Chapter 4

Dynamics of a ratio-dependent marine bacteriophage infection model with delay

4.1 Introduction

Present research in mathematical ecology and epidemiology has expanded drastically [9–11, 30, 31, 52, 53, 65, 68–71] after the work of Ross(1911). There are so many works on marine viruses [40, 46–51] but a simple mathematical model in connection with infected viruses (phages) at first was proposed by Beretta and Kuang [40] to describe epidemics of bacteriophages in a marine environment. Due to environmental fluctuations the bacteria bacteriophage interaction was studied by Beretta, Carletti and Solimano [46].

The study of models with variable population size due to demographic processes also illustrated the possibility of richer dynamics [72]. In the context of models with variable population size, the qualitative dynamics of such systems are controlled specifically by two thresholds. The first threshold is a demographic threshold $R_d$ and the second is the basic reproductive number $R_0$. $R_d > 1$ implies that each individual leaves more than one descendant on
average before it dies. On the other hand, $R_d < 1$ implies that the population will not survive.

The second threshold is the basic reproductive number $R_0$ for the epidemiological process. The dynamics of general epidemic models are reduced to the existence of $R_0$ that determines the stability and existence of non-trivial equilibria. In epidemiology the basic reproductive number $R_0$ is the number of secondary cases which one case would produce in a completely susceptible population. Therefore $R_0$ may vary considerably for different infectious diseases but also for the same disease in different populations. Because the magnitude of $R_0$ allows one to determine the amount of effort which is necessary either to prevent an epidemic or to eliminate an infection from a population, it is crucial to estimate $R_0$ for a given disease in a particular population. When $R_0 < 1$ the infection will die out in the long run; that is, the infection-free state, an equilibrium in an epidemic model, is locally asymptotically stable. If $R_0 > 1$ infection free-state loses its local stability and the infection is able to spread in a population and there exists a stable endemic state where the disease is always present.

Again we know that delay differential equations play an important role in ecology and epidemiological modelling [73–76]. In such type of delay models it is interesting to derive analytically the parameter thresholds for the existence of non-trivial equilibria (disease free) and to determine sufficient conditions for their asymptotic stability or the appearance of periodic solutions. Computer simulations are usually carried out to support analytical results because it is difficult to treat analytically.

The main aim of our work is to present a complete investigation of both the models (4.1) and (4.2). We organize the paper as follows: Section 4.2 demonstrates the basic assumptions and model construction for both the
systems; Section 4.3 studies mathematically the system (4.1) by deriving the conditions for boundedness and existence of solutions, stability analysis at different equilibria by the normal linearization approach; Hopf bifurcation by the approach in [56] and global stability; Section 4.4 studies mathematically the system (4.2) by showing it is bounded and dissipative; stability analysis at different equilibria; Hopf bifurcation by the same approach; in Section 4.5 we investigate both the models by numerical simulation and discussion and Section 4.6 contains conclusions.

4.2 Assumption and Model

Let at any time $t$ the total number of bacteria be $N$ ($[N] = \text{number of bacteria/liter}$) and the total number of virus be $V$ ($[V] = \text{number of viruses/liter}$). We formulate the model based on the following assumptions:

**A.1:** In the absence of viruses the growth of bacteria is according to the logistic law with carrying capacity $C$ ($C \in R_+$) and intrinsic birth rate $\alpha$ ($\alpha \in R_+$).

**A.2:** In presence of the virus the bacteria population $N$ is divided into susceptible class $S(t)$ and infected class $I(t)$ so that $N(t) = S(t) + I(t)$.

**A.3:** A susceptible bacteria $S(t)$ become infected under the attack of many virus particles. We assume that the rate of infection is according to $\frac{kSV}{S+I}$, which is the number of new infected bacteria per unit time and $k$ is the rate of infection.

**A.4:** The susceptible bacteria is emigrated at the rate $e$ and the natural
death rate constant is \( \lambda \).

**A.5:** The time from the instant of infection to bacterial cell-wall lysis is known as latent period \( (\tau > 0) \) and the lysis death rate constant \( \mu \) \((\mu \in \mathbb{R}_+)\) gives a measure of this latency period. Let the lysis of infected bacteria produces \( b \) virus particle \((b \in \mathbb{R}_+, b > 1)\). Also let \( d \) be the natural death rate of infected bacteria (the death other than cell lysis).

**A.6:** The virus particle have a natural death rate constant \( \delta \) \((\delta \in \mathbb{R}_+)\), which accounts all kinds of mortality of viruses. With these biological assumptions and with \( S + I < C \) we have the model

\[
\frac{dS}{dt} = \alpha S(1 - \frac{S + I}{C}) - \frac{kSV}{S + I} - (\lambda + \epsilon)S,
\]

\[
\frac{dI}{dt} = \frac{kSV}{S + I} - (\mu + d)I,
\]

\[
\frac{dV}{dt} = b\mu I - \delta V.
\]

**A.7:** The accumulated total number of infected cell in time \( t - \tau \) to \( t \) is

\[
I(t) = k \int_{t-\tau}^{t} \frac{e^{-\mu(t-u)}S(u)V(u)}{S(u) + I(u)} \, du.
\]

Thus we have the modified system (4.2)

\[
\frac{dS}{dt} = \alpha S(1 - \frac{S + I}{C}) - \frac{kSV}{S + I} - (\lambda + \epsilon)S,
\]

\[
\frac{dI}{dt} = \frac{kSV}{S + I} - dI - e^{-\mu\tau} \frac{kS(t - \tau)V(t - \tau)}{S(t - \tau) + I(t - \tau)},
\]

\[
\frac{dV}{dt} = b e^{-\mu\tau} \frac{kS(t - \tau)V(t - \tau)}{S(t - \tau) + I(t - \tau)} - \delta V.
\]

The initial conditions are \( S(u) = S_0(u) \geq 0, \ I(u) = I_0(u) \geq 0, V(u) = \)
\[ V_0(u) \geq 0, \; u \in [-\tau, 0] \text{ and } I_0(0) = k \int_{-\tau}^{0} \frac{e^{-\mu u} S_0(u)}{S_0(u) + I_0(u)} \; du. \]

### 4.3 Mathematical Study of System Without Delay

#### 4.3.1 Existence and Boundedness of Solutions

We rewrite the system (4.1) as \( \frac{dX}{dt} = F(X) \), where \( X = [S, I, V]^T \) and \( F = [f, g, h]^T \).

