A PREDATOR-PREY-DISEASE MODEL WITH IMMUNE RESPONSE IN INFECTED-PREY*

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Abstract. In this paper, a predator-prey-disease model with immune response in the infected prey is formulated. The basic reproduction number of the within-host model is defined and it is found that there are three equilibria: extinction equilibrium, infection-free equilibrium and infection-persistent equilibrium. The stabilities of these equilibria are completely determined by the reproduction number of the within-host model. Furthermore, we define a basic reproduction number of the between-host model and two predator invasion numbers: predator invasion number in the absence of disease and predator invasion number in the presence of disease. We have predator and infection-free equilibrium, infection-free equilibrium, predator-free equilibrium and a coexistence equilibrium. We determine the local stabilities of these equilibria with conditions on the reproduction and invasion reproduction numbers. Finally, we show that the predator-free equilibrium is globally stable.

Keywords: immuno-eco-epidemiology; Prey-predator model; age-since-infection; coexistence; reproduction numbers, invasion reproduction numbers; global stability.

AMS Subject Classification: 92D30, 92D40

1. Introduction

Mathematical biologists have been working on merging two major areas of interest Ecology [1, 2, 3] and Epidemiology [4] for a long time. Diseases that affect the prey in particular may affect the entire predator-prey system [5, 6, 7]. The pathogen may not infect the predator but it creates a differential pressure on the predator-prey dynamics, causing destabilization of equilibria or reducing natural oscillations. A key objective of these models is to investigate the correlation between the disease and the predator-prey system.

Predator-prey-pathogen models have been a topic of significant interest since the early 1980s. Anderson and May [9] in 1982 paved the way of merging ecological predator-prey models, which were initiated by Lotka and Volterra, and the epidemiological models,

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introduced by Kermack and McKendrick. Hethcote et. al [10] showed how the parasite population could affect the demographic behavior of the host population. The fusion of ecology and epidemiology is a comparatively new branch of study, now with a 30 year history, known as eco-epidemiology. Eco-epidemiological models could also address scenarios, such as the ones presented by Getz and Pickering in 1983 [11], where a parasitic disease has been found to regulate the host population density. Furthermore Bairagi et. al [12] showed that a disease might be the sole reason for co-existence of the species. They established that by combining an SI (Susceptible-Infected) disease model with a regular predator-prey N-P(Prey-Predator) model to obtain a eco-epidemiological ODE model.

In the paper [23] the author was successful in showing the effect of a predator on the prevalence of the disease in the prey. The simulations in the article show that existence of predator abundance creates oscillations in the SIR model of the prey population. Another scenario proposed by Bairagi et. al [12], suggests that predator may avoid infected prey and predate only on healthy susceptible ones which may lead to prey extinction. Their simulations show the existence of a bifurcation in the model.

Since then the field of eco-epidemiology has been attracting significant attention and many studies have been completed using eco-epidemiological modeling ([13] - [22]). All the studies mentioned above clearly demonstrate the volume of work going at present on the predator-prey dynamics where the prey population is infected. The infection in the prey population has many consequences for predator-prey dynamics and these models need more attention to elucidate the complex dynamics of predator-prey and disease.

Researchers interested in epidemiology have known for a long time that an intrinsic connection exists between the within-host status of the pathogen, its interaction with the immune system, and between-host ability of the pathogen to transmit and invade the host population. Even though there is a large body of literature treating within-host models and epidemiological models separately, it wasn't until the seminal work of Gilhrist and Sasaki [25] that the two fields were connected with an ODE within-host model nested in an epidemiological time-since-infection structured model. Since then the interest toward models linking within-host dynamics with epidemiological dynamics has been rising. Linked models have been also termed immuno-epidemiological models. Bridging the gap between the two fields [26] is now of primary interest not only for models of macro-parasitic infections, but also for micro-parasitic infections, such as HIV.

One area that has not been addressed this far is the impact of within-host dynamical interaction of a pathogen with the immune system and the between host distribution of the disease in the presence of a predator or a competition between species. There is still a lot to be learned on how ecological interaction of predation or competition affect the within-host dynamics of the pathogen with the immune system, how within-host interactions affect the distribution of disease on population level, and ultimately the predator-prey interaction.

In the present article we discuss a predator-prey PDE model where the prey population is infected by a pathogen. An immunological S-I model has been designed to represent the dynamics of the disease inside a host in the prey population. The major goal of this paper is to identify the probable characteristic of the disease and its major role in determining the dynamics of the predator-prey system. We investigate the long term behavior of the predator-prey dynamics in the light of the disease in the prey population. In the next section we introduce a predator-prey model with infected prey structured by immune status. We term these linked models immuno-eco-epidemiological models. In section 3 we present analysis of the within-host model. In section 4 we define the equilibria of the immuno-eco-epidemiological model and we investigate their local stabilities. In section 5 we obtain the global stability of the predator-free equilibrium. Section 6 contains a summary of our results.

2. Model

We consider the following model to represent the predator-prey interaction with the prey in the population being infected. We use an ODE model to describe the within-host-parasite dynamics. The virus particles present in a single infected prey over the infection period, plays an important role that decides the rate of infection among the prey population in a general epidemiological model. The following age-structured PDE model explains the prey-predator interaction in the epidemiological environment. Here $S(t)$ denotes the number of susceptible prey population at time t, $P(t)$ is the number of predators in the population. We use the variable $i(\tau, t)$ to represent the density of infected prey population at time t where τ is the age of infection in the prey population.

The model is given as follows.

$$
\begin{cases}
\dfrac{dS(t)}{dt} = \Lambda - S(t)\displaystyle\int_0^\infty \beta(\tau) i(\tau,t) d\tau - \dfrac{a_1 S(t) P(t)}{1+cS(t)} - m_0 S(t), \\
\dfrac{\partial i(\tau,t)}{\partial \tau} + \dfrac{\partial i(\tau,t)}{\partial t} = -m_0 i(\tau,t) - mV(\tau) i(\tau,t) - \alpha(\tau) P(t) i(\tau,t), \\
i(0,t) = S(t)\displaystyle\int_0^\infty \beta(\tau) i(\tau,t) d\tau, \\
\dfrac{dP(t)}{dt} = \dfrac{a_2 S(t) P(t)}{1+cS(t)} - dP(t) + kP(t)\displaystyle\int_0^\infty \alpha(\tau) i(\tau,t) d\tau,
\end{cases}
\tag{2.1}
$$

where Λ is the birth rate of the susceptible prey population and m_0 is the death rate of the prey population. $\beta(\tau)$ represents the infection rate in prey population with age of infection τ and is related to the number of virus particles $V(\tau)$ by the relation $\beta(\tau) = cV(\tau)$. We use a Holling function of Type II to represent the predation rate for the susceptible population, where a_1 is called the attack rate and the average time spent on processing a food item is called the handling time, given by c/a_1. α denotes the predation rate in the infected class, a_2/a_1 is the conversion efficiency of the prey into the body mass of the predator and d is the natural death rate of the predator; k is the conversion efficiency of the prey mass into the predator body mass, m is a scaling factor such that $mV(\tau)$ is the disease induced death rate.

The immunological model describing the dynamics of the host-parasite system which causes the disease in the prey population is given by the following ODE model.

$$
\begin{cases}
\dfrac{dV(\tau)}{dt} = rV(\tau)(1 - \dfrac{V(\tau)}{K}) - \eta V(\tau) z(\tau), \\
\dfrac{dz(\tau)}{dz} = \dfrac{\rho V(\tau) z(\tau)}{A + V(\tau)} - \mu z(\tau),
\end{cases}
\tag{2.2}
$$

where $V(\tau)$ represents the number of virus particles. The growth of the virus population has been modeled with a logistic equation, where K is the carrying capacity and r is the intrinsic growth rate. η is the elimination rate of the virus particles by the healthy immune system of the host. Holling function of Type II has been used to reflect the growth rate of the healthy immune cells $z(\tau)$ where μ is the death rate, A is the half saturation constant and ρ is maximum saturation constant.

3. Analysis of the Immune ODE Model.

In this section we set to investigate the equilibria of the model.

