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Global Dynamics and Sensitivity Analysis of a Vector-Host-Reservoir Model

Ibrahim M. ELmojtaba[1]*, Santanu Biswas[2] and Joydev Chattopadhyay[2]

*[1]*Department of Mathematics and Statistics, College of Science, Sultan Qaboos University P.O. Box 36, PC 123, Al-Khoud, Muscat, Sultanate of Oman; [2]Agricultural and Ecological Research Unit, Indian Statistical Institute, 203 B.T. Road, Kolkata 700108, India. *Email: elmojtaba@squ.edu.om.*

ABSTRACT: The role of animal reservoir in the disease dynamics is not yet properly studied. In the present investigation a mathematical model of a vector-host-reservoir is proposed and analyzed to observe the global dynamics of the disease. We observe that the disease free equilibrium is globally asymptotically stable if the basic reproduction number (R_0) is less than unity whereas unique positive equilibrium is globally asymptotically stable if $R_0 > 1$ and transcritical bifurcation occurs at $R_0 = 1$. Our numerical result suggests that the biting rate plays an important role for the propagation of the disease and the recovery rate has not such important contribution towards eradication of the disease. We also perform sensitivity analysis of the model parameters and the results suggest that the death rate of reservoir may be used as a control parameter to eradicate the disease.

Keywords: Vector-host-reservoir model; Basic reproduction number; Lyapunov function; Bifurcation analysis; Numerical simulation; Sensitivity analysis.

الديناميكية الشاملة وتحليل الحساسية لنموذج العائل-المستودع والناقل

إبراهيم محمد المجتبى*، سانتانو بيسواس و جويديف شاتوبادي

مستخلص: يعرف المستودع للمرض بأنه نوع حيواني يعتبر وجوده ضرورياً لانتشار المرض. لم تتم دراسة دور المستودع الحيواني في ديناميكية الأمراض بعد بصورة جيدة ، و لدراسة هذا الدور فقد قمنا باقتراح نموذج رياضي يصف ديناميكية مرض ينتشر بين ثلاثة مجتمعات ، العائل ، المستودع والناقل. لوحظ من خلال التحليل الرياضي للنموذج أن نقطة الإتزان الخالية من الوباء مستقرة عالمياً إذا كان العدد الأساسي لإعادة الإنتاج (R0) أقل من وحدة واحدة بينما هنالك نقطة إتزان موجبة وهي مستقرة عالمياً إذا كان (R0 > 1) ، ويحدث تشعب أمامي عند (R0 = 1). نتائج المحاكاة العددية أوضحت أن معدل العض يلعب دوراً أساسياً في إنتشار المرض بينما أن معدل التماثل للشفاء ليس له مساهمة ملموسة في القضاء على المرض. قمنا أيضاً بإجراء تحليل للحساسية لمعلمات النموذج ، والذي أظهر أن العدد الأساسي لإعادة الإنتاج يتأثر بشدة بمعدل وفيات المستودع ، مما يعني أنه يمكن إستخدامه كمعلمة تحكم للقضاء على المرض.

كلمات مفتاحية: نموذج العائل-المستودع والناقل، العدد الأساسي لإعادة الإنتاج، دالة ليبونوف، تحليل التشعب، المحاكاة العددية وتحليل الحساسية.

1. Introduction

Generally, a disease reservoir is defined as a species that is essential for the persistence and transmission of the disease [1]. There are several types of reservoirs depending on their role in the life cycle of the pathogen, some of which are not necessarily for the maintenance of the disease but they can get infected by the pathogen and transmit it [2].

Several studies showed that Lyme disease has many reservoir hosts; Salkeld *et al.* [3] observed an apparent statewide association between squirrel infection prevalence and *Lyme* disease incidence, which suggests that squirrels are an important reservoir host responsible for maintaining this zoonotic disease regionally through U.S.A., also Craine *et al.* [4] showed that gray squirrels are major reservoirs for *Lyme* disease in U.K., and Richter *et al.* [5] proved that American Robins act as reservoir hosts for *Lyme* disease *Spirochetes* across U.S.A.

Diniz *et al.* [6] showed that there are several potential reservoir hosts for *Leishmaniasis* such as domestic dog and hamsters; Dantas-Torres [7] also proved that dogs act as a reservoir for *Leishmainasis*, and Faiman *et al.* [8] found that voles and rodents also act as major reservoirs for *Leishmaniasis* in Israel; Quinnell *et al.* [9] discovered that wide range of wild and domestic animals play the role of reservoir for *Leishmaniasis* such as the crab-eating fox, *Cerdocyon thous*, opossums, *Didelphis spp.*, domestic cats, *Felis cattus*, and black rat, *Rattus rattus*.

Melaun *et al*. [10] showed that pets are suspected to be potential reservoirs for many viruses like Bwamba virus, Kaeng Khoi virus, Rift Valley fever virus, Toscana virus, Western equine encephalitis, Sindbis virus, Chikungunya virus, Ross River virus, the Eastern equine encephalitis virus, the Venezuelan equine encephalitis virus, Yellow fever, Japanese Encephalitis, West Nile fever, Dengue fever, St. Louis encephalitis, Zika virus and Tacaribe virus. Besides viruses, some parasites are known, which occur in bats and humans, and can be transmitted through hemorrhagic insects. The first one is the Chagas disease and the coccidian genus *Plasmodium*, which is the pathogenic agent of malaria.

Quite a good number of studies have been carried out to observe the disease dynamics with different settings and assumptions (for example, see [11, 12, 13]). As far our knowledge goes, no research has been done to describe the dynamics of a general vector-host-reservoir model. Keeping this factor in mind, we propose and analyze a non-fatal vector borne disease with reservoir. The basic aim of the present investigation is to observe the disease dynamics and to suggest some control strategies for eradication of the disease. In any epidemic model, the basic reproduction number plays an important role; we like to suggest the control strategies by sensitivity analysis of the model parameters related to basic reproduction number.

The article is organized as follows: an introduction is given in Section 1, the model is formulated in Section 2, the model is fully mathematically analyzed in Section 3, sensitivity analysis for the parameters of the model is carried out in Section 4, some numerical simulation is givn in Section 5 and the paper ends with a conclusion.

2. Model formulation and equations

To formulate this model, we will follow a model built by Elmojtaba *et al.* [14] to describe the dynamics of visceral leishmaniasis, see also [14, 15, 16]. Consider the transmission of a non fatal disease between our three different populations, human host population, $N_H(t)$, reservoir host population, $N_R(t)$, and vector population, $N_V(t)$. Human host population will be divided into three categories, susceptible individuals $S_H(t)$, infected individuals $I_H(t)$, and those who are recovered and have permanent immunity, $R_H(t)$. This implies that

$$N_H(t) = S_H(t) + I_H(t) + R_H(t).$$

Similarly, the reservoir host population will be divided into two categories, susceptible reservoirs, $S_R(t)$, and infected reservoirs, $I_R(t)$, such that

$$N_R(t) = S_R(t) + I_R(t)$$

and the vector population have two categories, susceptible vectors $S_V(t)$, and infected vectors $I_V(t)$, such that

$$N_V(t) = S_V(t) + I_V(t)$$

It is assumed that susceptible individuals are recruited into the population at a constant rate μ_h and acquire infection with following contacts with infected vectors at a per capita rate $ab\frac{I_V}{N_H}$, where a is the per capita biting rate of vectors on humans (or reservoirs), and b is the transmission probability per bite per human (as the case for malaria, [17, 18]). Infected humans recover and acquire permanent immunity at an average rate α. There is a per capita natural mortality rate μ_h in all human sub-population.

Susceptible reservoirs are recruited into the population at a constant rate μ_r, and acquire infection following contacts with infected vectors at a rate $ab\frac{I_V}{N_H}$ where a and b as described above. A per capita natural mortality rate μ_r occurs in the reservoir population.

Susceptible vectors are recruited at a constant rate μ_v, and acquire infection following contacts with infected humans or infected reservoirs at an average rate equal to $ac\frac{I_H}{N_H} + ac\frac{I_R}{N_R}$, where a is the per capita biting rate, and c is the transmission probability for vector infection. Vectors suffer natural mortality at a per capita rate μ_v regardless of their infection status.