Let \( R_+^3 = \{(S, I, V) : S \geq 0, I \geq 0, V \geq 0\} \). Obviously \( F : R_+^3 \rightarrow R_+^3 \) is \( C^1 \) and if \( X(0) = X_0 = (S_0, I_0, V_0) \in R_+^3 \), then it is easy to check that \( f_i(X) \mid_{X_i = 0} \geq 0 \). Therefore by Nagumo’s lemma [54] any solution of the system (4.1) with \( X_0 \in R_+^3 \), say \( X(t) = X(t; X_0) \), is such that \( X(t) \in R_+^3 \) for all \( t > 0 \). Hence all solutions of the system (4.1) exist in the region \( R_+^3 \), remain non-negative for all \( t > 0 \).

Again to check the boundedness of the solution of the system (4.1) we consider the following theorem.

**Theorem 4.3.1.** The solution of the system (4.1) is bounded in
\[ \Omega = \{(S, I, V) \in R_+^3 : 0 \leq S + I + \frac{1}{b}V \leq \frac{al}{\eta} + \epsilon, \; \forall \; \epsilon > 0\}, \]
where \( \eta = \min \{\lambda + e, d, \delta\} \) and \( l = \max(S(0), C) \).

**Proof.**

Let \( U(t) = S + I + \frac{1}{b}V \) and \( l = \max(S(0), C) \).

Now \( \frac{dU}{dt} = \alpha S(1 - \frac{S+I}{C}) - (\lambda + e)S - dI - \frac{\delta}{b}V \leq al - \{(\lambda + e)S + dI + \frac{\delta}{b}V\} \).

Let \( \eta = \min \{\lambda + e, d, \delta\} \), then \( \frac{dU}{dt} + \eta U \leq al \).

Now by the theory of differential inequality [55] we have,
\[ 0 \leq U(t) \leq \frac{al}{\eta} (1 - e^{-\eta t}) + x(0)e^{-\eta t}. \]

As \( t \rightarrow \infty \), then \( 0 \leq U(\tau) \leq \frac{al}{\eta} \).

Hence \( U(t) \) is a bounded quantity.
Hence the solutions of system (4.1) with initial value \((S_0, I_0, V_0) \in R^3_+\) are confined in the region

\[
\Omega = \{ (S, I, V) \in R^3_+ : 0 \leq S + I + \frac{1}{b} V \leq \frac{a}{\eta} + \epsilon, \quad \forall \ \epsilon > 0 \}.
\]

Before going to establish existence criterion of different equilibria we establish some criterion for which susceptible and infected bacteria or both going to extinction.

**Criterion for extinct of susceptible bacteria.**

**Result 1** If \(R_d < 1\) then \(\lim_{t \to \infty} S(t) = 0\) and \(\lim_{t \to \infty} I(t) = 0\), where \(R_d = \frac{\alpha}{\lambda + \epsilon}\).

**Proof:** From the first equation of the system (4.1) we have

\[
\frac{dS}{dt} \leq -(\lambda + \epsilon)(1 - R_d)S,
\]

where \(R_d = \frac{\alpha}{\lambda + \epsilon}\).

Thus by the theory of differential inequality [55] we have

\[
0 \leq S(t) \leq S(0)e^{-(\lambda + \epsilon)(1 - R_d)t}.
\]

Hence \(\lim_{t \to \infty} S(t) = 0\), provided \(R_d < 1\).

Again from first two equations of system (4.1) we have

\[
\frac{d}{dt}(S + I) \leq -(\lambda + \epsilon)(1 - R_d)S - (\mu + d)I.
\]

Let \(\nu = \min\{\mu + d, (\lambda + \epsilon)(1 - R_0)\}\) then \(\nu > 0\) and \(\frac{d}{dt}(S + I) \leq -\nu(S + I)\).

Thus by the theory of differential inequality [55] we have

\[
0 \leq S(t) + I(t) \leq \{S(0) + I(0)\}e^{-\nu t}.
\]

Hence \(\lim_{t \to \infty} \{S(t) + I(t)\} = 0\), provided \(R_d < 1\).

Again \(\lim_{t \to \infty} S(t) = 0\) hence \(\lim_{t \to \infty} I(t) = 0\).

### 4.3.2 Equilibria and Stability Analysis

The system (4.1) has following equilibria.

\[E_0(0, 0, 0), \ E_f(S_1, 0, 0), \text{ where } S_1 = \frac{C}{R_d}(R_d - 1) > 0 \text{ provided } R_d > 1 \text{ and }\]

\[E_+(S^*, I^*, V^*), \text{ where } S^* = \frac{CL}{\alpha R_0}, \ I^* = (R_0 - 1)S^* \text{ and } V^* = \frac{b\mu}{\delta}(R_0 - 1)S^* \text{ and } L = \theta - (\mu + d)(R_0 - 1) \text{ where } \theta = (\lambda + \epsilon)(R_d - 1). \ E_+ \text{ exists provided } \theta > (\mu + d)(R_0 - 1) \text{ and } R_0 = \frac{kb\mu}{\delta(\mu + d)} > 1.\]
Again the positive equilibrium point \( E_+ \) is feasible provided \( R_0 > 1 \). When \( R_0 \) approaches to 1, then \( I^* \to 0 \) and \( V^* \to 0 \), i.e. the positive equilibrium \( E_+ \) approaches to the boundary equilibrium \( E_f \) and \( E_+ \) collapses to \( E_f \) when \( R_0 = 1 \).

**Theorem 4.3.2.** The equilibrium \( E_f \) is locally asymptotically stable if \( R_0 < 1 \) and unstable for \( R_0 > 1 \).