Definition 3.1. *We define the basic reproduction number in the immunological model as* $$R_0 = \frac{\rho K}{\mu(A+K)}.$$

Theorem 3.1. *System 2.2 always has an extinction equilibrium* $\mathcal{E}_0 = (0,0)$ *and immune-response free equilibrium* $\mathcal{E}_1 = (K,0)$*. If* $R_0 > 1$ *then there is a unique infection equilibrium*

$$\mathcal{E}_2 = (\frac{\mu A}{\rho - \mu}, \frac{r}{\eta}(1 - \frac{\mu A}{K(\rho-\mu)})).$$

Proof. The equilibrium points are those where the solution does not change with time. We set the derivative equal to zero in order to investigate the equilibrium values. The equilibria in the ODE model are obtained by solving the following sets of equation.

$$\begin{cases} rV(1-\frac{V}{K}) - \eta V z = 0, \\ \frac{\rho V z}{A+V} - \mu z = 0. \end{cases} \tag{3.1}$$

The above sets of equations lead to three sets of solutions. These solutions represent corresponding equilibrium states , viz. virus-free immune-response free equilibrium or the extinction equilibrium ($\mathcal{E}_0 = (0,0)$), immune-response free equilibrium ($\mathcal{E}_1 = (K,0)$) and co-existence equilibrium ($\mathcal{E}_2 = (\frac{\mu A}{\rho-\mu}, \frac{r}{\eta}(1 - \frac{\mu A}{K(\rho-\mu)}))$). From the structure of the equilibrium points, it is clear that the extinction equilibrium and the immune response free equilibrium always exist. For the existence of the co-existence equilibrium, it is essential that $1 - \frac{\mu A}{K(\rho-\mu)} > 0$. This is true if and only if $R_0 > 1$. This completes the proof. □

Now we investigate the local stability of the model at the different equilibrium points.

Theorem 3.2. *The extinction equilibrium* $\mathcal{E}_0$ *is always unstable, the immune-response free equilibrium* $\mathcal{E}_1$ *is unstable if and only if* $R_0 > 1$ *and the co-existence equilibrium* $\mathcal{E}_2$ *is globally stable whenever it exists.*

Proof. Stability at $\mathcal{E}_0$: In order to investigate the stability of the model, the ODE was linearized about the equilibrium points to obtain the following Jacobian.

$$J(\mathcal{E}_0) = \begin{pmatrix} r & 0 \\ 0 & -\mu \end{pmatrix},$$

The stability of the equilibrium is obtained by evaluating the eigenvalues of the Jacobian. We observe that $det(J(\mathcal{E}_0)) < 0$. This means there is always an eigenvalue which is positive. Hence $\mathcal{E}_0$ is always unstable.

Stability at $\mathcal{E}_1$: In the same way we investigate the previous equilibrium we obtain the Jacobian corresponding to $\mathcal{E}_1$ as follows.

$$J(\mathcal{E}_1) = \begin{pmatrix} -r & -\eta K \\ 0 & \mu(R_0 - 1) \end{pmatrix},$$

We observe that $det(J(\mathcal{E}_1)) = -r\mu(R_0 - 1)$. For $R_0 > 1$ determinant is negative and with the argument presented in the previous case we can state that this equilibrium is unstable. For $R_0 < 1$ determinant is positive. Observe that $tr(J(\mathcal{E}_1)) < 0$ always. From Routh-Hurwitz criterion, all eigen values are negative or have negative real parts. Hence, we have local stability of this equilibrium when $R_0 < 1$.

Stability at $\mathcal{E}_2$:

Theorem 3.3. *The system [2.2] do not have any periodic solutions.*

Proof. Let us rewrite the system [2.2] as

$$\frac{dV}{d\tau} = f(V, z) \tag{3.2}$$

$$\frac{dz}{d\tau} = g(V, z) \tag{3.3}$$

where $f(V, z) = rV(\tau)(1 - \frac{V(\tau)}{K}) - \eta V(\tau)z(\tau)$ and $g(V, z) = z'(\tau) = \frac{\rho V(\tau)z(\tau)}{A+V(\tau)} - \mu z(\tau)$.

Let $\phi = \frac{1}{Vz}$. We observe that $\frac{\partial}{\partial V}(f\phi) + \frac{\partial}{\partial z}(g\phi) = -\frac{r}{zK}$,

which is always negative in the positive quadrant. Using BendixsonDulac theorem [14], the system [2.2] do not have any periodic solutions.

□

The theorem above excludes the possibility of a limit cycle.

Let us denote $\mathcal{E}_2 = (V^*, z^*)$. The Jacobian matrix obtained from the linearized model at the co-existent equilibrium point is given as follows.

$$J(\mathcal{E}_2) = \begin{pmatrix} -\dfrac{rV^*}{K} & -\eta V^* \\ \rho z^* \dfrac{A}{(A + V^*)^2} & 0 \end{pmatrix},$$

which clearly has a negative trace and a positive determinant. From Routh-Hurwitz criterion it follows that all eigenvalues of this matrix are negative or have negative real parts. Hence this equilibrium is always stable when it exists i.e. when $R_0 > 1$.

Note that for $R_0 > 1$ the other two equilibrium are both unstable. Hence, it can be shown that this equilibrium is globally Stable for $R_0 > 1$.

□

4. Analysis of the predator-prey PDE Model.

Before we proceed to explore the equilibrium values of the PDE model, we use the following definition to describe the reproduction numbers associated with this system.

Definition 4.1. *We define the basic reproduction number*

$$R_0 = \frac{\Lambda(a_2 - cd)}{m_0 d},$$

the disease invasion number as

$$R_0^P = \frac{\Lambda \int_0^\infty \beta(\tau) e^{-\mu(\tau)} d\tau}{m_0}, \quad \textit{where} \quad \mu(\tau) = \int_0^\tau (m_0 + mV(s)) ds,$$

and the predator invasion number as

$$R_i^P = \frac{a_2 \Lambda}{d(R_0^P m_0 + c\Lambda)} + \frac{k}{d}\Lambda \left(1 - \frac{1}{R_0^P}\right) \int_0^\infty \alpha(\tau) e^{-\int_0^\tau (m_0 + mV(s)) ds} d\tau.$$

Theorem 4.1. *There always exist a disease-free predator-free equilibrium* $E_1 = (\frac{\Lambda}{m_0}, 0, 0)$. *When* $\mathcal{R}_0 > 1$ *there exist a unique disease-free predator-prey equilibria* $E_2 = (S_2, 0, P_2)$ *and when* $\mathcal{R}_0^P > 1$ *there is a unique predator-free infection equilibrium* $E_3 = (S_3, i_3(\tau), 0)$.

Proof. We begin our proof by tracing the equilibrium points. The equilibria of the model is of the form $(S^*, i^*(\tau), P^*)$ which are solution of the sets of PDE equation and is always constant over time. The points are obtained by solving the following sets of equations.

$$\begin{cases} \Lambda - S^* \displaystyle\int_0^\infty \beta(\tau) i^*(\tau) d\tau - \frac{a_1 S^* P^*}{1 + cS^*} - m_0 S^* = 0, \\ \dfrac{di^*(\tau)}{d\tau} = -m_0 i^*(\tau) - mV(\tau) i^*(\tau) - \alpha(\tau) P^* i^*(\tau), \\ i^*(0) = S^* \displaystyle\int_0^\infty \beta(\tau) i^*(\tau) d\tau, \\ \dfrac{a_2 S^* P^*}{1 + cS^*} - dP^* + kP^* \displaystyle\int_0^\infty \alpha(\tau) i^*(\tau) d\tau = 0, \end{cases} \tag{4.1}$$

There are four sets of solution to the above array of equations. This proves the existence of four different equilibria in the model. The disease-free predator-free equilibrium which is given by $E_1 = (\frac{\Lambda}{m_0}, 0, 0)$ is always present as a solution to the equations (4.1).

The second equilibrium is given by $E_2 = (S_2, 0, P_2)$. This is a regular predator-prey equilibrium without any diseased prey in the population. This is what we call disease-free, predator-prey equilibrium is obtained as follows,

$$E_2 = (\frac{d}{a_2 - cd},\ 0,\ \frac{(\Lambda - m_0 S_2)(1 + cS_2)}{a_1 S_2}).$$

The equilibria exists if and only if the basic reproduction number for this immune ODE model, $\mathcal{R}_0$ as defined above is greater than one (> 1).