From the description of the terms, we get the following system of differential equations:

$$\begin{aligned} S_H' &= \mu_h N_H - abI_V\frac{S_H}{N_H} - \mu_h S_H \\ I_H' &= abI_V\frac{S_H}{N_H} - (\alpha + \mu_h)I_H \\ R_H' &= \alpha I_H - \mu_h R_H \end{aligned} \tag{1}$$

$$S_R^{'} = \mu_r N_R - abI_V \frac{S_R}{N_R} + \mu_r S_R$$

$$I_R^{'} = abI_V \frac{S_R}{N_R} - \mu_r I_R$$

$$S_V^{'} = \mu_v N_V - acS_V \frac{I_H}{N_H} - acS_V \frac{I_R}{N_R} - \mu_v S_V$$

$$I_V^{'} = acS_V \frac{I_H}{N_H} + acS_V \frac{I_R}{N_R} S_V - \mu_v I_V$$

Invariant region

All parameters of the model are assumed to be non-negative, furthermore since model (1) monitors living populations, it is assumed that all the state variables are non-negative at time $t = 0$. This shows that the biologically-feasible region: $\Omega = \{(S_H, I_H, R_H, S_R, I_R, S_V, I_V) \in R_+^7 : S_H, I_H, R_H, S_R, I_R, S_V, I_V \geq 0\}$ is positively-invariant domain, and thus, the model is epidemiologically and mathematically well posed, and it is sufficient to consider the dynamics of the flow generated by (1) in this positively-invariant domain Ω.

3. Analysis of the model

In this Section, we analyze system (1) to obtain the steady states of the system and their stability. We consider the equations for the proportions by first scaling the sub-populations for N_H, N_R and N_V using the following set of new variables

$$s_h = \frac{S_H}{N_H}, i_h = \frac{I_H}{N_H}, r_h = \frac{R_H}{N_H}, s_r = \frac{S_R}{N_R}, i_r = \frac{I_R}{N_R}, s_v = \frac{S_V}{N_V}, \text{ and } i_v = \frac{I_V}{N_V};$$

and let $m = \frac{N_V}{N_H}$ be the vector-human ratio defined as the number of vector per human host (see similar definition in malaria models, in [19, 20]). Note that the ratio m is taken as a constant because it is well known (see [21] pages 218-220) that a vector takes a fixed number of blood meals per unit time independent of the population density of the host. Similarly, we let $n = \frac{N_V}{N_R}$ be the vector-reservoir ratio defined as the number of vector per reservoir host.

Differentiating with respect to time t we get:

$$\begin{aligned}
s_h^{'} &= \mu_h - abmi_v s_h - \mu_h s_h \\
i_h^{'} &= abmi_v s_h - (\alpha + \mu_h) i_h \\
r_h^{'} &= \alpha i_h - \mu_h r_h \\
s_r^{'} &= \mu_r - abni_v s_r - \mu_r s_r \\
i_r^{'} &= abni_v s_r - \mu_r i_r \\
s_v^{'} &= \mu_v - ac(i_h + i_r) s_v - \mu_v s_v \\
i_v^{'} &= ac(i_h + i_r) s_v - \mu_v i_v
\end{aligned} \tag{2}$$

with the feasible region (i.e. where the model makes biological sense)
$\Gamma = \{(s_h, i_h, r_h, s_r, i_r, s_v, i_v) \in R_+^7 :$
$0 \leq s_h, i_h, r_h; s_h + i_h + r_h \leq 1; 0 \leq s_r, i_r; s_r + i_r \leq 1; 0 \leq s_v, i_v; s_v + i_v \leq 1\}$. It can be shown that the above region is positively invariant with respect to the system (2), where R_+^7 denotes the non-negative cone of R^7 including its lower dimensional faces.

3.1 Basic Reproduction Number of the Model

To calculate the basic reproduction number we will use the next generation approach [22, 23], define F as the column-vector of rates of the appearance of new infections in each compartment; $V = V^+ + V^-$, where V^+ is the column-vector of rates of transfer of individuals into the particular compartment; and V^- is the column-vector of rates of transfer of individuals out of the particular compartment. Hence, from our model we have

$$F = \begin{pmatrix} abmi_v s_h \\ abni_v s_r \\ ac(i_h + i_r)s_v \end{pmatrix}$$

and

$$V = \begin{pmatrix} (\alpha + \mu_h)i_h \\ \mu_r i_r \\ \mu_v i_v \end{pmatrix}.$$

then the matrices F and V from the partial derivatives of F and V with respect to the infected classes computed at the DFE are given by

$$F = \begin{pmatrix} 0 & 0 & abm \\ 0 & 0 & abn \\ ac & ac & 0 \end{pmatrix}, \quad and \quad V = \begin{pmatrix} (\alpha + \mu_h) & 0 & 0 \\ 0 & \mu_r & 0 \\ 0 & 0 & \mu_v \end{pmatrix}$$

Then the basic reproduction number, R_0 defined as the spectral radius of matrix FV^{-1};

$$\mathrm{R}_0 = \rho(FV^{-1}) = \sqrt{\frac{a^2bcn(\alpha + \mu_h) + a^2bcm\mu_r}{\mu_r\mu_v(\alpha + \mu_h)}}$$

3.2 Local Stability analysis of the disease-free equilibrium E_0

The disease-free equilibrium (DFE) of the system (2) is given by

$E_0 = (s_h^0, i_h^0, r_h^0, s_r^0, i_r^0, s_v^0, i_v^0) = (1,0,0,0,1,0,1,0)$.

using Theorem 2 of van den Driessche and Watmough [23], we have the following lemma:

Lemma 3.1. *The disease-free equilibrium is locally asymptotically stable if* $\mathrm{R}_0 < 1$ *and unstable if* $\mathrm{R}_0 > 1$.

3.3 Global Stability analysis of the disease-free equilibrium E_0

The following theorem shows that the DFE is globally asymptotically stable if $\mathrm{R}_0 < 1$.

Theorem 3.1. The disease-free equilibrium point is globally asymptotically stable if $\mathrm{R}_0 < 1$ **Proof**:

Consider the following Lyapunov function

$$L = ac\mu_r i_h + ac(\alpha + \mu_h)i_r + \mu_r(\alpha + \mu_h)i_v$$

with derivative

$$\begin{aligned}
L' &= ac\mu_r[abm(1-i_h-r_h)i_v - (\alpha+\mu_h)i_h] \\
&\quad + ac(\alpha+\mu_h)[abn(1-i_r)i_v - \mu_r i_r] \\
&\quad + \mu_r(\alpha+\mu_h)[ac(i_h+i_r)(1-i_v) - \mu_v i_v] \\
&\le [a^2bcm\mu_r + a^2bcn(\alpha+\mu_h) - \mu_r\mu_v(\alpha+\mu_h)]i_v - \mu_r a^2bcm(\alpha_2+\beta+\mu_h+(1-\sigma)\alpha_1)i_h i_v \\
&\quad - \mu_r a^2bcm(\alpha_2+\beta+\mu_h+(1-\sigma)\alpha_1)p_h i_v - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_h \\
&\quad - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)p_h - a^2bcn(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_r i_v \\
&\quad - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_r + \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_h \\
&\quad + \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)p_h + -\mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_r \\
&\quad - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_h i_v - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)p_h i_v \\
&\quad - \mu_r ac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_r i_v \\
&= \mu_r\mu_v(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)(\mathrm{R}_0^2-1)i_v \\
&\quad - \mu_r a^2bcm(\alpha_2+\beta+\mu_h+(1-\sigma)\alpha_1)i_h i_v - \mu_r a^2bcm(\alpha_2+\beta+\mu_h+(1-\sigma)\alpha_1)p_h i_v
\end{aligned}$$

$$-a^2bcn(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_ri_v-\mu_rac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_hi_v$$

$$-\mu_rac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)p_hi_v-\mu_rac(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)i_ri_v$$

$$\leq \mu_r\mu_v(\alpha_1+\delta+\mu_h)(\alpha_2+\beta+\mu_h)(\mathrm{R}_0^2-1)i_v$$

and hence $L' \leq 0$ if $\mathrm{R}_0 < 1$. We observe that our system has the maximum invariant set for $L' = 0$ if and only if $\mathrm{R}_0 \leq 1$ holds and $i_h = p_h = r_h = i_v = i_r = 0$. By Lyapunov-LaSallés Theorem [20], all the trajectories starting in the feasible region where the solutions have biological meaning approach the positively invariant subset of the set where $L' = 0$, so that as $t \to \infty$, $s_h(t) \to 1, s_r(t) \to 1$, and $s_v(t) \to 1$. This shows that all solutions in the set where $i_h = p_h = r_h = i_v = i_r = 0$, go to the disease-free equilibrium E_0. Thus, $\mathrm{R}_0 < 1$ is the necessary and sufficient condition for the disease to be eliminated from the community.

