as cited by [2]. See Table 1. Some values have been slightly perturbed to fit the description of our model.

The solution profiles in Figures 1 and 3 correspond to the cases in Lemma 2. Figure 1 shows that if all the parameters values are as in Table 2, then the basic reproduction number $R_0 = 8 > 1$, and the positive equilibrium point $(0.7, 0.583)$ is asymptotically stable. If the average mortality rate of the mosquitoes is increased past $0.4/day$ to $\mu = 0.5/day$ (Table 3), then the basic reproduction number $R_0 = 0.8 < 1$, and prevalence levels in both human host and mosquito decrease, and the solutions are approaching the trivial equilibrium point $(0, 0)$. Hence, the numerical results are in agreement with Lemma 2.

It is also interesting to note that with all the other parameter values as in Table 2, the number of female mosquitoes per human host would have to be decreased such that $m < 0.25$ for the prevalence levels in both human host and mosquitoes to decrease so that the solutions approach the trivial equilibrium $(0, 0)$. See Figures 5 and 6

Table 1: Definition and Ranges of Parameters

Parameter	Definition	Value/Range	References
a	Rate of biting on humans by a single mosquito	0.2-0.5/day	[6, 4]
b	Proportion of infected bites on humans that produce infection	0.5	[7, 14]
c	The transmission efficiency from human to mosquito	0.5	[7, 15]
m	Number of female mosquitoes per human host	2	[16, 17]
r	Average recovery rate of humans	0.01-0.05/day	[5, 4]
μ	Average mortality rate of mosquitoes	0.05-0.5/day	[5, 15]

Table 2: Definition of Parameters

Parameter	Definition	Value
a	Rate of biting on humans by a single mosquito	0.2
b	Proportion of infected bites on humans that profuce infection	0.5
c	The transmission efficiency from human to mosquito	0.5
m	Number of female mosquitoes per human host	2
r	Average recovety rate of humans	0.05
μ	Average mortality rate of mosquitoes	0.05

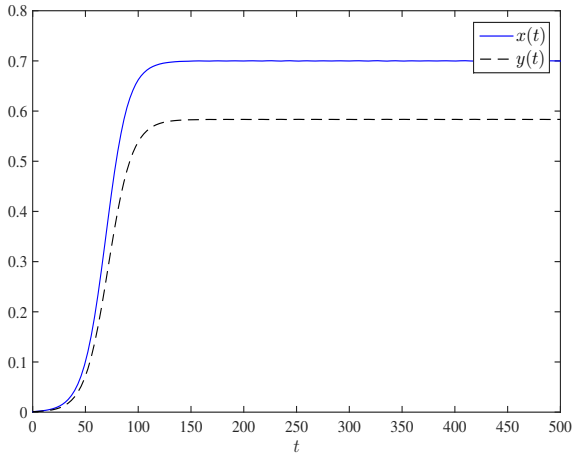

Figure 1: The plot of the $x(t)$ and $y(t)$ solutions when the values of parameters used are as in Table 2. The positive fixed point of the Ross-Macdonald model (1) is asymptotically stable, and the disease is endemic.

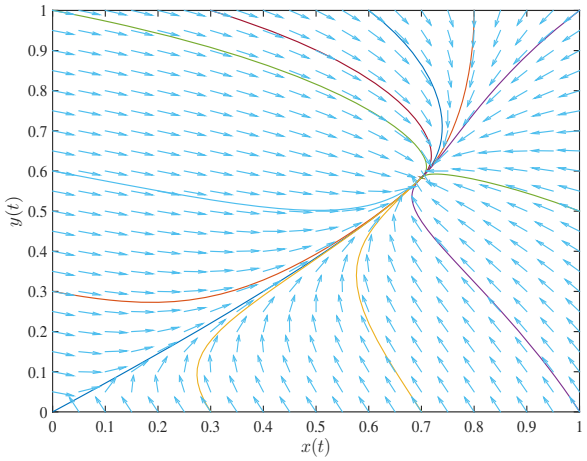

Figure 2: The phase portrait of the Ross-Macdonald model when the values of parameters used are as in Table 2. It agrees with Figure 1 that the positive fixed point of the Ross-Macdonald model (1) is asymptotically stable.