We obtain the third equilibrium point, where the healthy and diseased prey population co-exists, but there is no predator. This is called predator-free infection equilibrium, given by $\mathcal{P}_3 = (S_3, i_3(\tau), 0)$. The component of this equilibrium are obtained to be of the following form,

$$S_3 = \frac{1}{\int_0^\infty \beta(\tau) e^{-\mu(\tau)} d\tau}, \quad \text{where} \quad \mu(\tau) = \int_0^\tau (m_0 + mV(s)) ds,$$

$$i_3(\tau) = i_3(0) e^{-\mu(\tau)}, \quad \text{where} \quad i_3(0) = m_0 (\frac{\Lambda}{m_0 S_3} - 1).$$

This equilibrium exists if and only if the disease invasion number $R_0^P > 1$.

□

Theorem 4.2. *If $R_0^P > 1$ and $\frac{kc\Lambda}{d} > R_0 > R_0^P$ then there exists a non-trivial co-existence equilibrium to the system of equations (2.2).*

Proof. Finally we have the equilibrium solution where all the variables are present together. This is a solution where the diseased prey and healthy prey co-exits in the population together with the predator. This equilibrium is termed as disease-prey-predator coexistence equilibrium given by $E_4 = (S^*, i^*(\tau), P^*)$. The existence of a solution of this form has been explained in details below.

This equilibrium is obtained by solving the following set of equations.

$$\begin{cases} S^* \displaystyle\int_0^\infty \beta(\tau) e^{-\mu(\tau, P^*)} d\tau = 1, \\ \dfrac{a_2 S^*}{1 + cS^*} - d + k i^*(0) \displaystyle\int_0^\infty \alpha(\tau) e^{-\mu(\tau, P^*)} d\tau = 0, \\ i^*(0) = \Lambda - \dfrac{a_1 S^*}{1 + cS^*} - m_0 S^*, \end{cases} \tag{4.2}$$

where

$$\mu(\tau, P^*) = \int_0^\tau (m_0 + mV(s) + \alpha(s) P^*) ds.$$

Solving the first equation in (4.2) we can express S^* in terms of the P^* with the following relation,

$$S^* = f(P^*) = \frac{1}{\int_0^\infty \beta(\tau)e^{-\mu(\tau,P^*)}d\tau}.$$

Substituting the above solution in the second equation in (4.2) we have the following equation in P^*. $G(P^*) = 0$ where

$$G(P) = \frac{a_2 f(P)}{1+cf(P)} - d + k\left(\Lambda - \frac{a_1 P f(P)}{1+cf(P)} - m_0 f(P)\right)\int_0^\infty \alpha(\tau)e^{\mu(\tau,P^*)}d\tau.$$

The existence of a solution P^* in the above equation will automatically lead to the existence of the equilibrium point.

We observe that $f(0) = \frac{\Lambda}{m_0 R_0^P}$ and hence we have

$$\begin{aligned} G(0) &= \frac{(a_2 - cd)\frac{\Lambda}{m_0 R_0^P} - d}{1+cf(0)} + k\Lambda\left(1 - \frac{1}{R_0^P}\right)\int_0^\infty \alpha(\tau)e^{-\mu(\tau)}d\tau, \\ &= \frac{d(\frac{R_0}{R_0^P} - 1)}{1+cf(0)} + k\Lambda\left(1 - \frac{1}{R_0^P}\right)\int_0^\infty \alpha(\tau)e^{-\mu(\tau)}d\tau. \end{aligned}$$

Since $R_0^P > 1$ and $\frac{kc\Lambda}{d} > R_0 > R_0^P$, where R_0, R_0^P are the basic reproduction number and the prey invasion number as defined before. This implies $G(0) > 0$. Also if we make P in the equation of $G(P)$ very large as compared to other variables we observe that as $P \to \infty$ we have $G(P) \to$ a negative number. From the Intermediate Value Theorem we can claim that there is a positive solution of $P = P^*$ such that $G(P^*) = 0$. This positive solution of P^* proves the existence of a solution of the above equation. Hence, there exists a positive solution for the system and we have the existence of coexistent equilibrium. □

4.1. **Stability Analysis.**

4.1.1. *Stability of disease free predator free equilibrium.* In this section we shall proceed to investigate the stability of the corresponding equilibrium points. We begin with analyzing the equilibrium $E_1 = (\frac{\Lambda}{m_0}, 0, 0)$.

Theorem 4.3. *If $R_0^P > 1$ or $R_0 > 1$ the equilibrium E_1 is unstable. For $R_0^P < 1$ and $R_0 < 1$ the equilibrium E_1 is locally asymptotically stable.*

Proof. We investigate the local stability of the model. The idea is to expand the variables about the equilibrium point using Taylor expansion. The following sets of equations show

the expansion of the variables about the equilibrium point $\mathcal{E}_1$.

$$S(t) = \frac{\Lambda}{m_0} + \xi(t), \quad i(\tau, t) = \eta(\tau, t), \quad P(t) = n(t). \tag{4.3}$$

We substitute the above expansion of the variables in the PDE model (2.1) to obtain the following equations.

$$\xi'(t) = \Lambda - (\frac{\Lambda}{m_0} + \xi(t)) \int_0^\infty \beta(\tau)\eta(\tau, t)d\tau - \frac{a_1(\frac{\Lambda}{m_0} + \xi(t))n(t)}{1 + c(\frac{\Lambda}{m_0} + \xi(t))} - m_0(\frac{\Lambda}{m_0} + \xi(t)). \tag{4.4}$$

Since we are investigating the local stability of the model we neglect the higher order terms to obtain the following linearized version

$$\xi'(t) = -\frac{\Lambda}{m_0} \int_0^\infty \beta(\tau)\eta(\tau, t)d\tau - m_0\xi(t) - a_1 \frac{\Lambda}{m_0(1 + c\frac{\Lambda}{m_0})} n(t). \tag{4.5}$$

We continue the same idea for other variables as well. We substitute $i(\tau, t)$ and $P(t)$ in the given PDE equations and neglect the higher ordered terms to obtain the following sets of linear equations,

$$\begin{cases} \dfrac{\partial\eta(\tau, t)}{\partial\tau} + \dfrac{\eta(\tau, t)}{\partial t} = -m_0\eta - mV\eta, \\ \eta(0, t) = \dfrac{\Lambda}{m_0} \displaystyle\int_0^\infty \beta(\tau)\eta(\tau, t)d\tau, \\ \dfrac{dn(t)}{dt} = a_2 \dfrac{\Lambda}{m_0(1 + c\frac{\Lambda}{m_0})} n(t) - dn(t). \end{cases} \tag{4.6}$$

We transform the problem into an eigenvalue problem. We investigate solutions of the form

$$\xi(t) = \bar{\xi}e^{\lambda t}, \quad \eta(\tau, t) = \bar{\eta}(\tau)e^{\lambda t}, \quad n(t) = \bar{n}e^{\lambda t}.$$

We substitute these expressions in the linearized system and look for solutions of the eigenvalue λ. We observe here that if λ is negative or has negative real parts, then the perturbations η, n, ξ will asymptotically go to zero and the system will be locally stable and if the value is positive or have positive real part, then the system will diverge away from the equilibrium point. In this case we say that the equilibrium is unstable. The equation for η was found to be separable.

$$\bar{\eta}'(\tau) = -(\lambda + m_0 + mV(\tau))\bar{\eta}(\tau) \tag{4.7}$$

Solving the above equation we have

$$\eta(\tau) = \eta(0)e^{-\lambda\tau - \mu(\tau)},$$

where the definitions of $\mu(\tau)$ is as defined before in the text. Substituting this in the boundary condition we have the following characteristic equation

$$\mathcal{G}(\lambda) = 1, \quad \text{where} \quad \mathcal{G}(\lambda) = \frac{\Lambda}{m_0}\int_0^\infty \beta(\tau)e^{-\lambda\tau-\mu(\tau)}d\tau.$$

Solution of λ in this equation gives eigen values of the system (4.6). Observe that $G(0) = R_0^P$. Also $G(\lambda) \to 0$ as $\lambda \to \infty$. Hence if $R_0^P > 1$ there is a positive real λ such that $G(\lambda) = 1$ and hence the equilibrium is unstable.