**Proof.**

At the equilibrium \( E_f : (S_1, 0, 0) \), the variational matrix is

\[
V(E_f) = \begin{pmatrix}
-\frac{\alpha}{C}S_1 & -\frac{\alpha}{C}S_1 & -k \\
0 & -(\mu + d) & k \\
0 & b\mu & -\delta
\end{pmatrix}.
\]

The characteristic equation is \( x^3 + a_1x^2 + a_2x + a_3 = 0 \) where

\[
\begin{aligned}
a_1 &= \delta + \mu + d + (\lambda + e)(R_d - 1), \\
a_2 &= \delta(\mu + d)(1 - R_0) + (\lambda + e)(\delta + \mu + d)(R_d - 1), \\
a_3 &= \delta(\lambda + e)(\mu + d)(R_d - 1)(1 - R_0).
\end{aligned}
\]

Now \( a_1a_2 - a_3 \)
\[
= \delta(\mu + d)(\delta + \mu + d)(1 - R_0) + (\lambda + e)(\delta + \mu + d)^2(R_d - 1) \\
+ (\lambda + e)^2(\delta + \mu + d)(R_d - 1)^2.
\]

Since \( S_1 > 0 \) then \( R_d > 1 \). Therefore if \( R_0 < 1 \) then \( a_1 > 0, a_2 > 0, a_3 > 0 \) and \( a_1a_2 - a_3 > 0 \). Hence the equilibrium \( E_f \) is locally asymptotically stable. Again if \( R_0 > 1 \) then \( a_3 < 0 \) and hence the equilibrium \( E_f \) is unstable.

Now we study the global stability dynamics of the equilibrium \( E_f \) (see ref. [77,78] ) with the help of following theorem.

**Theorem 4.3.3.** If \( R_0 < 1 \), then \( E_f \) is globally asymptotically stable.
Proof.

From the last two equations of system (4.1), for \( t > t_1 \), we have

\[
\frac{dI}{dt} = \frac{kSV}{S + I} - (\mu + d)I \leq kV - (\mu + d)I,
\]

\[
\frac{dV}{dt} = b\mu I - \delta V.
\]

Consider the comparison equations

\[
\frac{dz_1}{dt} = kz_2 - (\mu + d)z_1, \tag{4.3}
\]

\[
\frac{dz_2}{dt} = b\mu z_1 - \delta z_2.
\]

Since \( R_0 < 1 \), that is \( kb\mu < \delta(\mu + d) \), it is easy to show system (4.3) has two negative eigenvalues. For any solution of system (4.3) with non-negative values, we have \( \lim_{t \to +\infty} z_i = 0; \, i = 1, 2 \).

Let \( 0 < I(0) < z_1(0), \, 0 < V(0) < z_2(0) \), by the comparison theorem [79], it follows that

\[
I(t) < z_1(t) \quad \text{and} \quad V(t) < z_2(t), \, \forall \, t > t_1 > 0.
\]

Therefore \( \lim_{t \to +\infty} I(t) = 0 \) and \( \lim_{t \to +\infty} V(t) = 0 \).

From the first equation of system (4.1), we can get

\[
\alpha S(1 - \frac{S + I}{C}) - kV - (\lambda + e)S \leq \frac{dS}{dt} \leq \alpha S(1 - \frac{S}{C}) - (\lambda + e)S
\]

This shows that there exists \( t_2 > 0 \), such that \( \lim_{t \to +\infty} S(t) = S_1 \) for all \( t > t_2 \).

Let \( t_0 = \max(t_1, t_2) \).

Therefore \( \lim_{t \to +\infty} S(t) = S_1, \, \lim_{t \to +\infty} I(t) = 0 \) and \( \lim_{t \to +\infty} V(t) = 0, \forall \, t > t_0 \).

This completes the proof.

**Theorem 4.3.4.** Let \( \phi = (kb\mu)^3 + \delta(L + \delta R_0^2)(kb\mu)^2 + \delta^2 R_0 L(L + 2\delta)(kb\mu) + \delta^4 R_0 L(L + \delta R_0) \) and \( \psi = R_0(kb\mu + \delta^2 R_0)(kb\mu)^2 \). If \( \phi > \psi \), then the equilibrium \( E_+ \) is locally asymptotically stable.
Proof.

At the equilibrium $E^+(S^*, I^*, V^*)$ the variational matrix is

$$V(E^*) = \begin{pmatrix}
\frac{k \mu L}{R^0_0} (R_0 - 1) - \frac{L}{R_0} & \frac{k \mu L}{R^0_0} (R_0 - 1) - \frac{L}{R_0} & -\frac{k}{R_0} \\
\frac{k \mu L}{R^0_0} (R_0 - 1)^2 & \frac{k \mu L}{R^0_0} (1 - 2R_0) & \frac{k}{R_0} \\
0 & b \mu & -\delta
\end{pmatrix}.$$  

The characteristic equation of $V(E^+)$ is

$$x^3 + b_1 x^2 + b_2 x + b_3 = 0,$$
where

- $b_1 = \delta + \frac{L}{R_0} + \frac{k \mu L}{R^0_0}$,
- $b_2 = \frac{L \delta}{R_0} + \frac{k \mu L}{R^0_0} \left\{ \frac{L}{R_0} + \frac{k \mu L}{R^2_0} (1 - R_0) \right\}$,
- $b_3 = \frac{k \mu L}{R_0^2} (R_0 - 1)$.

Under the existence criterion of $E^+$ we have $b_1 > 0$, $b_3 > 0$.

Also $b_1 b_2 - b_3$

$$= -\frac{k \mu L}{R^3_0} (R_0 - 1) + \left\{ \delta + \frac{L}{R_0} + \frac{k \mu L}{R^0_0} \right\} \left[ \frac{L \delta}{R_0} + \frac{k \mu L}{R^0_0} \left\{ \frac{L}{R_0} + \frac{k \mu L}{R^2_0} (1 - R_0) \right\} \right]$$

$$= \frac{1}{\delta^3 R^3_0} \left\{ (k \mu)^3 + \delta (L + \delta R^2_0) (k \mu)^2 + \delta^2 R_0 L (L + 2 \delta) (k \mu) \right\}$$

$$- \frac{1}{\delta^3 R^3_0} \left\{ -\delta^4 R_0 L (L + \delta R_0) + R_0 (k \mu + \delta^2 R_0) (k \mu)^2 \right\}$$

$$= \frac{1}{\delta^3 R^3_0} (\phi - \psi).$$

Thus if $\phi > \psi$ then $b_1 b_2 > b_3$ and hence $E^+$ is locally asymptotically stable.

