# Stability Analysis of an HBV Model with Delay in infection and in Viral Production

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## Abstract

The study focuses on a Hepatitis B infection model that includes saturation response, contamination delay, and cure of the infected cells. We examine the impact of time delay on the two equilibrium points' stability, the Hopf bifurcation condition, and permanence. The analytical results are confirmed by means of numerical simulations.

**Keywords:** HB Vinfection, time delay, stability, saturation response, Hopf bifurcation.

## 1. Introduction:

The hepatitis B virus (HBV) is one of the most hazardous viruses in the world as it may lead to liver cancer and cirrhosis. Persistent HBV infection can be exacerbated by a weak immune response or a cellular resistance. The primary way that HBV is transmitted is through contact with bodily fluids that contain blood or infectious blood. Eighty-seven to ninety percent of those infected with HBV either become immune to the virus or become persistent carriers.

Now a ketal. Propose dibasic mathematical model to analyses the HBV dynamics. Wangetal. Studied the intra cellular phase of the life cycle of virus taking the assumption that production of HBV lags behind the infection of a hepa tocyte by a delay $\tau$ . Are version rate constant was given by Lewinetal. and acytokine-induced "curing" of infected cells was discussed by Guidotti et al. for an HBV infection. Models with delays are also introduced by Abdelhadi Abta et al. and Sudipa Chauhan et al. to study the time between the entry of a viral particle into a target cell and the production of new virus particles.

In most HBV models, the rate of infection for both the virus V and the uninfected target cells $S_h$ is bilinear. However, the actual incidence rates may not be precisely linear in each variable across the whole range of V and Sh. For example, a smaller amount of linear response in V may occur when there is saturation at high virus concentration due to a high infectious fraction. As a result, it is safe to assume that the HBV infection model's infection rate in saturated mass action is $\dfrac{\beta S_h v^p}{1+\alpha v^q}$ where p and q are constants.

In this paper we encompass a time-lag in HBV model and a saturation response of the infection rate (p=q=1) .The model is given by

$$\left\{\begin{aligned} \frac{dS_h}{dt} &= A - \mu S_h(t) - \frac{\beta S_h(t)V(t-\tau)}{1+\alpha v(t-\tau)} + \delta I(t) \\ \frac{dI}{dt} &= \frac{\beta S_h(t)V(t-\tau)}{1+\alpha V(t-\tau)} - (c+\delta)I(t-\tau) \\ \frac{dV}{dt} &= pI(t-\tau) - \gamma V(t) \end{aligned}\right\} \quad (1)$$

Where $S_h(t) =$ concentration of the uninfected hepatocytes

$I(t) =$ Concentration of actively infected hepatocytes

$V(t) =$ Concentration of free pathogens

A= constant rate for production of uncontaminated hepatocytes

$\mu =$ Death rate of uninfected hepatocytes

$\beta =$ Infection rate constant

$\alpha =$ Half saturation constant of contamination

P=productivity rate of contaminated cells

$\gamma =$ rate of clearance of pathogen particle

$p/c =$ Pathogen particle produced by each actively infected hepatocyte during its life time.

## 2. BASIC PROPERTIES

**Let** $C = C\left(\left[-\tau, 0\right], R^3\right)$ be the Banach space of continuous functions, mapping the interval $\left[-\tau, 0\right]$ into $R^3$ amidst topology of uniform convergence, that is for $\varphi \in C^+$ the norm of $\varphi$ is defined as $\|\varphi\| = \sup_{-r \le \theta \le 0}\left\{\left|\varphi_1(\theta)\right|, \left|\varphi_2(\theta)\right|, \left|\varphi_3(\theta)\right|\right\}$. The positive cone of C is defined by $C^+ = C\left(\left[-\tau, 0\right], R_+^3\right)$.