If $R_0^P < 1$, let $\lambda = a + ib$ be a solution of the characteristic equation with $a \geq 0$. Then we have $|G(\lambda)| \leq G(0) = R_0^P < 1$. Hence, any λ with positive real part cannot be a solution to the characteristic equation $G(\lambda) = 1$.

We look for other eigen values in the linearized model when $R_0^P < 1$. Using the same strategy as explained we obtain the following expression for λ

$$\lambda = \frac{d}{1 + \frac{c\Lambda}{m_0}}\big(R_0 - 1\big). \tag{4.8}$$

This clearly shows that if $R_0 > 1$ we have a positive eigenvalue and the equilibrium is unstable. For $R_0 < 1$, all eigenvalues from this present model are negative or have negative real parts. Hence, this proves that the equilibrium is locally asymptotically stable in the case when $R_0 < 1$. □

4.1.2. *Stability of disease free predator -prey equilibrium.* We are now looking for the stability of the equilibrium $\mathcal{E}_2 = (S_2, 0, P_2)$.

Theorem 4.4. *When $R_0^P < R_0$ the equilibrium is locally asymptotically stable.*

Proof. As explained above, this equilibrium represents the state when the number of infected prey population does not exist, but the healthy prey and the predator coexists in the environment. The equilibrium point satisfy the following sets of equations.

$$\begin{aligned} \Lambda - \frac{a_1 S_2 P_2}{1 + cS_2} - m_0 S_2 = 0, \\ \frac{a_2 S_2 P_2}{1 + cS_2} - d = 0. \end{aligned} \tag{4.9}$$

We use our already defined technique to look for the local stability of this equilibrium point. As explained in the case of the disease free, predator free equilibrium before we expand the variables along the equilibrium values and linearize the model as given below. We set,

$$S(t) = S_2 + \xi(t), i(\tau, t) = \eta(\tau, t), P(t) = P_2 + n(t).$$

In order to expand the terms linearly about the equilibrium point, we replace this above mentioned expansion in the given model to obtain the following sets of equations.

$$\xi'(t) = \Lambda - (S_2 + \xi(t)) \int_0^\infty \beta(\tau)\eta(\tau, t)d\tau - \frac{a_1(S_2 + \xi(t))(P_2 + n(t))}{1 + c(S_2 + \xi(t))} - m_0(S_2 + \xi(t)).$$

Since we are looking for the local stability of the equilibrium point, i.e. we are looking if the initial value is very close to the equilibrium point, whether it will converge to the equilibrium point asymptotically or it will diverge away from it, we can neglect the non-linear terms. Hence, we are interested in the linear expansion and we ignore the higher order terms. Substituting the equilibrium values, we obtain the following expression

$$\xi'(t) = -S_2 \int_0^\infty \beta(\tau)\eta(\tau, t)d\tau - \frac{(a_1P_2\xi(t) + a_1S_2n(t))}{1 + cS_2} + \frac{ca_1S_2P_2\xi(t)}{(1 + cS_2)^2} - m_0(S_2 + \xi(t)).$$

Linearizing the terms, using the equilibrium conditions and removing the higher order terms we have the following form.

$$\begin{cases} \dfrac{\partial\eta(\tau, t)}{\partial\tau} + \dfrac{\partial\eta(\tau, t)}{\partial t} = -(m_0 + mV(\tau) + \alpha P_2)\eta(\tau, t), \\ \eta(0, t) = S_2 \displaystyle\int_0^\infty \beta(\tau)\eta(\tau, t)d\tau. \end{cases} \tag{4.10}$$

Using the techniques of differential equations, the solutions of a linear system are obtained by substituting functions of the form $\eta(\tau, t) = \bar{\eta}(\tau)e^{\lambda t}$ and investigating the values of λ, which results in a characteristic equation. The solutions of this characteristic equation gives the value of λ. Substituting in (4.10) we have,

$$\begin{cases} \dfrac{d\bar{\eta}}{d\tau} = -(\lambda + m_0 + mV(\tau) + \alpha P_2)\bar{\eta}, \\ \bar{\eta}(\tau) = \bar{\eta}(0)exp(-\lambda\tau - \mu(\tau, P_2)), \end{cases} \tag{4.11}$$

where

$$\mu(\tau, P_2) = \int_0^\tau (m_0 + mV(s) + \alpha(s)P_2)ds,$$

as defined before.

We substitute the above equation in the boundary condition of the linearized PDE model to obtain the following characteristic equation $H(\lambda) = 1$ where

$$H(\lambda) = S_2 \int_0^\infty \beta(\tau)e^{-\lambda\tau - \mu(\tau, P_2)}d\tau.$$

If λ is positive or has positive real part, then the solution blows up and hence the equilibrium is unstable. If it is negative, the perturbed term in the expansion asymptotically goes to zero and hence the equilibrium is locally asymptotically stable. Here, we

have assumed that the eigenvalues completely determine the local behavior of the PDE model.

We observe that

$$H(0) = \frac{\Lambda}{m_0 R_0} \int_0^\infty \beta(\tau) e^{-\mu(\tau, P_2)} d\tau.$$

Hence

$$H(0) \leq \frac{\Lambda}{m_0 R_0} \int_0^\infty \beta(\tau) e^{-\mu(\tau)} d\tau = \frac{\Lambda}{m_0 R_0 S_3} = \frac{R_0^P}{R_0}.$$

The following theorem gives the local stability of this equilibrium point.

Lemma 4.1. *When $R_0^P < R_0$ the characteristic equation $H(\lambda) = 1$ cannot have a root with positive real part.*

Proof of Lemma:

Let us assume that $H(\lambda) = 1$ for some $\lambda = a + ib$ where $a > 0$. Then we have

$$|H(\lambda)| \leq H(0) \leq \frac{R_0^P}{R_0} < 1,$$

which is a contradiction to our assumption that $H(\lambda) = 1$ for some $\lambda = a + ib$ where $a > 0$. Hence no solution exists for roots with positive real part. □

We have already shown that for the case $R_0^P < R_0$, the model involving η has only eigenvalues which are negative or with negative real parts.

When $R_0^P < R_0$ we look for other eigenvalues present in the model. We can claim that the system is locally asymptotically stable, only when all eigenvalues present in the model are negative or have negative real parts. This involves solving the following equations.

$$\begin{cases} \dfrac{d\xi(t)}{dt} = -\dfrac{(a_1 P_2 \xi(t) + a_1 S_2 n(t))}{1 + cS_2} + \dfrac{c a_1 S_2 P_2 \xi(t)}{(1 + cS_2)^2} - m_0 \xi(t), \\ \dfrac{dn(t)}{dt} = \dfrac{(a_2 P_2 \xi(t) + a_2 S_2 n(t))}{1 + cS_2} - \dfrac{c a_2 S_2 P_2 \xi(t)}{(1 + cS_2)^2} - dn(t). \end{cases}$$

Using the same concept explained above we look for eigenvalues of the equation in the form, $\xi(t) = \xi e^{\lambda t}$ and $n(t) = n e^{\lambda t}$. This leads to solving the following sets of equations.

$$\begin{cases} \lambda \xi = -\dfrac{(a_1 P_2 \xi + a_1 S_2 n)}{1 + cS_2} + \dfrac{c a_1 S_2 P_2 \xi}{(1 + cS_2)^2} - m_0 \xi, \\ \lambda n = \dfrac{(a_2 P_2 \xi + a_2 S_2 n)}{1 + cS_2} - \dfrac{c a_2 S_2 P_2 \xi}{(1 + cS_2)^2} - dn. \end{cases} \tag{4.12}$$

Since this reduces to a linear ODE model, looking for eigen values in the present model is same as finding the eigenvalues of the following Jacobian.