This completes the proof.

**Hopf bifurcation:** We first state the theorem (without proof) by Liu [56]
for the occurrence of Hopf bifurcation as follows.

Without knowing eigenvalues, Liu [56] proved that (specific result in our case) if
\[ b_1(\xi), b_3(\xi) \text{ and } D_2(\xi) = b_1(\xi)b_2(\xi) - b_3(\xi) \text{ are smooth functions of } \xi \text{ in an open interval of } \xi_0 \in R \text{ such that} \]
\( (E1): \quad b_3(\xi_0) > 0, \quad D_1(\xi_0) = b_2(\xi_0) > 0, \quad D_2(\xi_0) = 0 \quad \text{and} \)
\( (E2): \quad \text{at } \xi = \xi_0, \quad \frac{d}{d\xi}\{D_2(\xi)\} \neq 0 \)
then a simple hopf bifurcation occur at \( \xi = \xi_0 \).

**Result:** A simple Hopf bifurcation occur at \( k = k^* \).

**Theorem 4.3.5.** If \( R_0 > 1 \) then there is a Hopf bifurcation at \( \alpha = \alpha^* \) where \( \phi = \psi \).

**Proof.** Let \( D = b_1b_2 - b_3 \) then \( D = \frac{1}{\delta^3R_0}\phi - \psi \). We take the parameter \( \alpha \) as bifurcation parameter then \( D \) is a continuously differentiable function of \( \alpha \). Let at \( \alpha = \alpha^* \phi = \psi \) i.e., \( D(\alpha^*) = 0 \). Since \( R_0 \) and \( \psi \) is independent of \( \alpha \) then
\[ \left[ \frac{dD(\alpha)}{d\alpha} \right]_{\alpha=\alpha^*} = \frac{1}{\delta^3R_0}\left[ \frac{d\phi(\alpha)}{d\alpha} \right]_{\alpha=\alpha^*}. \]
Now
\[ \left[ \frac{d\phi(\alpha)}{d\alpha} \right]_{\alpha=\alpha^*} = \delta^2(\delta^2 + kb\mu)R_0L^* + \frac{(kb\mu)^3}{L^*}(R_0 - 1) \neq 0. \]
The two criteria \((CH.1)\) and \((CH.2)\) from Beretta and Kuang [40] are satisfied. Therefore, there is a Hopf bifurcation at \( \alpha = \alpha^* \).

### 4.3.3 Global Stability Result for \( E_0 \)

For a sufficiently virulent infection and small growth rate of the infected class, we observe that there is a singularity at \( E_0 \). To derive the global stability criterion of \( E_0 \) we use a ratio dependent transformation \((S, I, V) \rightarrow (x, y, z)\), where \( x = S, y = \frac{I}{S}, z = \frac{V}{S} \). Under this transformation the system (4.1)
reduced to
\[
\begin{align*}
\frac{dx}{dt} &= \alpha x \left(1 - \frac{x + xy}{C}\right) - \frac{kxz}{1 + y} - (\lambda + e)x, \\
\frac{dy}{dt} &= -\alpha y \left(1 - \frac{x + xy}{C}\right) + kz + (\lambda + e - \mu - d)y, \\
\frac{dz}{dt} &= -\alpha z \left(1 - \frac{x + xy}{C}\right) + b\mu y + (\lambda + e - \delta)z + \frac{kz^2}{1 + y}.
\end{align*}
\]

The steady states of the reduced system (4.4) are
\[
E_0(0, 0, 0), \quad E_f(x_1, 0, 0), \quad E_i(0, \bar{y}, \bar{z}) \quad \text{and} \quad E_+(x^*, y^*, z^*)
\]
where \(x_1 = \frac{C}{R_d}(R_d - 1) > 0\) provided \(R_d > 1\)
\[
\bar{y} = \frac{(\theta + \delta)(\theta + \mu + d) - bk\mu}{(\theta + \mu + d)(\mu + d - \delta) + bk\mu}, \quad \bar{z} = \frac{\theta + \mu + d}{k}\bar{y},
\]
where \(\theta = (\lambda + e)(R_d - 1)\)
\[
x^* = \frac{CL}{\alpha R_0}, \quad y^* = (R_0 - 1), \quad z^* = \frac{b\mu}{\delta}(R_0 - 1) \quad \text{and} \quad L = \theta - (\mu + d)(R_0 - 1).
\]
\(\bar{E}_+\) exists provided \(\theta > (\mu + d)(R_0 - 1)\) and \(R_0 = \frac{bk\mu}{\delta(\mu + d)} > 1\).

Now \(\bar{E}_i\) is nonnegative if \(\delta < \mu + d\) and \(R_0 < \frac{(\theta + \delta)(\theta + \mu + d)}{\delta(\mu + d)}\).

The nontrivial steady states are preserved because \(\bar{E}_f = E_f\) and \(\bar{E}_+ = E_+\) but \(E_0\) has been blown up into two steady states: \(\bar{E}_0\) and \(\bar{E}_i\). To find a global stability result for \(E_0\), we first prove the following theorem:

**Theorem 4.3.6.** If \(R_d > 1\), the equilibria \(\bar{E}_0\) and \(\bar{E}_i\) are unstable.

**Proof.**

At the equilibrium \(\bar{E}_0 : (0, 0, 0)\), the variational matrix is
\[
V(\bar{E}_0) = \begin{pmatrix}
\theta & 0 & 0 \\
0 & -(\theta + \mu + d) & k \\
0 & b\mu & -(\delta + \theta)
\end{pmatrix}.
\]

Since \(R_d > 1\), \(\theta > 0\) and hence one eigenvalue of the variational matrix \(V(\bar{E}_0)\) is positive.
Thus \( E_0 \) is an unstable saddle.