The initial conditions of system (1) are

$$S_h(\theta) = \varphi_1(\theta), I(\theta) = \varphi_2(\theta), V(\theta) = \varphi_3(\theta) \quad (2)$$

where $R_+^3 = \{(x_1, x_2, x_3), x_i \geq 0, i = 1,2,3\} \varphi_1 \geq 0, \varphi_2 \geq 0, \varphi_3 \geq 0, \theta \in [-\tau, 0], \varphi_1 > 0, \varphi_1 > 0, \varphi_1 > 0$

## 2.1 Positivity and boundedness of solutions

Under the above initial conditions every solutions of system (1)are non-negative and ∃ an M >0 ∋ every solution satisfies $S_h(t) < M, I(t) < M, V(t) < M$ following sufficiently large t time.

Define G= $\left\{\varphi = (\varphi_1, \varphi_2, \varphi_3) \in C^+ / Sh \geq \varphi_1 \geq 0, \varphi_2 \geq 0, \varphi_3 \geq 0\right\}$.

Let us verify that $S_h(t)$ is non-negative, and let us consider the contrary that is, let $t_1 > 0$ is the first time such that $S_h(t_1) = 0$. We have $S_h^{'}(t_1) = A > 0$ from the first equation of (1).Which says $S_h(t) < 0$ for t $\in (t_1 - \varepsilon, t_1)$ where $\varepsilon$ is an arbitrary small non-negative constant that leads to contradiction it follows that $S_h(t)$ is always positive.

Determining $I(t_1) > 0$ and $V(t_1) > 0 \ \forall t_1 > 0$, we have

$$I(t_1) = \exp\left[-(c+\delta)(t_1 - \tau)\right]\left[I(0) + \int_0^{t_1} \frac{\beta S_h(t)V(\theta-\tau)}{1+\alpha v(\theta-\tau)} \exp\left[-(c+\delta)(\theta-\tau)\right] d\theta\right] > 0 \tag{3}$$

$$V(t_1) = \exp\left[-\gamma t_1\right]\left[V(0) + \int_0^{t_1} pI(\theta-\tau)\exp\left[\gamma\theta\right] d\theta\right] > 0 \tag{4}$$

Let $t_1 \in [0, T]$.We have $\theta - T \in [0, T] \forall \theta \in [0, T]$.As we've $S_h(\theta) = \varphi_1(\theta), I(\theta) = \varphi_2(\theta), V(\theta) = \varphi_3(\theta)$ and through (4) we conclude that $V(t) \geq 0, t_1 \in [0, T]$.

In accordance with $S_h(\theta), I(\theta) and V(\theta)$ and from equation (3) we conclude that $S_h(\theta), I(\theta) and V(\theta)$ are all positive on the interval $[0, T]$.

Now let us prove that system is bounded that is an M>0 ∋ for any non-negative solution of $[S_h(\theta), I(\theta) and V(\theta)]$ of system (1),I(t)<M,V(t)<M ∀ large t.

Set $U(t) = S_h(t) + I(t)$

therefore U(t)=A-$\mu S_h(t) - cI(t)$

$\leq$ A-h$\left(S_h(t)+I\left(t\right)\right)$ where h=min$\left\{\mu,c\right\}$.

By standard comparison theorem we dissolve that $\limsup_{t\to\infty}\left(S_h(t)+I\left(t\right)\right)\leq\frac{A}{h}$

Therefore we get the boundedness of U (t), i.e $\exists\ t_2>0$ and $M_1>0\ \ni$ U$\left(t\right)<M_1$ *for* t>$t_2$.

Then I (t) has an eventually upper bound, let the maximum is an M i.e

$$\frac{dV}{dt}=pI-\gamma V\leq\frac{Ap}{h}-\gamma V$$

$$\therefore\ \limsup_{t\to\infty}V(t)\leq\frac{Ap}{h\gamma}$$

Let us define $W(t)=S_h(t)+I(t)+(c/np)V(t)$ for n>>1.