$$J = \begin{bmatrix} -m_0 - \dfrac{a_1 P_2}{(1+cS_2)^2} & -\frac{a_1 S_2}{(1+cS_2)} \\ \dfrac{a_2 P_2}{(1+cS_2)^2} & 0 \end{bmatrix}.$$

Clearly we have $Det(J) > 0$ and $tr(J) < 0$. Hence all eigenvalues are negative or have negative real parts. This proves that when $R_0^P < R_0$, the equilibrium is locally asymptotically stable. □

4.1.3. *Stability of Predator free equilibrium.* Now we turn to the third equilibrium, where the predator goes to extinction, but the prey population co-exists in both the healthy and diseased individuals. The equilibrium is given by $E_3 = (S_3, i_3(\tau), 0)$ where the variables satisfy the following equations.

$$\begin{cases} \Lambda - S_3 \displaystyle\int_0^\infty \beta(\tau) i_3(\tau) d\tau - m_0 S_3 = 0, \\ \dfrac{di_3(\tau)}{d\tau} = -(m_0 + mV(\tau)) i_3(\tau), \\ i_3(0) = S_3 \displaystyle\int_0^\infty \beta(\tau) i_3(\tau) d\tau. \end{cases} \tag{4.13}$$

Theorem 4.5. *The equilibrium E_3 defined above is locally asymptotically if and only if the predator invasion reproduction number $R_i^p < 1$ and unstable if and only if $R_i^P > 1$.*

Proof. To achieve the local stability of the model, we follow the same technique defined in the previous part of this article viz. linearizing and analyzing the asymptotic behavior of the perturbed term. We linearize the system about the equilibrium points as follows,

$$S(t) = S_3 + \xi(t), i(\tau, t) = i_3(\tau) + \eta(\tau, t), P(t) = n(t).$$

We substitute this expansion in the original equation to observe the behavior. This reduces the system to the following form.

$$\begin{cases} \dfrac{d\xi(t)}{dt} = \Lambda - (S_3 + \xi(t)) \displaystyle\int_0^\infty \beta(\tau)(i_3(\tau) + \eta(\tau, t)) d\tau \\ \qquad\qquad - \dfrac{a_1 (S_2 + \xi(t)) n(t)}{1 + c(S_2 + \xi(t))} - m_0 (S_2 + \xi(t)), \\ \dfrac{\partial \eta(\tau, t)}{\partial \tau} + \dfrac{\partial \eta(\tau, t)}{\partial t} = -(m_0 + mV(\tau)) \eta(\tau, t) - \alpha(\tau) i_3(\tau) n(t), \\ \eta(0, t) = S_3 \displaystyle\int_0^\infty \beta(\tau) \eta(\tau, t) d\tau + \xi(t) \int_0^\infty \beta(\tau) i_3(\tau) d\tau \end{cases} \tag{4.14}$$

The predator equation in the similar way reduces to the form given below.

$$\begin{aligned}\frac{dn(t)}{dt} &= \left(\frac{(a_2-cd)\frac{\Lambda}{m_0R_0^P}-d}{1+cS_3}+k\Lambda(1-\frac{1}{R_0^P})\int_0^\infty \alpha(\tau)e^{-\mu(\tau)}d\tau\right)n(t)\\ &= \left(\frac{d(\frac{R_0}{R_0^P}-1)}{1+cS_3}+k\Lambda(1-\frac{1}{R_0^P})\int_0^\infty \alpha(\tau)e^{-\mu(\tau)}d\tau\right)n(t) \qquad (4.15)\\ &= f_1 n(t),\end{aligned}$$

where

$$f_1 = \frac{d(\frac{R_0}{R_0^P}-1)}{1+cS_3}+k\Lambda(1-\frac{1}{R_0^P})\int_0^\infty \alpha(\tau)e^{-\mu(\tau)}d\tau.$$

This shows that the predator equation is a linear ODE and it can be solved using the methods for solving the linear Ordinary Differential Equations. Solving the equation we have

$$n(t) = n(0)e^{f_1 t}.$$

Note that $R_i^P > 1 \Rightarrow f_1 > 0$. Since f_1 is an eigenvalue of the system, it is clear that the system is unstable if $R_i^P > 1$.

Also $R_i^P < 1 \Rightarrow f_1 < 0$ and hence we have $n(t) \to 0$ as $t \to \infty$. In the case when $R_i^P < 1$ we look for the solution of $\eta(\tau, t)$ and $\xi(t)$. To investigate the system we let $\eta(\tau, t) = \eta(\tau)e^{\lambda t}$ and $\xi(t) = \xi e^{\lambda t}$. This leads to the following set of equations.

$$\frac{d\eta(\tau)}{d\tau} = -(\lambda + m_0 + mV(\tau))\eta(\tau) \Rightarrow \eta(\tau) = \eta(0)e^{-\lambda\tau-\mu(\tau)}. \qquad (4.16)$$

Substituting the solution in the boundary condition leads to the following form of the equation, which will finally lead to the characteristic equation. Details of the computational work have been explained below,

$$\eta(0) = \xi\int_0^\infty \beta(\tau)i_3(\tau)d\tau + S_3\int_0^\infty \beta(\tau)\eta(\tau)d\tau.$$

From (4.14) we have

$$\xi = \frac{-\eta(0)}{\lambda+m_0}.$$

Substituting in the previous equation, we have the following characteristic equation.

$$R(\lambda) = 1,$$

where

$$R(\lambda) = \frac{-1}{\lambda+m_0}\int_0^\infty \beta(\tau)i_3(\tau)d\tau + S_3\int_0^\infty \beta(\tau)e^{-\mu(\tau)-\lambda\tau}d\tau.$$

As we have explained before, the roots of this characteristic equation will give the local stability of this equilibrium point. The form of the perturbations assumed in the text,

tells us that if the root λ is negative or has a negative real part, then local stability can be established in the model, otherwise the solutions will diverge and the equilibrium will be unstable. The following Lemma below establishes the result.

Lemma 4.2. *$R(\lambda) = 1$ cannot have roots with positive real parts.*

Proof of Lemma: We begin our proof by the method of contradiction. Let us assume $G(\lambda) = 1$ for some $\lambda = a + ib$ for some $a \geq 0$. This reduces the equation $R(\lambda) = 1$ to the following form,

$$1 + \frac{1}{\lambda + m_0} \int_0^\infty \beta(\tau) i_3(\tau) d\tau = S_3 \int_0^\infty \beta(\tau) e^{-\mu(\tau) - \lambda\tau} d\tau. \tag{4.17}$$

Since $\Re(\lambda) > 0$ we have

$$\left| S_3 \int_0^\infty \beta(\tau) e^{-\mu(\tau) - \lambda\tau} d\tau \right| < S_3 \int_0^\infty \beta(\tau) e^{-\mu(\tau)} d\tau = 1.$$

But the LHS of the equation (4.17) is

$$1 + \frac{1}{\lambda + m_0} \int_0^\infty \beta(\tau) i_3(\tau) d\tau = 1 + \frac{k}{\lambda + m_0},$$

where

$$k = \int_0^\infty \beta(\tau) i_3(\tau) d\tau > 0.$$

Hence we have

$$|LHS| > \Re(LHS) = 1 + \frac{k(a + m_0)}{(a + m_0)^2 + b^2} > 1.$$

Which is a contradiction. This establishes the theorem.

This result proves that this equilibrium is locally asymptotically stable when $R_i^P < 1$.

□

5. Global stability of the predator-free equilibrium.

In this section we are going to prove the global stability of the equilibrium with no predator under certain conditions. We first establish the following Proposition and Lemma before we state the final theorem.

Proposition: The semiflow Ψ defined by the solution of the equation 2.1 is

$$\Psi(t, S^0, i^0, P^0) := (S(t), i(., t), P(t)),$$

is a mapping $\Psi : [0, \infty) \times \chi_+ \to \chi_+$ with $\Psi(t, \Psi(s, .)) = \Psi(t + s, .), \forall t, s \geq 0$. and $\Psi(0, .)$ being the identity map. A set K in χ_+ is called global compact attractor for Ψ, if K is

a maximal compact invariant set and if for all bounded sets B of $\chi_+, \exists r > 0$ such that $\Psi(t, B) \subset U, \forall t \geq r$.