3.4 Existence of the endemic equilibrium E_1

In order to prove the existence of E_1 we equate the right hand sides of system (2) to zeros, and substitute $s_h = 1 - i_h - r_h$, $s_r = 1 - i_r$ and $s_v = 1 - i_v$, to obtain

$$abmi_v(1-i_h-r_h) = (\alpha+\mu_h)i_h \tag{3}$$

$$\alpha i_h = \mu_h r_h \tag{4}$$

$$abni_v(1-i_r) = \mu_r i_r \tag{5}$$

$$(aci_h + aci_r)(1-i_v) = \mu_v i_v \tag{6}$$

From equations (4) and (5) we have:

$$r_h^* = \frac{\alpha}{\mu_h} i_h^* \tag{7}$$

$$i_r^* = \frac{abni_v^*}{abni_v^* + \mu_r} \tag{8}$$

Now substituting equations (7) and (8) in equations (3) and (6), respectively, then solving equations (3) and (6) we have either $i_v^* = 0$, which gives the DFE, or i_v^* satisfies the following equation:

$$A(i_v^*)^2 + Bi_v^* + C = 0 \tag{9}$$

where

$$A = -a^3b^2cmn\left(\frac{\alpha+2\mu_h}{\mu_h}\right)$$

$$B = -A - \mu_v\mu_r(\alpha+\mu_h)(\mathrm{R}_0^2-1) - \mu_v(\alpha+\mu_h)\left[\frac{ab}{\mu_h}(m\mu_r+n\mu_h)+\mu_r\right]$$

$$C = \mu_v\mu_r(\alpha+\mu_h)(\mathrm{R}_0^2-1)$$

We note that $A < 0$, and $C > 0$ when $\mathrm{R}_0 > 1$, hence we have one and only one positive solution for equation (9) when $\mathrm{R}_0 > 1$, and then we have the following lemma:

Lemma 3.2. *The system (2) has precisely one positive endemic equilibrium E_1 given by $E_1 = (s_h^*, i_h^*, r_h^*, s_r^*, i_r^*, s_v^*, i_v^*)$ and i_v^* satisfying equation (9), when $\mathrm{R}_0 > 1$.*

3.5 Local Stability analysis of the endemic equilibrium E_1

To investigate the local stability of the endemic equilibrium, we use the center manifold theorem, particularly, Theorem 5 in Castillo-Chavez and Song [25].
The Jacobian of the system (2) at the disease-free equilibrium E_0 is given by:

$$\mathrm{J}\ (E_0) = \begin{pmatrix} -\mu_h & 0 & 0 & 0 & 0 & 0 & -\Phi m \\ 0 & -(\alpha+\mu_h) & 0 & 0 & 0 & 0 & \Phi m \\ 0 & \alpha & -\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_r & 0 & 0 & -\Phi n \\ 0 & 0 & 0 & 0 & -\mu_r & 0 & \Phi n \\ 0 & -ac & 0 & 0 & -ac & -\mu_v & 0 \\ 0 & -ac & 0 & 0 & -ac & 0 & -\mu_v \end{pmatrix}$$

Consider the case when $\mathrm{R}_0 = 1$ and suppose that $\Phi = ab$ is chosen as a bifurcation parameter, then it can be shown that the jacobian of the system (2) has a right eigenvector given by $W = (w_1, w_2, w_3, w_4, w_5, w_6, w_7)^T$, where

$$w_1 = -\frac{\Phi m}{\mu_h} w_7$$

$$w_2 = \frac{\Phi m}{\alpha+\mu_h} w_7$$

$$w_3 = \frac{\Phi \alpha m}{\mu_h(\alpha+\mu_h)} w_7$$

$$w_4 = -\frac{\Phi n}{\mu_r} w_7$$

$$w_5 = \frac{\Phi n}{\mu_r} w_7$$

$$w_6 = -w_7$$

and a left eigenvector given by $V = (v_1, v_2, v_3, v_4, v_5, v_6, v_7)$, where

$$v_1 = v_3 = v_4 = v_6 = 0$$

$$v_2 = \frac{ac}{\alpha+\mu_h}$$

$$v_5 = \frac{ac}{\mu_r}$$

It can be shown that:

$$a^* = -[\frac{acm^2\Phi^2}{\mu_h(\alpha+\mu_h)} + \frac{acm\Phi}{\alpha+\mu_h} + \frac{acn\Phi}{\mu_r}(\frac{n\Phi}{\mu_r} - 1)]v_7 w_7^2$$

$$b^* = acm[\frac{1}{\alpha+\mu_h} + \frac{1}{\mu_r}]v_7 w_7$$

it is clear that $a^* < 0$ and $b^* > 0$, hence our System (2) undergoes a regular transcritical bifurcation at $\mathrm{R}_0 = 1$, before the bifurcation the disease-free equilibrium is stable and there exists an unstable positive endemic equilibrium, and after the bifurcation the disease-free equilibrium became unstable the endemic equilibrium became stable. Then we have the following result:

Lemma 3.3. The endemic equilibrium is locally asymptotically stable for $\mathrm{R}_0 > 1$.

3.6 Global Stability of Endemic Equilibrium

To prove the global stability of the endemic equilibrium we first start with some preliminaries.

Lemma 1. *(Lemma 2.1 in [26]) Let $A(t)$ be a continuous, cooperative, irreducible, and ω-periodic $n \times n$ matrix function. Let $\Phi_{A(.)}(t)$ be the fundamental matrix of the linear non-autonomous differential equation $\dot{x} = A(t)x$, where x is a $n \times 1$ vector. Let $\mu = \frac{1}{\omega}\ln r(\Phi_{A(.)}(\omega))$, where, $r(\Phi_{A(.)}(\omega))$ is the spectral radius of the monodromy matrix $\Phi_{A(.)}(\omega)$. Then there exists a positive, ω-periodic function $v(t)$ such that $e^{\mu t}v(t)$ is a solution of $\dot{x} = A(t)x$.*

Definition 1 *System (2) is uniformly persistent if* $\exists$ *an* $\eta > 0$ *(depending only on parameter values not on initial condition) such that for any initial value* $(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in \mathrm{R}_+ \times$ *int(*R_+*)* $\times$ *int(*R_+*)* $\times$ R_+ $\times$ *int(*R_+*)* $\times$ R_+ $\times$ *int(*R_+*)*

such that every solution $(s_h(t), i_h(t), r_h(t), s_r(t), i_r(t), s_v(t), i - v(t))$ of the system (2) satisfies

$\lim_{t\to\infty}\inf s_h(t) \ldots \eta$, $\lim_{t\to\infty}\inf i_h(t) \ldots \eta$, $\lim_{t\to\infty}\inf r_h(t) \ldots \eta$, $\lim_{t\to\infty}\inf s_r(t) \ldots \eta$, $\lim_{t\to\infty}\inf i_r(t) \ldots \eta$, $\lim_{t\to\infty}\inf s_v(t) \ldots \eta$, $\lim_{t\to\infty}\inf i_v(t) \ldots \eta$.

Definition 2 *The system (2) is said to be permanent if there exists a compact region* $\Omega_0 \in$ *int(*Ω*) such that every solution of the system (2) with initial condition* $(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in \mathrm{R}_+ \times$ *int(*R_+*)* $\times$ R_+ $\times$ *int(*R_+*)* $\times$ R_+ $\times$ *int(*R_+*) will eventually enter and remain in region* Ω_0.

Clearly, for a dissipative dynamical system proving permanence is equivalent to proving uniform persistence. Consider following sets:

$X = \mathrm{R}_+^7$, $X_0 = \mathrm{R}_+ \times \mathrm{int}(\mathrm{R}_+) \times \mathrm{int}(\mathrm{R}_+) \times \mathrm{R}_+ \times \mathrm{int}(\mathrm{R}_+) \times \mathrm{R}_+ \times \mathrm{int}(\mathrm{R}_+)$, $\partial X_0 = X \setminus X_0$.

Let, $f : X \to X$ be a continuous map and we define following set

$M_\partial = \{x \in \partial X_0 : f^n(x) \in \partial X_0, n \ldots 0\}$.

Following lemma will be used to show uniform persistence of the system (2)

Lemma 2. *([27]) Assume that*

1. $f(X_0) \subseteq X_0$ and f has a global attractor A.
2. There exists a finite sequence $\mathrm{M} = \{M_1, M_2, ..., M_k\}$ of disjoint, compact, and isolated invariant sets in ∂X_0 such that

- $\Omega(M_\delta) = \cup_{x\in M_\partial} \omega(x) \subset \cup_{i=1}^k M_i$;
- no subset of M forms a cycle in ∂X_0;
- M_i is isolated in X;
- $W^s(M_i) \cap X_0 = \varnothing$ for each 1,, i ,, k

Then there exists $\eta > 0$ such that $\liminf_{n\to\infty} d(f^n(x), \partial X_0) \ldots \eta$ for all $x \in X_0$.

We claim the following result

Proposition 1 *If* $R_0 > 1$ *then the solutions of the system (2) is uniformly persistent.*

Proof. Consider the periodic semi-flow $T : \mathrm{R}_+^7 \to \mathrm{R}_+^7$ associated with the system (2) defined by:

$T(t)x = u(t, x)$, $\forall x \in \mathrm{R}_+^7$.

Let P_1 be the associated Poincaré map defined as $P_1 := T(\omega)$. We first show that P_1 is uniformly persistent with respect to $(X_0, \partial X_0)$. It is clear that the set X and X_0 are positively invariant for the system (2). Now the bounded set Ω ($\Omega = \Gamma$) attracts every solution of the system (2) and also Ω is compact. Thus the Poincaré map P_1 is point dissipative and compact on X. Therefore, it follows from Theorem 1.1.3 in [27] there is a global attractor A of P_1 that attracts each bounded set in X. For the system (2) the set M_∂ is defined as $M_\partial = \{(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in \partial X_0 : P_1^n(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in \partial X_0, \quad \forall n \ldots 0\}$.