Taking the time derivative along the system (1)

$$\frac{dW}{dt}=A-\mu S_h(t)-\frac{c(n-1)}{n}I(t)-\gamma V(t)$$

$$\frac{dW}{dt}=A-\eta W(t)\ \text{where}\ \eta=\min\left\{\frac{c(n-1)}{n},\mu,\gamma\right\}$$

By positivity of the solutions it follows that $\frac{dW}{dt}+\eta W(t)<A.$

Using a theorem in differential inequalities we acquire

$$W(t)\leq\frac{A}{\eta}+\left[W\left(S_h(0),I(0),V(0)\right)-\frac{A}{\eta}\right]e^{-\eta t}$$

Therefore $\limsup_{t\to\infty}W(t)<\frac{A}{\eta}$. Thus , $S_h$(t).I(t),V(t) are all bounded for t>0,that conclude the proof.

### 3. LOCAL STABILITY OF THE STEADY STATE

Let us -examine the local stability, of the non-contaminated equilibrium state $E_1$and the contaminated state $E_2$using the characteristic equation for the equation (1)

Let $E^*\left(S_h^*, I^*, V^*\right)$ be an arbitrary- equilibrium

The characteristic, equation is -given by

$$\begin{vmatrix} -\mu - \frac{\beta v^*}{1+\alpha v^*} - \lambda & \delta & -\frac{\beta s_h^*}{\left(1+\alpha v^*\right)^2} e^{-\lambda\tau} \\ \frac{\beta v^*}{1+\alpha v^*} & -\left(c+\delta\right)e^{-\lambda\tau} - \lambda & \frac{\beta s_h^*}{\left(1+\alpha v^*\right)^2} e^{-\lambda\tau} \\ 0 & pe^{-\lambda\tau} & -\gamma - \lambda \end{vmatrix} = 0 \quad (5)$$

There are two types of plausible positive equilibria named as Infection free equilibrium $E_1$ and endemic equilibrium $E_2$

Equating $\frac{ds}{dt} = 0$ and taking I=V=0(1) we get

$$\frac{ds}{dt} = A - \mu S\left(t\right) = 0$$

S=A/$\mu$

Therefore $E_1 = \left(S, 0, 0\right)$

Equating $\frac{dv}{dt} = 0$ in equation (1)

$$\frac{dv}{dt} = p\, I(t) - \gamma\, v(t) = 0$$

$$pI(t) = \gamma\, v(t)$$

$$I(t) = \frac{\gamma v(t)}{p}$$

Equating $\frac{dI}{dt}=0$

$$\frac{dI}{dt}=\frac{\beta s(t)\,v(t)}{1+\alpha\,v(t)}-\frac{(c+\delta)\gamma\,v(t)}{p}=0$$

$$p\beta s(t)\,v(t)-(c+\delta)\gamma v(t)(1+\alpha v(t))=0$$

$$v(t)\left[p\beta s(t)-(c+\delta)\gamma-\alpha\,v(t)\,(c+\delta)\gamma\right]=0$$

$$\alpha v(t)(c+\delta)\gamma=p\beta s(t)-(c+\delta)\gamma$$

$$v(t)=\frac{p\beta s(t)-(c+\delta)\gamma}{\alpha\,(c+\delta)\gamma}$$

And $s(t)=\dfrac{(c+\delta)(Ap+c\gamma)}{p\mu\alpha(c+\delta)+p\beta\,c}$

The basic- reproduction ratio, for the -system (1) is given by: $R_0=\frac{p\beta S}{(c+\delta)\gamma}$ , it describes the expected number ,of new, free contaminated pathogens obtained from –a- single contamination pathogen particle at the starting of contamination process.

**Theorem 3.1**(1) If $R_0$<1.0 then,, the non-contaminated equilibrium state $E_1$ is locally – asymptotically- stable for any, time-lag $\tau \geq 0$0..

Biologically the non-contaminated equilibrium state $E_1$ implies the, cellular contamination; by the- hepatitis- B pathogen would vanish.

(2) When $R_0>1$, then $E_1$ is unstable for any time lag $\tau \geq 0$.

Proof: For $E_1$ equation (5) reduces to

$$\left(-\mu-\lambda\right)\left|\lambda^2+\lambda\gamma+\gamma\left(c+\delta\right)e^{-\lambda\tau}+\lambda\left(c+\delta\right)e^{-\lambda\tau}-p\beta S_h{}^{*}e^{-2\lambda\tau}\right|=0 \quad (6)$$

It is evident that equation (6) has the latent root $\lambda=-\mu<0$.