Again at the equilibrium \( E_i : (0, \bar{y}, \bar{z}) \), the variational matrix is

\[
V(E_i) = \begin{pmatrix}
\theta - \frac{k\bar{z}}{1+\bar{y}} & 0 & 0 \\
\frac{\alpha}{c}\bar{y}(1 + \bar{y}) & -(\theta + \mu + d) & k \\
\frac{\alpha}{c}\bar{z}(1 + \bar{y}) & b\mu - \frac{k\bar{z}^2}{(1+\bar{y})^2} & -(\delta + \theta) + \frac{2k\bar{z}}{1+\bar{y}}
\end{pmatrix}.
\]

The eigenvalues of \( V(E_i) \) are

\[
\lambda_1 = \frac{\delta(\mu+d)(R_0-1)-\delta\bar{y}}{\theta+\mu+d} \quad \text{which is negative if } R_0 < \frac{\theta+\mu+d}{\mu+d}.
\]

and other two eigenvalues \( \lambda_2, \lambda_3 \) are the roots of \( x^2 + p_1 x + p_2 = 0 \), where \( p_1 = \delta + \mu + d + 2\lambda_1 \) which is positive if \( \lambda_1 < -\frac{1}{2}(\mu + d + \delta) \)

and \( p_2 = (\theta + \mu + d)(\theta + \delta - \frac{2k\bar{z}}{1+\bar{y}}) - bk\mu + \frac{k^2\bar{z}^2}{(1+\bar{y})^2} = -(\theta + \mu + d)^2 \frac{\bar{y}}{1+\bar{y}} < 0 \).

Since \( p_2 < 0 \) then by Routh-Hurwitz criterion for \( 2 \times 2 \) matrix, we conclude that \( E_i \) is an unstable saddle.

**Theorem 4.3.7.** If \( R_0 > \frac{(\theta+\delta)(\theta+\mu+d)}{\delta(\mu+d)} \) then \( \lim_{t \to +\infty} \sup(y(t), z(t)) = (+\infty, +\infty) \)

**Proof.**

Let \((x(t), y(t))\) be the solution of the system

\[
\frac{dy}{dt} = -\alpha y(1 - \frac{x + xy}{C}) + kz + (\lambda + e - \mu - d)y \geq (-\theta - \mu - d)y + kz,
\]

\[
\frac{dz}{dt} = -\alpha z(1 - \frac{x + xy}{C}) + b\mu y + (\lambda + e - \delta)z + \frac{kz^2}{1+y} \geq b\mu y + (-\theta - \delta)z.
\]

Let \((Y(t), Z(t))\) be the solution of the system

\[
\frac{dY}{dt} = (-\theta - \mu - d)y + kz,
\]

\[
\frac{dZ}{dt} = b\mu y + (-\theta - \delta)z. \tag{4.5}
\]

\((Y, Z) = (0, 0)\) is the only steady state of (4.5) and is unstable when \( R_0 > \frac{(\theta+\delta)(\theta+\mu+d)}{\delta(\mu+d)} \).

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Since there are no other steady states, $Y, Z$ are unbounded, and system (4.5) is a co-operative, monotone system and $\lim_{t \to +\infty} I(t) = +\infty$ and $\lim_{t \to +\infty} V(t) = +\infty$.

Let $y_0 = Y_0$ and $z_0 = Z_0$, then by the comparison theorem, $(y(t), z(t)) \geq (Y(t), Z(t)), t > 0$. Therefore, $\limsup_{t \to +\infty} y(t) \geq \liminf_{t \to +\infty} y(t) \geq \lim_{t \to +\infty} Y(t) = +\infty$ and

$$\limsup_{t \to +\infty} z(t) \geq \liminf_{t \to +\infty} z(t) \geq \lim_{t \to +\infty} Z(t) = +\infty.$$ 

Hence $\lim_{t \to +\infty} \inf_{y(t)} k \geq \lim_{t \to +\infty} \inf_{z(t)} k \geq (\theta + \delta)/(\mu + d)$ and $\lim_{t \to +\infty} \inf_{x(t)} k = 0$.

**Theorem 4.3.8.** $R_0 > (\theta + \delta)/(\mu + d)$ then $\lim_{t \to +\infty} \inf_{x(t)} k = 0$.

**Proof.**

To prove that $E_0$ is globally stable, we need it to be the only steady state in $R^3_+$. Therefore, set $\mu + d < \delta$ to ensure that $E_i$ no longer exists.

Since $\frac{dx}{dt} = \alpha x (1 - \frac{x + cy}{C}) - \frac{kxz}{1 + y} - (\lambda + \epsilon)x < (\theta - \frac{kz}{1 + y})x$,

it is sufficient to show $\lim_{t \to +\infty} \inf_{y(t)} k > 0$.

Let $\phi(t) = \frac{kz(t)}{1 + y(t)}$, then

$$\frac{d\phi}{dt} = \frac{k}{1 + y} \frac{dz}{dt} - \frac{kz}{(1 + y)^2} \frac{dy}{dt} \geq bk\mu \frac{y}{1 + y} - \{\theta - (\theta + \mu + d) \frac{y}{1 + y}\} \phi(t).$$

Since $\lim_{t \to +\infty} \frac{y(t)}{1 + y(t)} = 1$ then $\exists \epsilon > 0$ and $t > t'$ such that $\frac{y}{1 + y} > 1 - \epsilon$.

Therefore $\frac{d\phi}{dt} > bk\mu (1 - \epsilon) - \{\theta + \delta - (\theta + \mu + d)(1 - \epsilon)\} \phi(t)$.

Let $\gamma(\epsilon) = \theta + \delta - (\theta + \mu + d)(1 - \epsilon)$ then $\gamma(\epsilon) > 0$ if $\mu + d < \delta$.

Solving the equation $\frac{d\phi}{dt} + \gamma(\epsilon) \phi > bk\mu (1 - \epsilon)$ we have

$$\lim_{t \to +\infty} \inf_{\phi(t)} > bk\mu (1 - \epsilon) > \frac{\delta(\mu + d)R_0(1 - \epsilon)}{\delta + \theta} > \theta + (\theta + \mu + d)(1 - \epsilon) > \theta.$$

Hence $\lim_{t \to +\infty} \inf_{k} > \theta$ and hence $\lim_{t \to +\infty} \inf_{x(t)} k = 0$. 