We claim that, $M_\partial = \{(s_h, 0, 0, s_r, 0, s_v, 0) : s_h \ldots 0, s_r \ldots 0, s_v \ldots 0\}$. It is clear that

$\{(s_h, 0, 0, s_r, 0, s_v, 0) : s_h \ldots 0, s_r \ldots 0, s_v \ldots 0\} \subseteq M_\partial$. Now, let

$(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in \partial X_0 \setminus \{(s_h, 0, 0, s_r, 0, s_v, 0) : s_h \ldots 0, s_r \ldots 0, s_v \ldots 0\}$. If

$i_h(0) = 0, r_h(0) = 0, i_r(0) = 0, i_v > 0$, then we get $s_h(0) > 0, s_r(0) > 0, s_v(0) > 0, i_v(0) > 0$. From second equation of the system (2) we have,

$i_h'(0) > abmi_v(0)s_h(0) > 0$.

$r_h'(0) > \alpha i_h(0) > 0$.

$i_r'(0) > abni_v(0)s_r(0) > 0$.

and $i_v^{'}(0) > acs_v(0)(i_h(0)+i_r(0)) > 0$. Similarly, for other cases also.

Therefore, $(s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \notin \partial X_0$ for all $0 < t = 1$. This implies that $M_\partial = \{(s_h, 0, 0, s_r, 0, s_v, 0) : s_h \ldots 0, s_r \ldots 0, s_v \ldots 0\}$.

Now, P_1 has a unique fixed point $E_0(s_h, 0, 0, s_r, 0, s_v, 0)$ in M_∂. It is easy to show that $\{E_0\}$ is isolated in X and as E_0 is global attracting in M_∂ therefore we have, $\Omega(M_\partial) = \cup_{x \in M_\partial} \omega(x) \subseteq \{E_0\}$, where, $\omega(x)$ is the omega limit set of x. It is clear that no subset of $\{E_0\}$ can forms a cycle in ∂X_0.

Now, we shall show that, $W^s(E_0) \cap X_0 = \varnothing$, where, $W^s(E_0)$ is the stable set of E_0.

Let $x^0 = (s_h(0), i_h(0), r_h(0), s_r(0), i_r(0), s_v(0), i_v(0)) \in W^s(E_0) \cap X_0$.

Since $x^0 \in X_0$, therefore by continuity of solution with respect to initial conditions we have, for any $\varepsilon \in (0,1)$, there exists a $\delta > 0$ such that $\forall x^0 \in X_0$ satisfying $\| x^0 - E_0 \| < \delta$, implies $\| u(t, x^0) - u(t, E_0) \| < \varepsilon \quad \forall t \in [0, \omega]$.

We claim that $\lim_{m \to \infty} \sup \| P_1^m(x^0) - E_0 \| \ldots \delta \quad \forall x^0 \in X_0$. Suppose if possible $\exists x^0 \in X_0$ such that $\lim_{m \to \infty} \sup \| P_1^m(x^0) - E_0 \| < \delta$. Without loss of generality, we can assume that $\| P_1^m(x^0) - E_0 \| < \delta$ for all $m \ldots 0$. Therefore, we have $\| u(t, P_1^m(x^0)) - u(t, E_0) \| < \varepsilon$, $\forall t \in [0, \omega]$ and $\forall m \ldots 0$.

For any, $t \ldots 0$, let $t = m\omega + t_1$, where $t_1 \in [0, \omega]$ and $m = [\frac{t}{\omega}]$ is the greatest positive integer less than or equal to $\frac{t}{\omega}$.

Then we have, $\| u(t, P_1^m(x^0)) - u(t, E_0) \| = \| u(t_1, P_1^m(x^0)) - u(t_1, E_0) \| < \varepsilon$ for all $t \ldots 0$.

Let, $(s_h(t), i_h(t), r_h(t), s_r(t), i_r(t), s_v(t), i_v(t)) = U(t, x^0)$. It follows from previous argument that, $1 - \varepsilon < s_h(t) < 1 + \varepsilon,$, $1 - \varepsilon < s_r(t) < 1 + \varepsilon$, $1 - \varepsilon < s_v(t) < 1 + \varepsilon$, $0 < i_h(t) < \varepsilon$, $0 < r_h(t) < \varepsilon$, $0 < i_r(t) < \varepsilon$, $0 < i_v(t) < \varepsilon$, $\forall t \ldots 0$.

From the system (2) we have:

$$\begin{aligned} \frac{di_h}{dt} &\ldots abmi_v(1-\varepsilon) - (\alpha + \mu_h) i_h \\ \frac{di_r}{dt} &\ldots abni_v(1-\varepsilon) - \mu_r i_r \\ \frac{di_v}{dt} &\ldots aci_h(1-\varepsilon) + aci_r(1-\varepsilon) - \mu_v i_v \end{aligned} \tag{10}$$

Let, $M_\varepsilon(t) = \begin{pmatrix} 0 & 0 & abm\varepsilon \\ 0 & 0 & bn\varepsilon \\ ac\varepsilon & ac\varepsilon & 0. \end{pmatrix}$,

Hence we obtain,

$$\frac{d}{dt}[i_h, i_r, i_v]^T \ldots [F(t) - V(t) - \varepsilon M_\varepsilon(t)][i_h, i_r, i_v]^T.$$

Now, choosing $\varepsilon > 0$ sufficiently small so that $r(\Phi_{F(.)-V(.)-\varepsilon M_\varepsilon(.)}(\omega)) > 1$. Thus by lemma 1 and standard comparison theorem [28] $\exists$ ω-periodic function $f(t)$ such that $x(t) \ldots f(t)e^{s_1 t}$, where, $x(t) = [i_h, i_r, i_v]$ and

$$s_1 = \frac{1}{\omega} \ln r(\Phi_{F(.)-V(.)-\varepsilon M_\varepsilon(.)}(\omega)) > 0.$$

This implies as $t \to \infty$, $i_h(t) \to \infty$, $i_r(t) \to \infty$ and $i_v(t) \to \infty$. This is a contradiction as $\lim_{t \to \infty} \sup \| P_1^m(x^0) - E_0 \| < \delta$. Therefore, we have, $\lim_{t \to \infty} \sup \| P_1^m(x^0) - E_0 \| \ldots \delta \quad \forall x^0 \in X_0$. Which is again impossible as $x^0 \in W^s(E_0)$ (as $x \in W^s(E_0)$ implies $\lim_{t \to \infty} \| P_1^m(x^0) - E_0 \| = 0$). Thus we have, $W^s(E_0) \cap X_0 = \varnothing$.

Therefore, by lemma 2 we have P_1 is uniformly persistent with respect to $(X_0, \partial X_0)$. Therefore, by Theorem 3.1.1 in [27] the periodic semi-flow T is uniformly persistent in X.

Thus, if $R_0 > 1$ then solution of the system (2) is uniformly persistent.

Next, we claim the following result

Proposition 2. *If $R_0 > 1$ then the endemic equilibrium E_1 is globally asymptotically stable.*

Proof. Let, $E_1 = (\bar{s}_h(t), \bar{i}_h(t), \bar{r}_h(t), \bar{s}_r(t), \bar{i}_r(t), \bar{s}_v(t), \bar{i}_v(t))$.

We shall first show that $(\bar{s}_h(t), \bar{i}_h(t), \bar{p}_h(t), \bar{r}_h(t), \bar{s}_r(t), \bar{i}_r(t), \bar{s}_v(t), \bar{i}_v(t))$ is globally asymptotically stable

We construct following Lyapunov function

$$L(t) = |s_h(t) - \bar{s}_h(t)| + |i_h(t) - \bar{i}_h(t)| + |r_h(t) - \bar{r}_h(t)| + |s_r(t) - \bar{s}_r(t)| + |i_r(t) - \bar{i}_r(t)| + |s_v(t) - \bar{s}_v(t)| + |i_v(t) - \bar{i}_v(t)|.$$

We use following formula,

$$|x|' = sgn(x)x',$$

to calculate the upper right-hand derivative (Dini's derivative) of $L(t)$. Therefore, we have

$$\begin{aligned} D^+L(t) ,, & -|s_h - \bar{s}_h|\mu_h - |i_h - \bar{i}_h|\mu_h - |r_h - \bar{r}_h|\mu_h \\ & - |s_r - \bar{s}_r|\mu_r - |i_r - \bar{i}_r|\mu_r - |s_v - \bar{s}_v|\mu_v - |i_v - \bar{i}_v|\mu_v \end{aligned} \tag{11}$$

Let, $K = \min\{\mu_r, \mu_v, \mu_h\}$. Therefore, $K > 0$.