Table 3: Definition of Parameters

Parameter	Definition	Value
a	Rate of biting on humans by a single mosquito	0.2
b	Proportion of infected bites on humans that profuce infection	0.5
c	The transmission efficiency from human to mosquito	0.5
m	Number of female mosquitoes per human host	2
r	Average recovety rate of humans	0.05
μ	Average mortality rate of mosquitoes	0.5

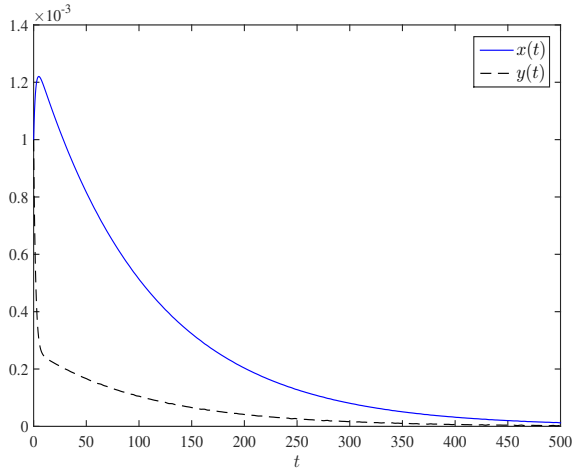

Figure 3: The plot of the $x(t)$ and $y(t)$ solutions when the values of parameters used are as in Table 3. The prevalence level decrease when the average mortality rate of mosquitoes is increased.

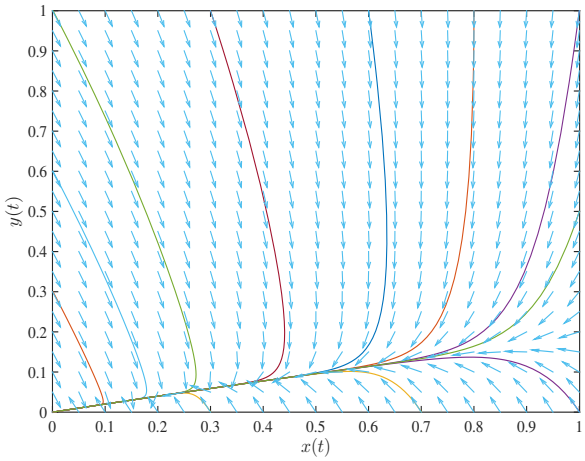

Figure 4: The phase portrait of the Ross-Macdonald model when the values of parameters used are as in Table 3. It agrees with Figure 3 that the prevalence level decrease when the average mortality rate of mosquitoes is increased.

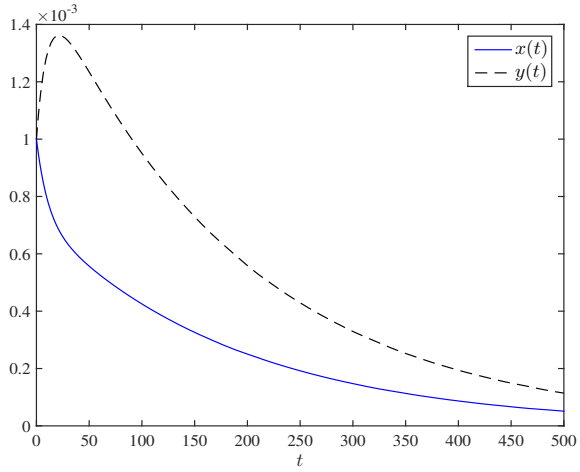

Figure 5: The plot of the $x(t)$ and $y(t)$ solutions when the values of parameters used are as in Table 2 and $m = 0.2$.

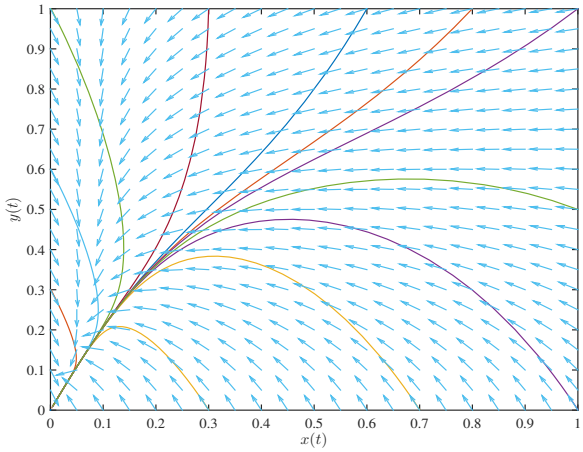

Figure 6: The phase portrait of the Ross-Macdonald model when the values of parameters used are as in Table 2 and $m = 0.2$. It agrees with Figure 5 that the prevalence level decrease.

5 Conclusion

We have presented a simple finite dimensional model for the interaction between the infected proportions of the human host population and the mosquito vector population. The primary objective of this paper is to give relevance of the well-posednes of the finite dimensional evolution process and to obtain a numerical validation of the theoretical results. For future research work, extension to the infinite dimensional case would be considered.

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