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4.4 Mathematical Study of System with Delay

4.4.1 Boundedness of Solutions

The following result shows that solutions of the system (4.2) are bounded and lie in a compact set and exist for all $t > 0$

**Theorem 4.4.1.** The system (4.2) is dissipative.

**Proof.**

Let $V(t, S(t), I(.), V(.)) = S + I + \frac{1}{b}V$.

The derivative of $V$ along the trajectories of (4.2) is

$$\frac{dV}{dt} = \alpha S(1 - \frac{S + I}{C}) - (\lambda + \epsilon)S - dI - \frac{\delta}{b}V$$

$$\leq \alpha l - \{(\lambda + \epsilon)S + dI + \frac{\delta}{b}V\}$$

where $l = \max\{C, S(0)\}$.

If $S(\eta) \leq S(t)$ for $t - \tau \leq \eta \leq t$, by a classical Liapunov-Razumikhin theorem about boundedness [79] the system (4.2) is dissipative.

4.4.2 Equilibria and Stability Analysis

The system (4.2) has following equilibria

$E'_0(0, 0, 0), E'_f(\frac{\theta C}{\alpha}, 0, 0)$, provided $\theta > 0$ i.e. $R_d > 1$ and $E'_+(S', I', V')$, where

$S' = Ce^{\mu \tau} \left\{ \frac{(\theta + d) e^\mu - (\theta \delta + bkd)}{e^\mu - 1} \right\}$, $I' = \left( \frac{bk}{\delta} e^{-\mu \tau} - 1 \right) S'$ and $V' = \frac{bdI'}{\delta(e^\mu - 1)}$.

$E'_+$ exists provided $\tau_0 = \frac{1}{\mu} \log \left\{ \frac{\theta \delta + bkd}{\delta(\theta + d)} \right\} < \tau < 1 \log \left\{ \frac{bk}{\delta} \right\} = \tau^*$ (say).

Again the positive equilibrium $E'_+$ is feasible provided $\tau_0 < \tau < \tau^*$. When $\tau$ approaches to $\tau^*$, then $I' \to 0$ and $V' \to 0$, i.e. the positive equilibrium $E'_+$ approaches to the boundary equilibrium $E'_f$ and $E'_+$ collapses to $E'_f$ when $\tau = \tau^*$. Again if $\theta \to 0$ then $\tau_0 \to \tau^*$ and hence $E'_f \to E'_0$. Hence stability analysis at $E'_0$ of system (4.2) is same as the stability analysis at $E_0$ of system (4.1).

**Theorem 4.4.2.** The equilibrium $E'_f$ is locally asymptotically stable if $\tau > \tau^*$.
Proof.

At the equilibrium \( E'_f : \left( \frac{\theta C}{\alpha}, 0, 0 \right) \), the variational matrix is

\[
V(E'_f) = \begin{pmatrix}
-\theta & -\theta & -k \\
0 & -d & ke^{-\mu \tau} \\
0 & 0 & bke^{-\mu \tau} - \delta
\end{pmatrix}.
\]

Since \( \theta > 0 \) then \( R_d > 1 \). Therefore if \( \tau > \tau^* \) then all eigenvalues of \( V(E'_f) \) has negative real part. Hence the equilibrium \( E'_f \) is locally asymptotically stable.

**Theorem 4.4.3.** If \( \tau > \tau' = \frac{1}{\mu} \log \left( \frac{b-1}{\xi-1} \right) \), then \( E'_f \) is globally asymptotically stable.

**Proof.**

From the last two equations of system (4.2), for \( t > t' \), we have

\[
\frac{d}{dt}(I + V) \leq kV - dI + (b-1)ke^{-\mu \tau}V(t-\tau) - \delta V.
\]

Consider the functional \( W(t) = I(t) + V(t) + (b-1)ke^{-\mu \tau} \int_{t-\tau}^{t} V(\xi)d\xi \). Then we have \( W'(t) \leq -dI - k\{(\frac{\delta}{\xi} - 1) - (b-1)ke^{-\mu \tau}\}V \), provided \( (\frac{\delta}{\xi} - 1) > (b-1)ke^{-\mu \tau} \) which gives \( \tau > \tau' = \frac{1}{\mu} \log \left( \frac{b-1}{\xi-1} \right) \).

So \( W(t) \) is a Liapunov functional for global asymptotic stability of the equilibrium \((0, 0)\) of the last two equations of the system (4.2) i.e., \( \lim_{t \to \infty} I(t) = 0 \) and \( \lim_{t \to \infty} V(t) = 0 \).

From the first equation of system (4.2), we can get

\[
\alpha S(1 - \frac{S+I}{C}) - kV - (\lambda + \epsilon)S \leq \frac{dS}{dt} \leq \alpha S(1 - \frac{S}{C}) - (\lambda + \epsilon)S.
\]

This shows that there exists \( t'_1 > 0 \), such that \( \lim_{t \to +\infty} S(t) = \frac{\theta C}{\alpha} \) for all \( t > t'_1 \).

Let \( t'_0 = \max(t', t'_1) \).
Therefore \( \lim_{t \to +\infty} S(t) = \frac{\theta C}{\alpha} \), \( \lim_{t \to +\infty} I(t) = 0 \) and \( \lim_{t \to +\infty} V(t) = 0 \), for all \( t > t'_0 \).

This completes the proof.

**Local stability of system (4.2) at \( E'_+ \)**

Let \( u(t) = \text{col}(s(t), i(t), v(t)) = \text{col}(S(t) - S', I(t) - I', V(t) - V'), u \in R^3_+ \), for \( t > 0 \).

Then the system (4.2) can be written in the vector form as

\[
\frac{d}{dt} u(t) = F(u(t); u(t - \tau)).
\]  

(4.6)

where \( F : C([-\tau, 0], R^3_+) \to R^3 \) is a continuously differentiable function.