Proposition: The semiflow Ψ has a global compact attractor.

Proof. We show that Ψ satisfies the assumptions of the Lemma 3.2.3 and Theorem 3.4.6 in .

We split the function Ψ into two parts given as follows.

$$\Psi(t, u^0) = \hat{\Psi}(t, u^0) + \tilde{\Psi}(t, u^0),$$

such that $\hat{\Psi}(t, u^0) \to 0$ as $t \to \infty, \forall u^0 \in \chi$, where the corresponding functions are represented by the following form.

$\hat{\Psi}(t, u^0) = (0, 0, \hat{i}(., t))$ and $\tilde{\Psi}(t, u^0) = (S(t), P(t), \tilde{i}(., t))$ where the functions $\hat{i}$ and $\tilde{i}$ are solutions of the following system.

$$\begin{cases} (\delta_t + \delta_\tau)\hat{i} = -m_0\hat{i} - mV(\tau)\hat{i} - \alpha(\tau)P\hat{i}, \\ \hat{i}(0, t) = 0, \\ \hat{i}(\tau, 0) = i_0(\tau) \end{cases} \tag{5.1}$$

and

$$\begin{cases} (\delta_t + \delta_\tau)\tilde{i} = -m_0\tilde{i} - mV(\tau)\tilde{i} - \alpha(\tau)P\tilde{i}, \\ \tilde{i}(0, t) = S(t)\displaystyle\int_0^\infty \beta(\tau)i(\tau, t)d\tau, \\ \tilde{i}(\tau, 0) = 0. \end{cases} \tag{5.2}$$

PDE are not satisfied in a strict, but integral sense. Moreover the functions $\hat{i}, \tilde{i}$ are non-negative. First we show that $\tilde{i} \to 0$ as $t \to \infty$.

Let $\nu(t) = \int_0^\infty \hat{i}(\tau, t)d\tau$. Integrating the equation for $\hat{i}$, over $\tau \in [0, \infty)$ we obtain,

(5.3)

$$\delta_t\nu(t) + \hat{i}(\infty, t) - \hat{i}(0, t) = -m_0 - m\int_0^\infty V(\tau)\hat{i}(\tau, t)d\tau - P(t)\int_0^\infty \alpha(\tau)\hat{i}(\tau, t)d\tau,$$

$$\nu' = -\hat{i}(\infty, t) - m_0\nu - m\int_0^\infty V(\tau)i(\tau, t)d\tau - P(t)\int_0^\infty \alpha(\tau)\hat{i}(\tau, t)d\tau$$

Since $\hat{i}(0, t) = 0$. We observe that

$$\nu' \leq -m_0\nu.$$

Solving the equation we obtain $\nu(t) \leq e^{-m_0 t}\nu(0)$. This implies that $\left|\left|\hat{\Psi}(t, u)\right|\right| \leq e^{-m_0 t}\,||u||$. Let us define a function $k(t, r) = e^{\mu t}r$. Since $\hat{i}$ and $\tilde{i}$ are non-negative functions, we have

$$\hat{\Psi} \leq \Psi, \tilde{\Psi} \leq \Psi.$$

Note that, if $||\Psi(t,u_0)|| = N(t)$ and $m = min(m_0, d)$, then $N(t)$ satisfies the following equation.

$$N' \leq \Lambda - mN \Rightarrow N(t) \leq (||u_0|| + \frac{\Lambda}{m})e^{-mt}\frac{\lambda}{m}. \tag{5.4}$$

This shows that

a) for every ball with radius $r > \frac{\Lambda}{m}$ is invariant and attracts all bounded sets or Ψ is bounded dissipative.

b) The orbits of all bounded sets are bounded i.e. $\forall c_1 > 0, \exists c_2 > 0$ such that $||\Psi(t,u_0)|| \leq c_2, \forall t \geq 0$, whenever $||u_0|| \leq c_1$.

$\hat{\Psi}$ and $\tilde{\Psi}$ also has these properties.

Next, suppose the initial data are in a bounded set, e.g. a ball, i.e., $||u_0|| = |S^0| + |P^0| + ||i^0|| \leq K$, where K is some constant.

We will show that for a fixed time t, the family of functions,

$$(S(t), P(t), \tilde{\tilde{i}}(.,t)) = \tilde{\Psi}(t,u_0),$$

is a compact family of functions. Then Ψ will be asymptotically smooth by Lemma 3.2.3 and have a compact attractor by Theorem 3.4.6. Hence by previous observation, $\{\Psi(t,u_0) : t \geq 0, ||u_0|| \leq K\}$ is bounded.

To show compactness we use Frechet-Kolmogorov theorem for compactness in L^1. Boundedness is trivial. We need to show that

$$\begin{aligned}
\lim_{r\to\infty} \int |\tilde{\tilde{i}}(\tau+h,t) - \tilde{\tilde{i}}(\tau+h,t)|d\tau &= 0, \\
\int |\tilde{\tilde{i}}(\tau+h,t) - \tilde{\tilde{i}}(\tau+h,t)|d\tau &\leq \int |\pi(\tau+h)||B(t-\tau-h) - B(t-\tau)|d\tau \\
&\quad + \int |B(t-\tau)||\pi(t+\tau-h) - B(\tau)|d\tau.
\end{aligned}$$

From the model equation we have $S' \leq \Lambda - B(t) - m_0 S$ and $i_\tau + i_t \leq -m_0 i$. Integrating the second equation with respect to τ we have, $-B(t) + I' \leq -m_0 I$, where $I(t) = \int_0^\infty i(\tau,t)d\tau$. Adding the two equations and using the notation $N = S + I$ we have $N' \leq \Lambda - m_0 N$. Integrating leads to $N \leq \frac{\lambda}{m_0} + Ce^{-m_0 t}$. This proves that $S+I$ is bounded. Hence P is also bounded. Let each of them is bounded by the total population bound say M. Let us assume that β, α, V are bounded functions and $\beta(\tau) \leq \overline{\beta}, \alpha(\tau) \leq \overline{\alpha}, V(\tau) \leq \overline{V}$

From the definition of $B(t) = S(t)\int_0^\infty \beta(\tau)i(\tau,t)d\tau \leq M\overline{\beta}M$ since S, I are bounded. Differentiating the equation we have

$$\begin{aligned} B' &= S'\int_0^\infty \beta(\tau)i(\tau,t)d\tau + S\int_0^\infty \beta(\tau)i_t(\tau,t)d\tau \\ &= S'\int_0^\infty \beta(\tau)i(\tau,t)d\tau + S\int_0^\infty \beta(\tau)[-i_\tau - mVi + \alpha Pi]d\tau \\ &\leq ||S'||\overline{\beta}M + M\beta(0)B(t) + M\overline{\beta}M + Mm\overline{\beta V}M + M\overline{\beta}\overline{\alpha}M \\ &= K + LB \leq R. \end{aligned} \tag{5.5}$$

From the previous equation we have

$$|B(t-\tau-h) - B(t-\tau)|d\tau \leq |B'(\xi)|h \leq Rh.$$

Also note that $\pi(\tau+h)$ is bounded in L^1 norm. The second integral can be shown to be uniformly convergent by using the inequality for $0 \leq x, y \leq M$,

$$|e^{-x} - e^{-y}| \leq \frac{e^{2M}}{2M}|x-y|.$$

The uniform continuity of B implies that the integral can be made arbitrarily small independent of the family of functions. This proves the compactness of $\tilde{\Psi}$ □

Theorem 5.1. *The predator free boundary equilibrium is globally asymptotically stable when $R_0^P > 1$ and $R_0 < R_0^P$, under the circumstances that the predator feeds on the prey selectively, i.e. the predator only feeds on healthy prey and ignore the diseased ones.*

Proof. In this section we show the global stability of this equilibrium in the case when $\alpha = 0$ i.e. the predator does not feed on diseased prey. The equilibrium is given as $\mathcal{E}_3 = (S_3, i_3(\tau), 0)$. We develop the following Lyapunov function, $V(t)$ given by $V(t) = V_s(t) + V_i(t)$. We set up each of the parts as follows.