Now, $D^+L(t) ,, -K(|s_h - \bar{s}_h| + |i_h - \bar{i}_h| + |r_h - \bar{r}_h| + |s_r - \bar{s}_r| + |i_r - \bar{i}_r| + |s_v - \bar{s}_v| + |i_v - \bar{i}_v|)$.

Which implies L is non-increasing on $[0, +\infty)$.

Thus we have, $\lim_{t\to\infty} L(t) = 0$. Therefore it follows that

$\lim_{t\to\infty} |s_h - \bar{s}_h| = 0$, $\lim_{t\to\infty} |i_h - \bar{i}_h| = 0$, $\lim_{t\to\infty} |r_h - \bar{r}_h| = 0$, $\lim_{t\to\infty} |s_r - \bar{s}_r| = 0$, $\lim_{t\to\infty} |i_r - \bar{i}_r| = 0$, $\lim_{t\to\infty} |s_v - \bar{s}_v| = 0$, $\lim_{t\to\infty} |i_v - \bar{i}_v| = 0$.

Thus, $(\bar{s}_h(t), \bar{i}_h(t), \bar{p}_h(t), \bar{r}_h(t), \bar{s}_r(t), \bar{i}_r(t), \bar{s}_v(t), \bar{i}_v(t))$ is globally asymptotically stable.

4. Sensitivity Analysis of R_0

R_0 is considered one of the most important quantities in epidemic theory [29], therefore studying the sensitivity of R_0 to the other parameters will give some more insight ideas about the best way of interventions to reduce R_0 below unity.

There are many ways of conducting sensitivity analysis, all resulting in a slightly different sensitivity ranking [30]. Following [31, 32, 33] we used the normalized forward sensitivity index also called elasticity as it is the backbone of nearly all other sensitivity analysis techniques [30] and are computationally efficient [31]. The normalized forward sensitivity index of the basic reproduction number, R_0 with respect to a parameter value, P is given by:

$$S_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{P}{R_0} \tag{12}$$

because our R_0 contains square root, then it is convenient to use this version of equation 12:

$$S_p^{R_0} = \frac{1}{2}\frac{\partial R_0^2}{\partial p} \times \frac{P}{R_0^2} \tag{13}$$

Using equation 13 together with parameter values given in the Table 1, we have our sensitivity indices for R_0 with respect to the other model parameters, which is presented in Table 2.

Table 1. Parameter values for sensitivity analysis.

Parameter	Parameter description	Value	Source
μ_h	Natural mortality rate of humans	0.00004 day^{-1}	[34]
μ_r	Natural mortality rate of reservoirs	0.000274 day^{-1}	[14]
μ_v	Natural mortality rate of vectors	0.189 day^{-1}	[35]
a	Biting rate of vectors	0.285	[36]
b	Progression rate of the disease in vectors	0.22	[36]
c	Progression rate of the disease in human and reservoir	0.0714	[37]
α	Recovery rate	0.1,0.5,0.9	Assumed
m	Vector-human ratio	5	Assumed
n	Vector-reservoir ratio	10	Assumed

It can be seen from Table 2 that the sensitivity index of a, b, c, n and μ_v are fixed for all values of α, which means that the effect of these parameters on R_0 is not affected by the recovery rate (i.e. different values of α), where a, b, c and n has positive effect on R_0, for example if the biting rate is increased by 10%, then R_0 will increase by 10%, and if c is decreased by 10% then R_0 will decrease by 5%, while μ_v has a negative impact on R_0, therefor if for example μ_v is decreased (increased) by 10% then R_0 will increase (decrease) by 5%.

Table 2. Sensitivity indices of R_0.

Parameter	Sensitivity Index		
	$\alpha = 0.1$	$\alpha = 0.5$	$\alpha = 0.9$
a	+1	+1	+1
b	+0.5	+0.5	+0.5
c	+0.5	+0.5	+0.5
n	+0.499	+0.499	+0.499
m	+0.0006	+0.0001	+0.00001
α	-0.0006	-0.0001	-0.00001
μ_h	-2.7e-7	-1.1e-8	-3.4e-9
μ_r	-4.99	-0.99	-0.55
μ_v	-0.5	-0.5	-0.5

It is also clear that m, α and μ_h have a very small effect on R_0 because their sensitivity indexes are very small (less than 0.001). However when the recovery rate, α, is small, then R_0 became very sensitive to μ_r, for example if μ_r is decreased (increased) by 10% then R_0 will increase (decrease) by 49.9%, this is also can be seen from Figure 1, for example when $\alpha = 0.1$, then R_0 ranges between 5.6 and 15.5 for different values of μ_r, and when $\alpha = 0.5$ R_0 ranges between 1.1 and 3.9 for the same values of μ_r and when $\alpha = 0.9$ R_0 ranges between 0.83 and 2.1 for the same values of μ_r, which shows the effect of μ_r on R_0, and that effect is really clear for small values of α.

Different Scenarios Regarding Disease Control:

- If the animal reservoir is kept out of the system (assuming that there is no transmission between reservoir and vector, or if the animal reservoir is kept away from humans so vectors can't transmit the disease from reservoir to human), then the threshold for the disease to invade the human population can be kept less than 1 easily, i.e. the disease can be eliminated.
- If the human population is kept out of the system (assuming that all vectors stay near to the animal reservoir population to the their blood meal) then the threshold cannot be kept smaller than one which means that the disease will always persist in the reservoir and vector populations.
- Considering the full system, then the threshold can be kept less than one using one of the following control strategies:
  - Applying human treatment at a very high rate, which is not cost-effective.
  - Decrease the animal reservoir population throw culling and apply human treatment at a medium rate, which is not ethical and also not so cost-effective.
  - Keep the vector biting rate in a low level either by using pesticides or changing the human behavior, and applying human treatment at a low rate.

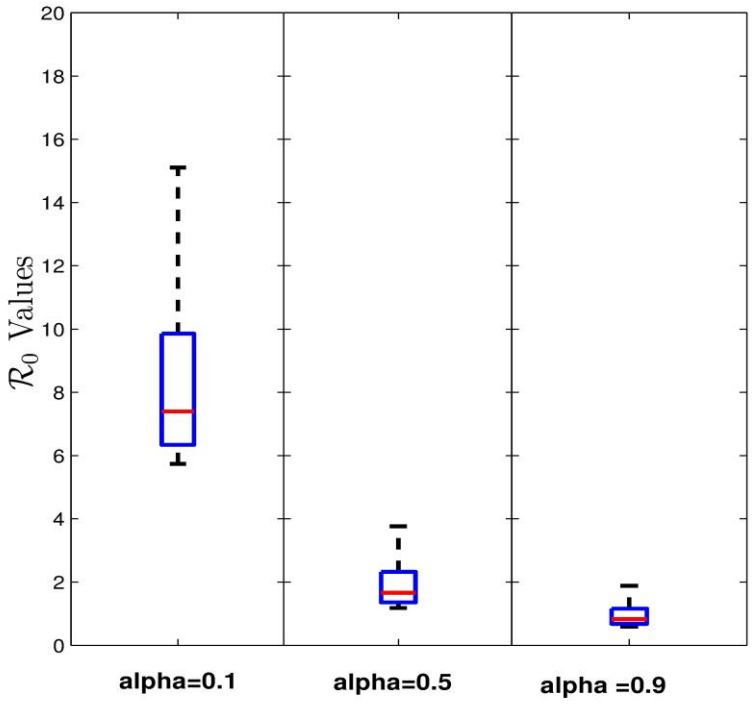

Figure 1. Values of R_0 for different values of μ_r with: (a) $\alpha = 0.1$, (b) $\alpha = 0.5$, (c) $\alpha = 0.9$.

5. Numerical Simulation of the Model

In this section we solve our model numerically with initial conditions: $s_h^0 = 0.9, i_h^0 = 0.1, r_h^0 = 0, s_r^0 = 0.9, i_r^0 = 0.1, s_v^0 = 0.8, i_v^0 = 0.2$. Some of the parameter's values were obtained from literature, and some of them were assumed or made varying in order to study their role. The parameter values used are in Table 3.

Table 3. Parameter values for numerical simulation.

Parameter	Parameter description	Value	Source
μ_h	Natural mortality rate of humans	0.00004 day^{-1}	[34]
μ_r	Natural mortality rate of reservoirs	0.000274 day^{-1}	[14]
μ_v	Natural mortality rate of vectors	0.189 day^{-1}	[35]
a	Biting rate of vectors	Variable	Variable
b	Progression rate of the disease in vectors	Variable	Variable
c	Progression rate of the disease in human and reservoir	Variable	Variable
α	Recovery rate	Variable	Variable
m	Vector-human ratio	Variable	Variable
n	Vector-reservoir ratio	Variable	Variable

Varying the values of a, the biting rate of vectors

Simulation results show that when the biting rate of vectors is small that leads to some delay in the time needed for the epidemic curve to reach the peak in the infected human population; however, the peak itself remains the same for all values of the biting rate, therefore reducing the biting rate of vectors helps in reducing the prevalence of the disease in the human population; however, to reduce the epidemic's peak other intervention is needed. Nonetheless, it seems to have less effect on other population as can be seen from Figure 2.