Let us define two real \( 3 \times 3 \) matrices \( A \) and \( B \) as

\[
A = \left[ \frac{\partial F}{\partial u(t)} \right]_{u=0}; \quad B = \left[ \frac{\partial F}{\partial u(t-\tau)} \right]_{u=0}.
\]

Therefore the system (4.2), linearized around 0, takes the form

\[
\frac{d}{dt} u(t) = Au(t) + Bu(t - \tau).
\]  

(4.7)

Now the characteristic equation of this linearized system (4.7) is

\[
det[A + Be^{-\Lambda t} - \Lambda I_3] = 0.
\]

or

\[
\begin{vmatrix}
(2\rho - \frac{\theta\delta}{bk})e^{\mu\tau} - \Lambda & (2\rho - \frac{\theta\delta}{bk})e^{\mu\tau} & -\frac{\delta}{b}e^{\mu\tau} \\
\sigma - \sigma e^{-\tau(\nu+\Lambda)} & -d - \rho e^{\mu\tau} + \rho e^{-\tau\Lambda} - \Lambda & \frac{\delta}{b}e^{\mu\tau} \\
b\sigma e^{-\mu\tau} & b\sigma & -\delta + \delta e^{-\tau\Lambda} - \Lambda
\end{vmatrix} = 0.
\]

(4.8)

Where \( \rho = \frac{\delta d}{bk} \left( \frac{bk - e^{\mu\tau}}{e^{\mu\tau} - 1} \right) \) and \( \sigma = \frac{\delta d (bk - e^{\mu\tau})^2}{bk - e^{\mu\tau} - 1} \).

The equivalent form of this characteristic equation is

\[
\Lambda^3 + p_1\Lambda^2 + p_2\Lambda + p_3 = q_1\Lambda e^{-\tau\Lambda} + q_2\Lambda e^{-\tau\Lambda} + q'_2\Lambda e^{-2\tau\Lambda} + q_3 e^{-\tau\Lambda} + q'_3 e^{-2\tau\Lambda}. 
\]  

(4.8)
\[ p_1 = (d + \delta - \rho + \frac{\theta \delta}{bk}) e^{-\mu \tau}, \quad q_1 = \rho + \delta, \]
\[ p_2 = (d + \delta + \sigma + \rho e^{\mu \tau}) \left( \frac{\theta \delta}{bk} - 2\rho \right) e^{\mu \tau} + \delta(d + \sigma + \rho e^{\mu \tau}), \]
\[ q_2 = \delta(d + \rho + \rho e^{\mu \tau}) + \left( \frac{\theta \delta}{bk} - 2\rho \right) (\delta + \sigma + \rho e^{\mu \tau}), \quad q'_2 = \rho \delta, \]
\[ p_3 = \delta(d + \rho e^{\mu \tau} - \sigma e^{\mu \tau}) + \left( \frac{\theta \delta}{bk} - 2\rho \right) b\sigma^2(d + \rho e^{\mu \tau} - \sigma e^{2\mu \tau}), \]
\[ q_3 = \delta(d + \rho + \rho e^{\mu \tau}) + \left( \frac{\theta \delta}{bk} - 2\rho \right) \delta \sigma (1 + \sigma) + \sigma(\rho e^{-\mu \tau} - \sigma \delta), \]
\[ q'_3 = \left( \frac{\theta \delta}{bk} - 2\rho \right) \rho \delta e^{\mu \tau}. \]

The stability of \( E'_+ \) can be determined according to the sign of the real parts of the roots \( \Lambda \) of equation (4.8). Let \( \Lambda = \beta + i\nu \), where \( \Lambda, \beta, \nu \) are functions of delay parameter \( \tau \). Substituting in equation (4.8) and equating real and imaginary parts we have the following equations

\[ \beta^3 - 3\beta \nu^2 + p_1(\beta^2 - \nu^2) + p_2 \beta + p_3 = e^{-\tau \beta} \left[ q_1 \{ (\beta^2 - \nu^2) \cos \tau \nu + 2\beta \nu \sin \tau \nu \} + q_2(\beta \cos \tau \nu + \nu \sin \tau \nu) + q_3 \cos \tau \nu \} + e^{-2\tau \beta} \left[ q'_2(\beta \cos 2\tau \nu + \nu \sin 2\tau \nu) + q'_3 \cos 2\tau \nu \right], \] (4.9)

\[ 3\beta^2 \nu + 2p_1 \beta \nu + p_2 \nu = e^{-\tau \beta} \left[ q_1 \{ 2\beta \nu \cos \tau \nu - (\beta^2 - \nu^2) \sin \tau \nu \} + q_2(\nu \cos \tau \nu - \beta \sin \tau \nu) - q_3 \sin \tau \nu \} + e^{-2\tau \beta} \left[ q'_2(\nu \cos 2\tau \nu - \beta \sin 2\tau \nu) - q'_3 \sin 2\tau \nu \right]. \]

A necessary condition for stability change of \( E'_+ \) is that the characteristic equation (4.8) has purely imaginary root \( \Lambda = i\nu \). Let \( \hat{\tau} \) be such that \( \beta(\hat{\tau}) = 0, \)
then we have the reduced equation

\[ p_3 - \nu^2 p_1 = (q_3 - q_1) \cos \tau \nu + q_2 \nu \sin \tau \nu + q'_2 \nu \sin 2\tau \nu + q'_3 \cos 2\tau \nu, \]

\[ p_2 \nu = (q_1 \nu^2 - q_3) \sin \tau \nu + q_2 \nu \cos \tau \nu + q'_2 \nu \cos 2\tau \nu - q'_3 \sin 2\tau \nu. \]

Analytically it is complicated to solve the equation (4.10) for \( \nu \) and \( \tau \). So we check the Hopf bifurcation conditions numerically for the parameter \( \tau \) at \( \tau = \hat{\tau} \) by satisfying

(i) \( \beta(\hat{\tau}) = 0 \) and (ii) \[ \left[ \frac{d\beta(\tau)}{d\tau} \right]_{\tau=\hat{\tau}} \neq 0 \] in the next section.