$$V_s(t) = \frac{1}{S_3}\left(\frac{a_2}{1+cS_3}(S - S_3 - S_3\ln(\frac{S}{S_3})) + a_1P\right). \tag{5.6}$$

Differentiating V_s with respect to time t, we have

$$\begin{aligned} \frac{dV_s}{dt} &= \frac{1}{S_3}\left[\frac{a_2}{1+cS_3}\left(1-\frac{S_3}{S}\right)\left(\Lambda - m_0S - \frac{a_1SP}{1+cS} - S\int_0^\infty \beta(\tau)i(\tau,t)d\tau\right) + a_1\big(\frac{a_2SP}{1+cP} - dP\big)\right] \\ &= \frac{1}{S_3}\left[\frac{a_2}{1+cS_3}\left(1-\frac{S_3}{S}\right)\left(m_0(S_3-S) - \frac{a_1SP}{1+cS}\right) + a_1\Big(\frac{a_2SP}{1+cS} - dP\Big)\right] \\ &\quad + \frac{1}{S_3}\left(\frac{a_2}{1+cS_3}(1-\frac{S_3}{S})\right)\left(S_3\int_0^\infty \beta(\tau)i^*(\tau)d\tau - S\int_0^\infty \beta(\tau)i(\tau,t)d\tau\right) \end{aligned} \tag{5.7}$$

which can be rearranged in the form,

$$\begin{aligned}\frac{dV_s}{dt} &= -\frac{a_2 m_0}{SS_3(1+cS_3)}(S-S_3)^2 + \frac{a_1 a_2 P}{S_3(1+cS)}\left(S - \frac{S-S_3}{1+cS_3}\right) - \frac{a_1 dP}{S_3} \\ &\quad +(1-\frac{S_3}{S})\int_0^\infty \beta(\tau) i_3(\tau)\left(1-\frac{Si(\tau,t)}{S_3 i_3(\tau)}\right)d\tau \\ &= -\frac{a_2 m_0}{SS_3(1+cS_3)}(S-S_3)^2 + \frac{a_1 P}{S_3}\left(\frac{a_2 S_3}{1+cS_3} - d\right) \\ &\quad +l\int_0^\infty \beta(\tau) i_3(\tau)\left(1-\frac{Si(\tau,t)}{S_3 i_3(\tau)} + \frac{i(\tau,t)}{i_3(\tau)} - \frac{S_3}{S}\right)d\tau \\ &= -\frac{a_2 m_0}{SS_3(1+cS_3)}(S-S_3)^2 + M + lH,\end{aligned}$$

where

$$M = \frac{a_1 P}{S_3}\left(\frac{a_2 S_3}{1+cS_3} - d\right) < 0,$$

when $R_i^P < 1$ and

$$H = \int_0^\infty \beta(\tau) i_3(\tau)\left(1-\frac{Si(\tau,t)}{S_3 i_3(\tau)} + \frac{i(\tau,t)}{i_3(\tau)} - \frac{S_3}{S}\right)d\tau$$

and

$$l = \frac{a_2 S_3}{1+cS_3}.$$

We define

$$V_i(t) = l\int_0^\infty z(\tau) g(\frac{i(\tau,t)}{i_3(\tau)})d\tau,$$

where the function

$$g(x) = x - 1 - \ln(x), \quad \text{and} \quad z(\tau) = \int_\tau^\infty \beta(s) i_3(s) ds.$$

With this formation we have the function changes to

$$V_i(t) = l\int_0^\infty z(\tau) g(\frac{B(t-\tau)}{i_3(0)})d\tau = l\int_{-\infty}^t z(t-s) g(\frac{B(s)}{i_3(0)})ds, \tag{5.8}$$

using the transformation $s = t - \tau$

Differentiating the above form of V_i we have

$$V_i'(t) = z(0) g(\frac{B(t)}{i_3(0)}) + \int_{-\infty}^t z'(t-s) g(\frac{B(s)}{i_3(0)})ds \tag{5.9}$$

Using the derivative of $z'(\tau) = -\beta(\tau) i_3(\tau)$ we have

$$\begin{aligned}V_i'(t) &= l\int_0^\infty \beta(\tau) i_3(\tau)\left(g(\frac{i(0,t)}{i_3(0)}) - g(\frac{i(\tau,t)}{i_3(\tau)})\right)d\tau \\ &= l\int_0^\infty \beta(\tau) i_3(\tau)\left(\frac{i(0,t)}{i_3(0)} - \frac{i(\tau,t)}{i_3(\tau)} - \ln(\frac{i(0,t)}{i_3(0)}) + \ln(\frac{i(\tau,t)}{i_3(\tau)})\right)d\tau.\end{aligned} \tag{5.10}$$

Since we have $V' = V_s' + V_i' = P + lH + V_i'$. Let us consider the term, $lH + V_i'$.

$$\begin{aligned} lH + V_i' &= \int_0^\infty \beta(\tau) i_3(\tau) \Big(1 - \frac{Si(\tau,t)}{S_3 i_3(\tau)} \\ &\quad - \frac{S}{S_3} + \frac{i(0,t)}{i_3(0)} - \ln(\frac{i(0,t)}{i_3(0)}) + \ln(\frac{i(\tau,t)}{i_3(\tau)})\Big) d\tau. \end{aligned} \tag{5.11}$$

We observe that

$$\int_0^\infty \beta(\tau) i_3(\tau) \Big(\frac{i(0,t)}{i_3(0)} - \frac{Si(\tau,t)}{S_3 i_3(\tau)}\Big) d\tau = 0.$$

This reduces the equation to

$$lH + V_i' = \int_0^\infty \beta(\tau) i_3(\tau) \Big(1 - \frac{S}{S_3} - \ln(\frac{i(0,t)}{i_3(0)}) + \ln(\frac{i(\tau,t)}{i_3(\tau)})\Big) d\tau. \tag{5.12}$$

We also have the relation

$$\int_0^\infty \beta(\tau) i_3(\tau) \Big(1 - \frac{Si(\tau,t)}{S_3 i_3(\tau)} \frac{i_3(0)}{i(0,t)}\Big) d\tau = 0.$$

Adding this to the equation $lH + V_i'$ we have the following form

$$lH + V_i' = \int_0^\infty \beta(\tau) i_3(\tau) C(\tau) d\tau,$$

where

$$\begin{aligned} C(\tau) &= 2 - \frac{i(\tau,t)}{i_3(\tau)} \frac{S}{S_3} \frac{i_3(0)}{i(0,t)} - \frac{S_3}{S} - \ln(\frac{i(0,t)}{i_3(0)}) + \ln(\frac{i(\tau,t)}{i_3(\tau)}) + \ln(\frac{S}{S_3}) - \ln(\frac{S}{S_3}) \\ &= \Big(1 - \frac{S}{S_3} + \ln(\frac{S}{S_3})\Big) + \Big(1 - \frac{i(\tau,t)}{i_3(\tau)} \frac{S}{S_3} \frac{i_3(0)}{i(0,t)} + \ln(\frac{i(\tau,t)}{i_3(\tau)} \frac{S}{S_3} \frac{i_3(0)}{i(0,t)})\Big) \leq 0. \end{aligned}$$

Hence $lH + V_i' \leq 0$. We have already shown $P \leq 0$. This proves that $V' \leq 0$ although $V \geq 0$. Note that $V' = 0$ if and only if $S = S_3, i(\tau,t) = i_3(\tau), P = 0$. from Lassale's invariance principle we can show that the equilibrium is globally stable when $R_0^P > 1$ and $R_0 < R_0^P$.

□

6. Numerical simulations

In this section we simulate the behavior of the immuno-eco-epidemiological model (2.2)-(2.1). We use Matlab to solve the model. We use Matlab's `ode23s` routine to solve the ODE model (2.2) and a finite difference numerical scheme to solve the PDE (2.1). As a first scenario, we simulate the case for which global stability occurs, that is when $R_0^P > 1$ and $R_0 < R_0^P$. Figure 1 illustrate the behavior.