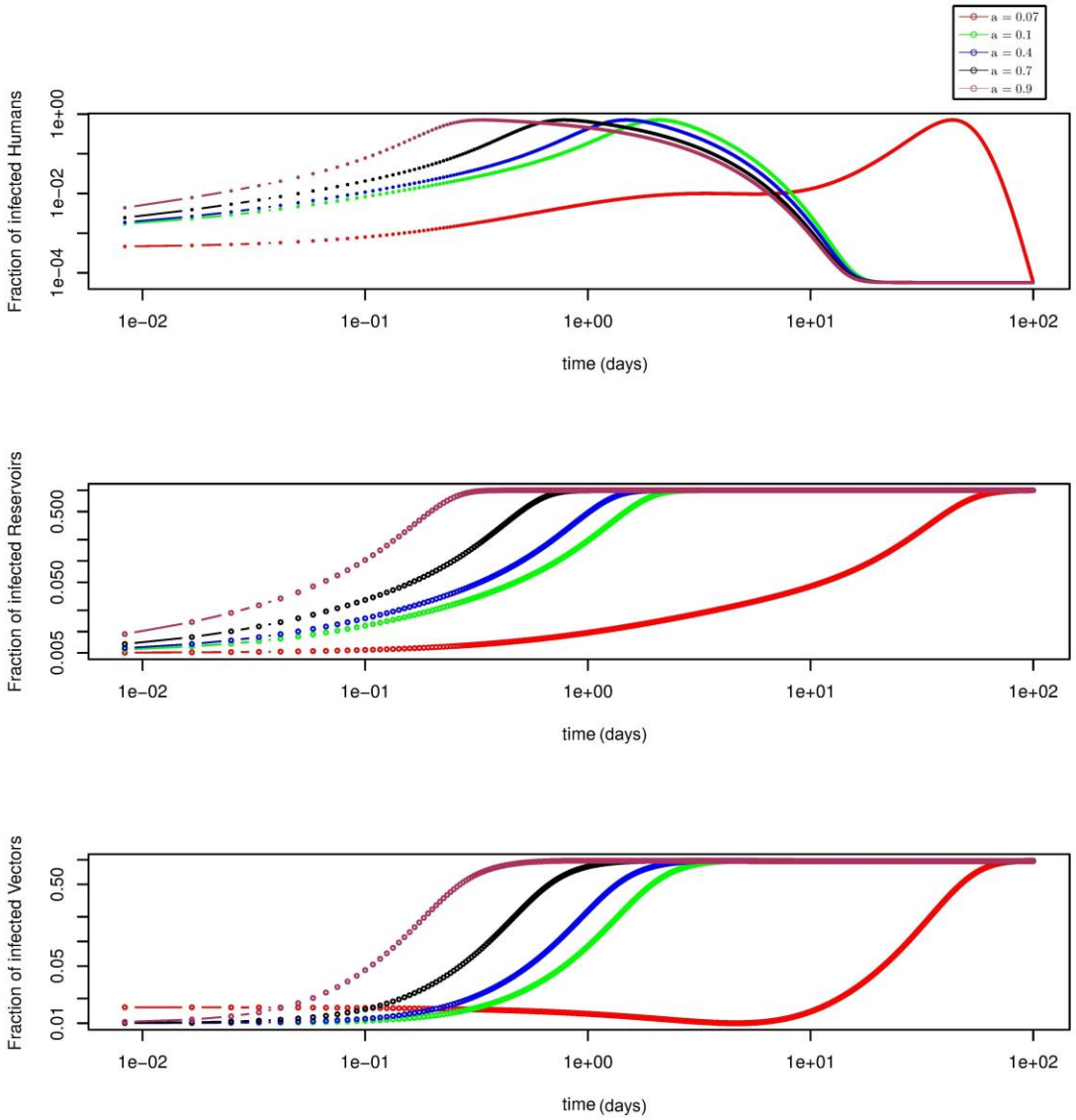

Figure 2. Simulation results for different values of *a*.

Varying the values of b, the progression rate of the disease in vectors

Simulation results show that the epidemic curve remains the same for small and big values of b and it just shifted to the right, which means that when the time needed for the pathogen to progress within vectors is big, the disease will need more time to hit the population which gives a window for some interventions, as seen from Figure 3. However, as we know this parameter is out of control.

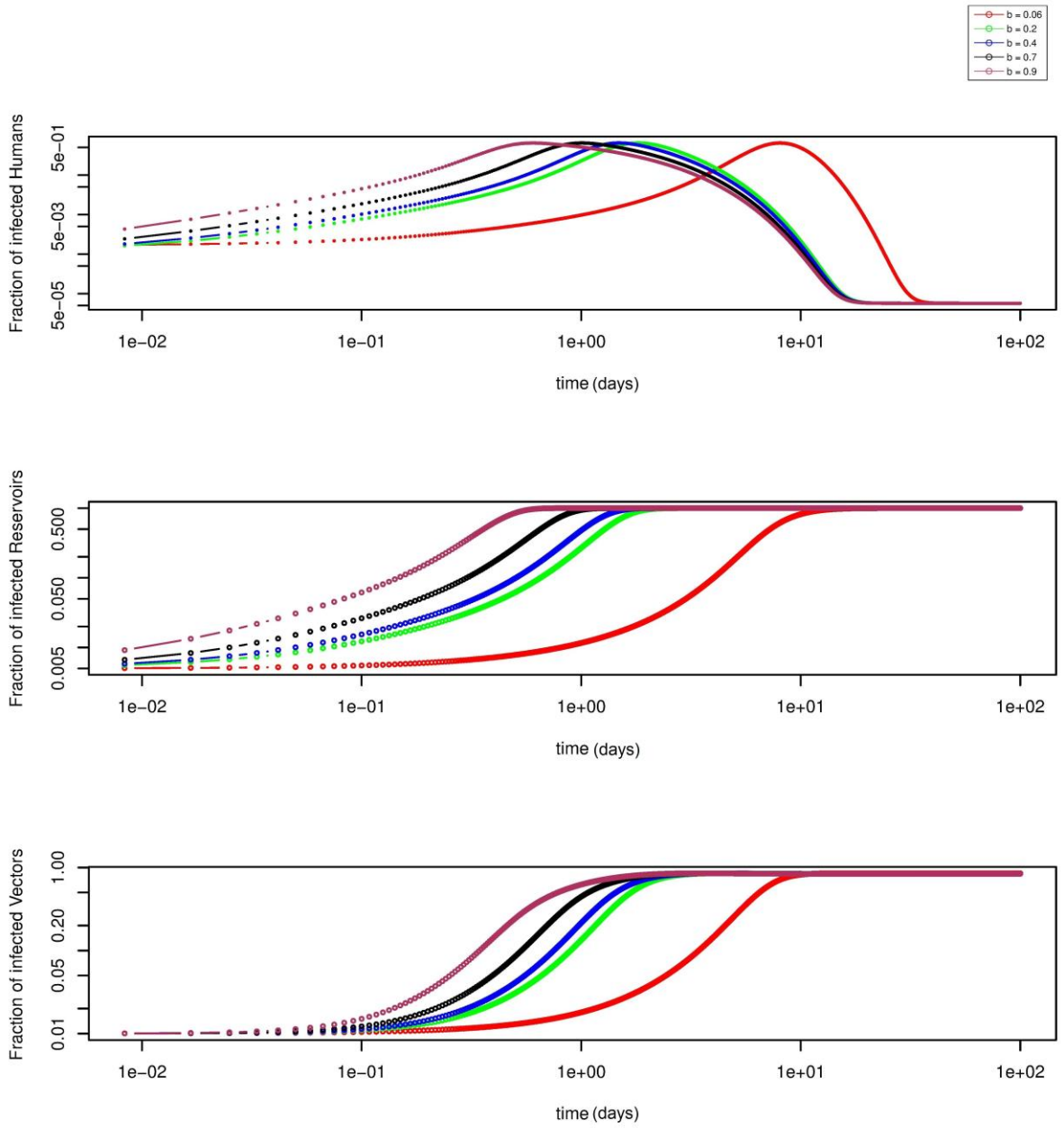

Figure 3. Simulation results for different values of *b*.

Varying the values of c, the progression rate of the disease in humans and reservoirs

It can be seen from Figure 4 that the effect of changing the values of c is almost the same as changing the values of b ; but the differences between the curves of the small value and big value of c is less than the differences between the curves of the small value and big value of b in infected human and infected reservoir populations, and the curves of different values of b and c are the same for the population of infected vectors, which means that the progression time of the pathogen within the vector has more effect than the progression time of the pathogen within the host or within reservoir. This is due to the fact that the vector population is much bigger than the other populations and the recruitment rate of the vector population is big compared to the recruitment rate of the other populations.