4.5 Numerical Simulation

We try to analyze the behaviour of \( E_+ \) and \( E'_+ \) of the systems (4.1) and (4.2) respectively using numerical simulation. For this we select our parameters values satisfying the existence criteria of the interior equilibrium. The hypothetical parameters values are given in the Table 4.1, where \( d = 1 \) day.

<table>
<thead>
<tr>
<th>Parameter Name</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha ) (intrinsic growth rate)</td>
<td>1.34</td>
<td>( d^{-1} )</td>
</tr>
<tr>
<td>( C ) (carrying capacity)</td>
<td>10</td>
<td>( \text{ml}^{-1} )</td>
</tr>
<tr>
<td>( k ) (infection rate)</td>
<td>0.14</td>
<td>( \text{ml}d^{-1} )</td>
</tr>
<tr>
<td>( \lambda ) (death rate susceptibles)</td>
<td>0.05</td>
<td>( d^{-1} )</td>
</tr>
<tr>
<td>( e ) (emigration rate)</td>
<td>0.02</td>
<td>( d^{-1} )</td>
</tr>
<tr>
<td>( \mu ) (lysis rate)</td>
<td>0.02</td>
<td>( d^{-1} )</td>
</tr>
<tr>
<td>( d ) (death rate of infectives)</td>
<td>0.003</td>
<td>( d^{-1} )</td>
</tr>
<tr>
<td>( b ) (burst coefficient)</td>
<td>3.0</td>
<td>\text{virus/lysis}</td>
</tr>
<tr>
<td>( \delta ) (death rate of virus)</td>
<td>0.11</td>
<td>( d^{-1} )</td>
</tr>
</tbody>
</table>

Table 4.1: Definitions, values and units of the parameters.

With this set of parameters values as given in Table 4.1 we have \( R_0 = 3.3202 \) and \( R_d = 19.1429 \). Taking initial value of population \((S_0, I_0, V_0) = \)
(2.5, 3.2, 5), we have Figure 4.1 which illustrates that the system (4.1) without delay and system (4.2) with delay (time $\tau = 0.95$) are stable. If we decrease the value of delay time from 0.95 to 0.70 then we have Figure 4.2 which illustrates that system (4.1) is stable but system (4.2) with delay is unstable.

Again for $k = 0.115, \tau = 0.95, b = 4.75$ and all other parameters values as in Table 4.1 we have Figure 4.3 which illustrates that system (4.1) without delay is stable but system (4.2) with delay is unstable. Taking $\tau = 0.95$ but increasing the infection rate $k$ from 0.14 to 0.99, we observe that the system (4.1) bifurcates from positive equilibria. So infection rate may also act as stability switch. If we study the system (4.2) by changing the parameter $k$ (as before) then we have Figure 4.4 which illustrates that system (4.1) is unstable and system (4.2) is ultimately going to extinct for $k = 0.99, \tau = 0.95$. For this reason we draw the bifurcation diagram (Figure 4.5) for system (4.1) varying $k$ from 0.5 to 1.3 and observe that a simple Hopf-bifurcation occur.
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Figure 4.2: For delay time $\tau = 0.7$ the system (4.1) without delay is stable and system (4.2) with delay is unstable.

Figure 4.3: For $k = 0.115, \tau = 0.95, b = 4.75$ and all other parameters values as in Table 4.1 the system (4.1) without delay is stable but system (4.2) with delay is unstable.
Figure 4.4: This figure illustrates that system (4.1) is unstable and system (4.2) is ultimately going to extinct for $k = 0.99, \tau = 0.95$.

at $k = k^* = 0.785$ (approx.).

Again for $k = 0.3, \tau = 2.9$ we have Figure 4.6 which illustrates that system (4.1) is stable and system (4.2) is asymptotically stable near positive equilibria. But if we decrease the value of $\tau$ from 2.9 to 1.7 the we have Figure 4.7 which illustrates that system (4.1) is stable but system (4.2) is unstable near positive equilibria.

Also taking $k = 0.3, \tau = 0.7$ and all other parameters values as in Table 4.1 we have Figure 4.8 which illustrates bifurcation of system (4.2) for $\alpha \in (0.6, 2)$. So the effect of growth rate $\alpha$ can not be ignored.

Lastly taking $k = 0.115, \tau = 0.7$ and varying $b$ we have bifurcation diagram in Figure 4.9 which illustrates bifurcation of system (4.2) for $b \in (0.3, 4.5)$. In this figure the virus population dynamics is shown for large range of $b$. 
Figure 4.5: Bifurcation diagram for the system (4.1) varying $k$ from 0.5 to 1.3.

Figure 4.6: For $k = 0.3, \tau = 2.9$ the system (4.1) is stable and system (4.2) is asymptotically stable.
Figure 4.7: For $k = 0.3, \tau = 1.7$ the system (4.1) is stable but system (4.2) is unstable.

Figure 4.8: Bifurcation diagram of system (4.2) for $k = 0.3, \tau = 0.7$ and $\alpha \in (0.6, 2)$. 
4.6 Conclusion

In this chapter we have proved that the disease free steady state \( E_f \) is globally stable for \( R_o < 1 \) and \( E'_f \) is also globally stable for \( \tau > \tau' \). After that we have proved that if \( R_0 > 1 \) the endemic steady state \( E_+ \) is feasible and stable for \( \phi > \psi \). The stability of \( E_0 \) is studied by using a transformation of state variables in ratio dependent form. For such transformation corresponding to the equilibrium \( E_0 \) we have two steady states of the transform system but under the condition \( R_d > 1 \) they are unstable. We also derive the condition \( R_0 > \frac{(\theta+\delta)(\theta+\mu+d)}{\delta(\mu+d)} \) under which \( E'_0 \) is globally stable but \( E'_i \) is unstable. The numerical study shows that delay does not preserve the stability but we can find out the condition under which the stability turns over. So we conclude that under restricted time delay (\( \tau \in (0, 1) \)) the system changes its stability for change of the parameters \( k \) and \( \alpha \) and \( \tau \). So inclusion of delay in our model gives positive result.