Figure 1 gives the time-dependent behavior of three curves. The top panel represents the growth in the number of virus V. The middle panel shows the total infected prey

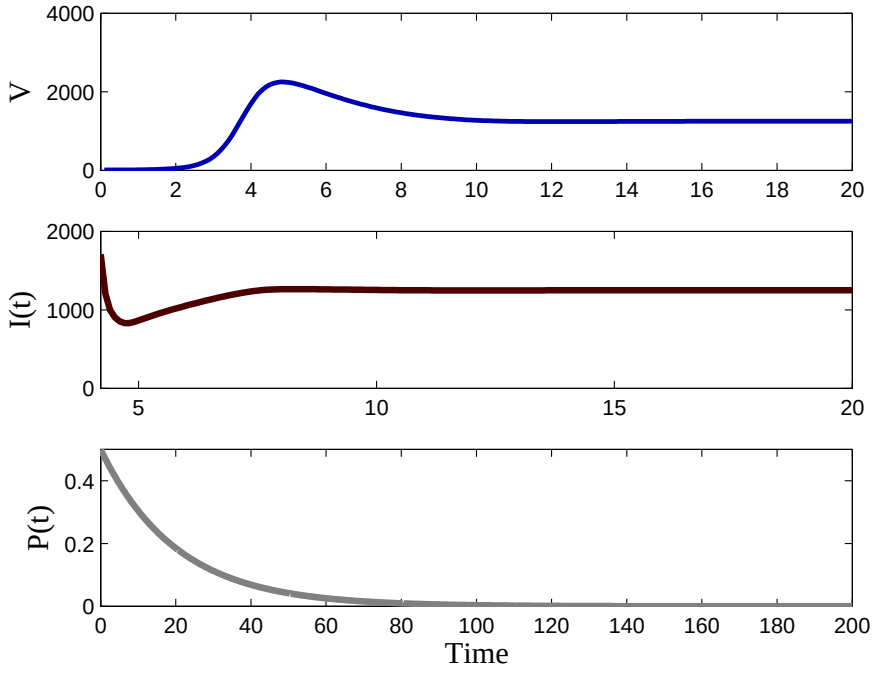

FIGURE 1. Plots of $V(\tau)$, $I(t)$ and $P(t)$ with parameters as in text.

population $I(t)$ where

$$I(t) = \int_0^\infty i(\tau, t)d\tau.$$

The bottom panel shows the number of predator $P(t)$ with respect to time. The parameters for the immune system are $r = 10, K = 10000, \eta = 0.5, \rho = 0.5, A = 5000, \mu = 0.1$ and the parameters for the epidemiological system are $\Lambda = 1000, m_0 = 0.5, a_1 = 0.2, a_2 = 0.05, m = 0.01, d = 0.1, k = 0.5, c = 0.1$. In this case $\alpha = 0$. The approximate values of the reproductive numbers computed by the code are $R_0 = 900$, $R_0^P \approx 4.7 * 10^9$, and $R_i^P \approx 2.1 * 10^{-7}$. The Figure shows that the number of infected prey population is globally stable as it approaches a finite non-zero value whereas the number of predator population dies out eventually. The virus within the prey stabilizes at a positive value. The numerical simulation clearly demonstrates our result presented in the manuscript on global stability.

In the second simulation we consider a different scenario, where the disease dies out, while the predator persists. We simulate this scenario in Figure 2.

Figure 2 shows that when the predator predates on infected individuals, the predator may persist while the disease is eliminated from the prey population. Panel one in the

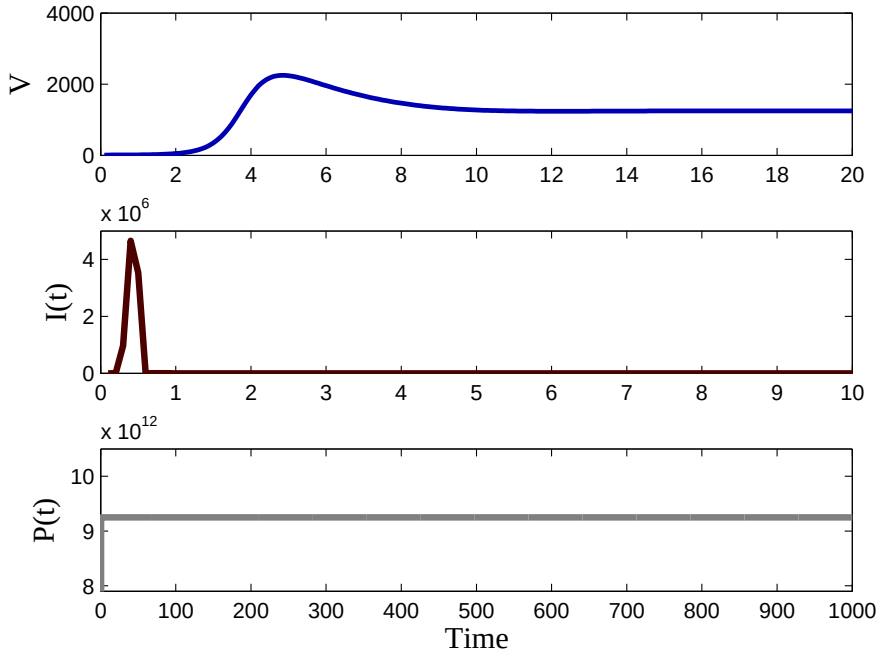

FIGURE 2. Plots of $V(\tau)$, $I(t)$ and $P(t)$ with parameters as in text.

figure again represents the growth in the number of virus V. Panel two shows the total infected prey population $I(t)$ and panel three demonstrates the number of predator $P(t)$ with respect to time. The parameters for the immune system are $r = 10, K = 10000, \eta = 0.5, \rho = 0.5, A = 5000, \mu = 0.1$ and the parameters for the epidemiological system are $\Lambda = 1000, m_0 = 0.5, a_1 = 0.2, a_2 = 0.1, m = 0.01, d = 0.1, k = 0.5, c = 0.1$. In this case α is not zero and is given by the step function

$$\alpha(\tau) = \begin{cases} 0 & \tau < 0.25 \\ 2 & \tau > 0.25. \end{cases}$$

The values of the reproduction numbers with this choice of parameters are $R_0 = 1900$, $R_0^P \approx 4.7 * 10^9$ and $R_i^P \approx 7.2 * 10^8$. The graph clearly shows that for this particular choice of parameters the number of infected prey population approaches zero whereas the number of predator population stabilizes at non-zero values. This numerical simulation extends the analytical results in the manuscript.

7. CONCLUSIONS

This paper is focused on a model merging three separate branches of study namely ecology, epidemiology and immunology. This model is termed an immuno-eco-epide-

miological model. The role of the within-host status of the pathogen in the prey has not been given much attention. Consideration of the number of virus particles and the status of the immune response inside an infected prey individual in a predator-prey dynamics gives an entirely different approach to the predator-prey-disease system. How the predator-prey dynamics impacts the immunological factors in the diseased prey and conversely, how the within-host pathogen dynamics impacts the predator-prey dynamics are questions of paramount importance. Significant amount of further study is necessary to fully understand their mutual interrelation.

In this article we investigate what we believe is the first immuno-eco-epidemiological model. We define within-host reproduction number and between-host reproduction number of the diseases as well as two invasion numbers of the predator: one predator invasion number in the absence of disease and another – in the presence of disease. We find that the predator-prey-disease system has four equilibria: disease and predator-free equilibrium, predator-free equilibrium, predator-prey disease-free equilibrium and coexistence equilibrium. Furthermore, we find that the predator and disease-free equilibrium is locally asymptotically stable if both the reproduction number of the disease and the predator invasion number in the absence of disease are less than one. The disease-free predator-prey equilibrium is locally stable if the predator invasion number in the absence of disease is smaller than the disease reproduction number. The predator-free prey-disease equilibrium is locally stable if the predator invasion number in the presence of disease is smaller than one, and unstable if the predator invasion number in the presence of disease is larger than one. Finally we show that the predator-free prey-disease equilibrium is globally asymptotically stable. We establish the global stability result using a Lyapunov's function.

This paper assumes the disease in a prey population only, which can be extended to include the disease dynamics inside the predator population. The general model involving both infected predator and prey populations, can be used as a greater measure how the balance in the eco-system can be maintained.

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