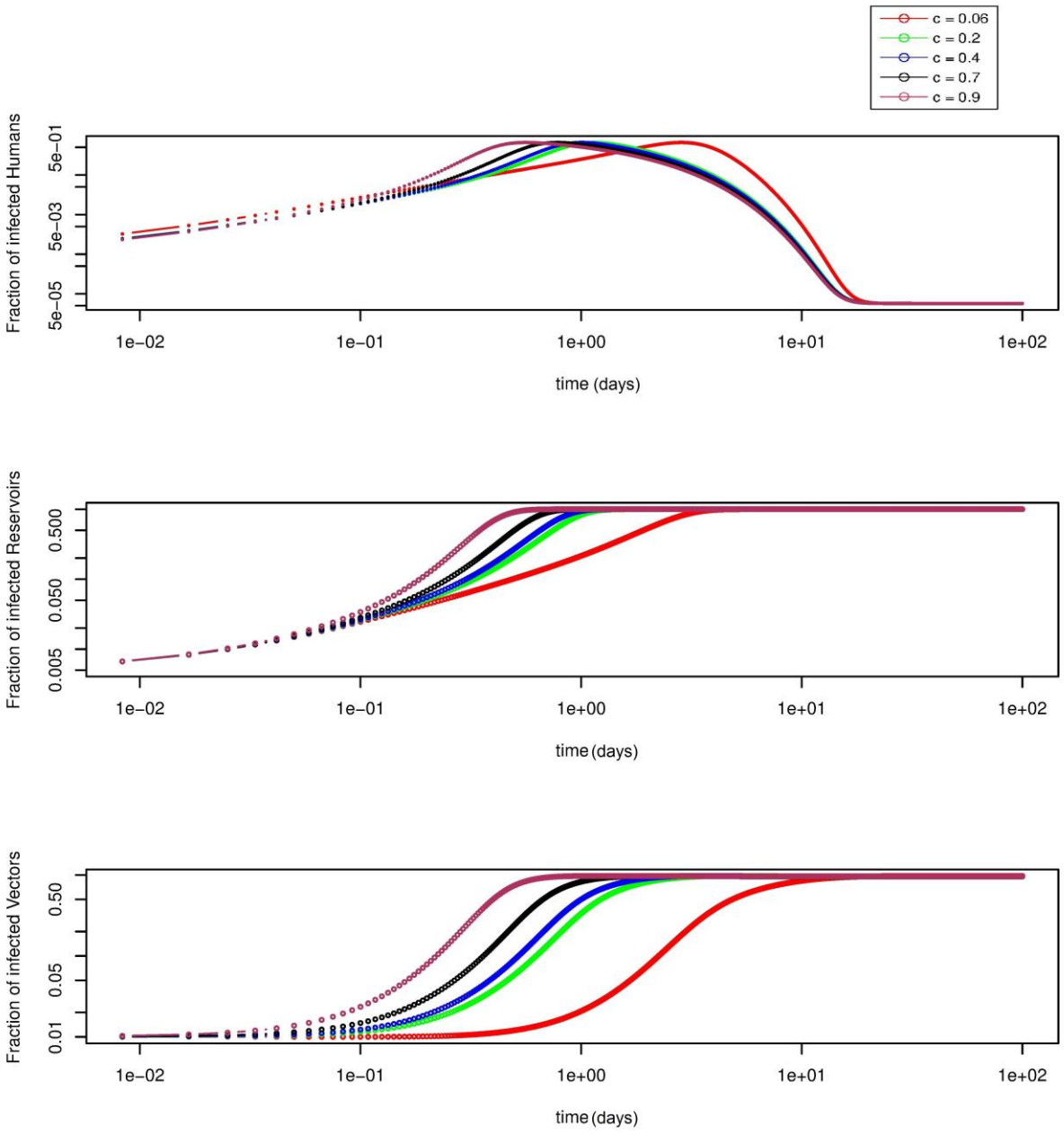

Figure 4. Simulation results for different values of *c*.

Varying the values of m, the vector-human ratio, and n, the vector-reservoir ratio

Results show that there is a positive relationship between m and the fraction of infected humans, and there is almost no relationship between m and the fraction of infected reservoir, which is something predictable, as seen from Figure 5. Also, there is a positive relationship between n and the fraction of infected reservoirs, and there is almost no relationship between n and the fraction of infected humans, as seen from Figure 6. From Figures 5 and 6 it can be shown that the effect of different values of m on the population of vectors is the same as the effect of different values of n on the population of vectors, and that is because it is assumed that vectors take a fixed amount of blood despite the available number of hosts or reservoirs, and also because it is assumed that vectors do not prefer humans over reservoirs.

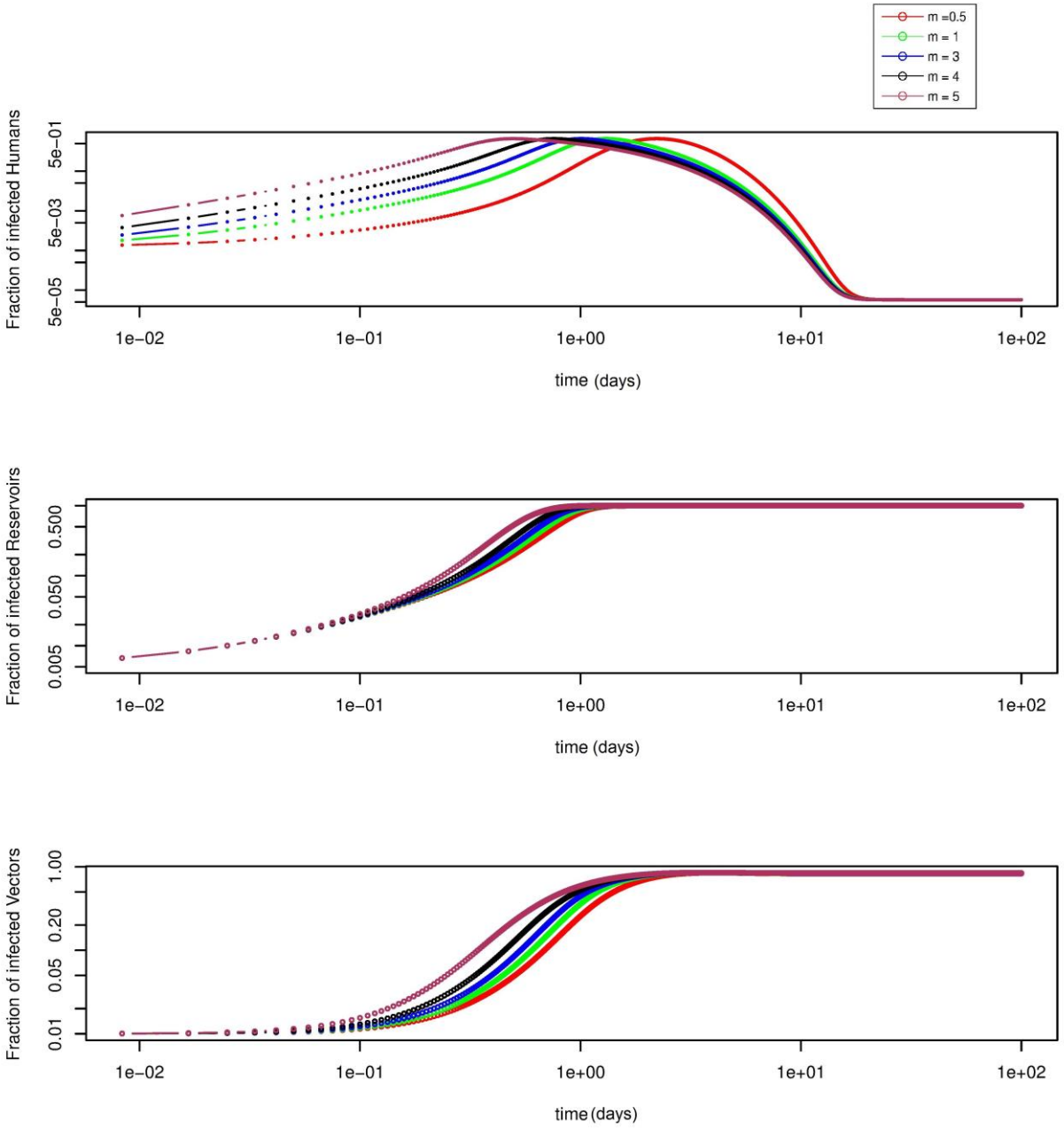

Figure 5. Simulation results for different values of *m.*

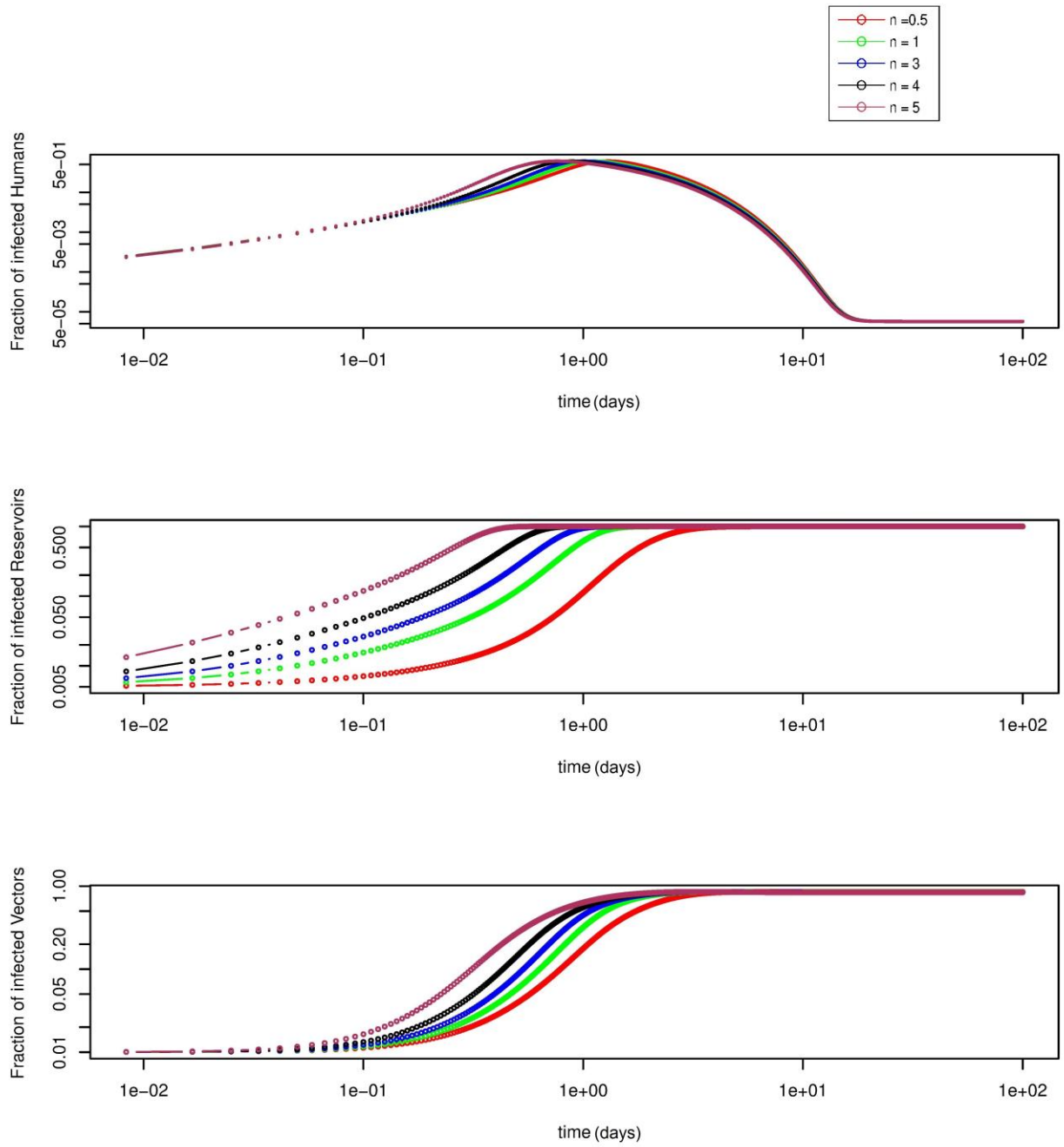

Figure 6. Simulation results for different values of *n*.

Varying the values of α (the recovery rate)

Simulation results show that recovery rate has a strong impact on the population of infected humans, and it has no effect on the reservoir population nor on the vector population; which shows that although the recovery rate is an important factor in the fight against the disease, it is not enough for eradication, and it should be accompanying other interventions on the other populations, as seen from Figure 7.

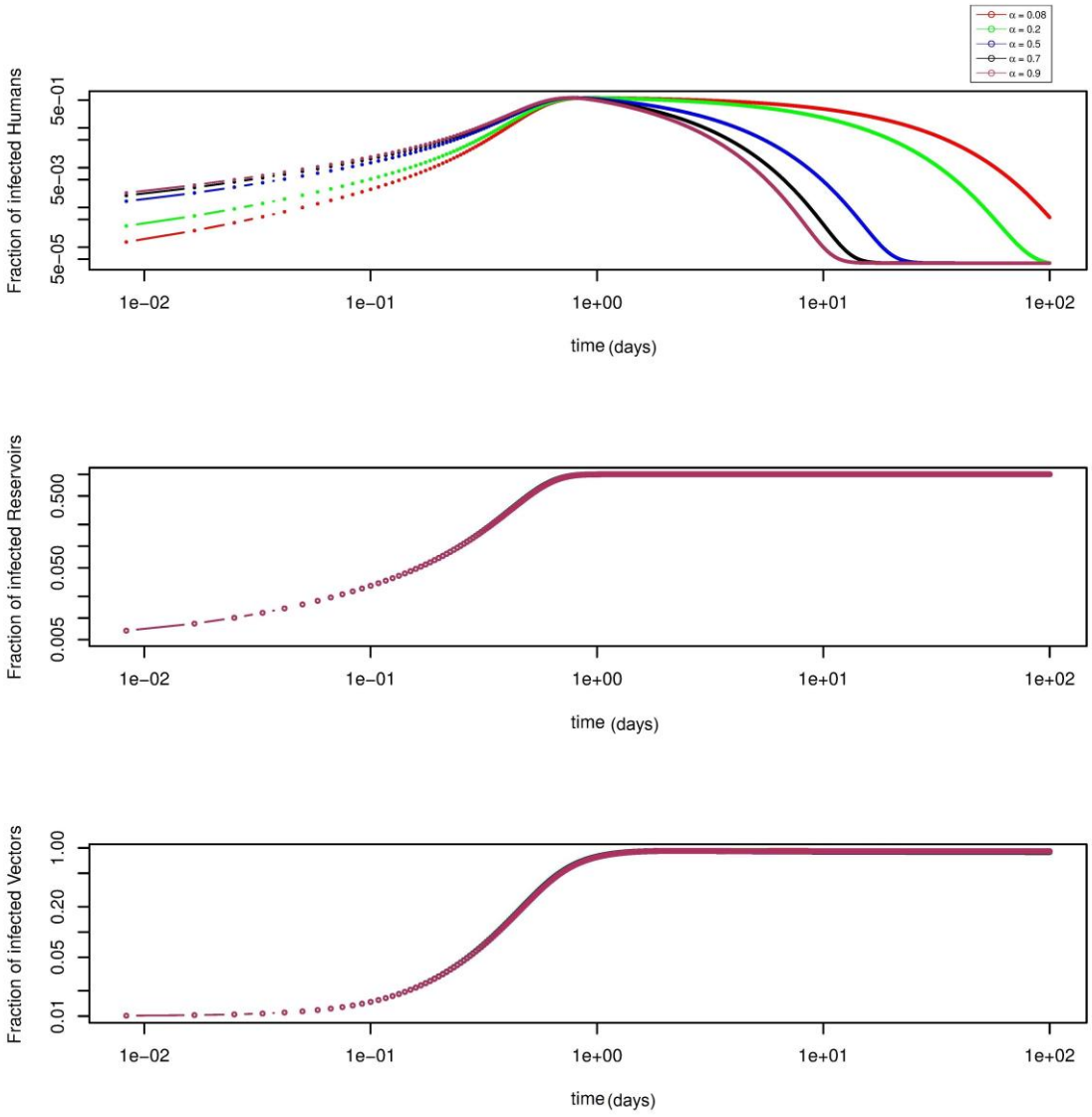

Figure 7. Simulation results for different values of α.

6. Conclusion

We have developed a general model for the dynamics of a vector-host-reservoir model. Our analysis of the model showed that the disease-free equilibrium is globally asymptotically stable when R_0 is less than unity; and unstable when R_0 is greater than unity, and our system posses only one endemic equilibrium which is globally asymptotically stable when R_0 is greater than unity.

Our sensitivity analysis shows that R_0 is sensitive to all of the parameters of the model either positively or negatively, and the most influential has been the natural death of the reservoir, μ_r which indicates that the best control strategy is culling the infected animals, and the second one is the biting rate, a which indicates that reducing the biting rate by using, for example, bed-nets is the second best control strategy against the disease.

Numerical simulations were used to examine the effect of all of the parameters of the model, and the results showed that reducing the biting rate of vectors helps in reducing the prevalence of the disease in the human population. However, to reduce the epidemic's peak other interventions are needed; nonetheless, it seems to have less effect on other populations.

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