Let us consider the polynomial

$$\left|\lambda^2+\lambda\gamma+\gamma(c+\delta)e^{-\lambda\tau}+\lambda(c+\delta)e^{-\lambda\tau}-p\beta s^* e^{-2\lambda\tau}\right|=0 \quad (7)$$

If $\tau=0$ then the above equation can be given as $\left|\lambda^2+\lambda\gamma+\gamma(c+\delta)+\lambda(c+\delta)-p\beta s_h^*\right|=0$

$$\left|\lambda^2+\lambda\gamma+\lambda c+\lambda\delta+\gamma(c+\delta)-p\beta s_h^*\right|=0$$

$$\left|\lambda^2+\lambda(c+\delta+\gamma)+\gamma(c+\delta)-p\beta s_h^*\right|=0$$

$$\left|\lambda^2+\lambda f_1+f_2+f_3\right|=0$$

let $f_1=(c+\delta+\gamma);\ f_2=\gamma(c+\delta);\ f_3=-p\beta s_h^*$

We can establish $f_1>0,\ f_2+f_3=\gamma(c+\delta)-p\beta s_h^*$

$$\gamma(c+\delta)\left[1-\frac{p\beta s_h^*}{\gamma(c+\delta)}\right]$$

$$\gamma(c+\delta)\left[1-R_0\right].$$

If $R_0<1$, then non-contaminated equilibrium state $E_1$ of the system (1) is locally asymptotically stable when $\tau=0$.

If $\left|\lambda^2+\lambda\gamma+\gamma(c+\delta)e^{-\lambda\tau}+\lambda(c+\delta)e^{-\lambda\tau}-p\beta s_h^* e^{-2\lambda\tau}\right|=0$

$$\left|\lambda^2+\lambda\gamma+\gamma(c+\delta)e^{-\lambda\tau}+\lambda(c+\delta)e^{-\lambda\tau}-p\beta s_h^* e^{-2\lambda\tau}\right|=0$$

$$\left|\lambda^{2}+\lambda\gamma+e^{-\lambda\tau}\left(q_{1}\lambda+q_{2}\right)\right|=0 \quad (8)$$

$$q_{1}=\left(c+\delta\right);\ q_{2}=\gamma\left(c+\delta\right)-p\beta s_{h}{}^{*}e^{-\lambda\tau}$$

If the equation (8) has pure imaginary root $\lambda=i\omega$ for $\omega>0,\tau>0.$ Then from the equation we have $\lambda^{2}+\lambda\gamma+e^{-\lambda\tau}\left(q_{1}\lambda+q_{2}\right)=0$

$$\omega^{4}+\omega^{2}(q_{1}{}^{2}+\gamma^{2})+q_{2}{}^{2}=0 \quad (9)$$

We perceive that

$$q_{1}{}^{2}+\gamma^{2}=\left(c+\delta\right)^{2}+\gamma^{2}>0,$$

$$q_{2}^{2}=\gamma^{2}\left(c+\delta\right)^{2}\left(1-\frac{p^{2}\beta^{2}s_{h}^{*2}}{\gamma^{2}\left(c+\delta\right)^{2}}\right)$$

$$q_{2}^{2}=\gamma^{2}\left(c+\delta\right)^{2}\left(1+R_{0}\right)\left(1-R_{0}\right)$$

Therefore if $R_0<1$ then $q_2^2>0$ hence equation (9) has no non-negative roots. So the equilibrium E1 is locally asymptotically stable for any lag $\tau\geq 0$.

Let us indicate h by $h\left(\lambda\right)=\lambda^{2}+\lambda\gamma+e^{-\lambda\tau}\left(q_{1}\lambda+q_{2}\right)=0$

If $R_0>1$ we have h (0) $=q_2=\gamma\left(c+\delta\right)\left(1-R_{0}\right)<0$ and $\lim_{t\to\infty}h\left(\lambda\right)=+\infty$ .

The continuity of the function $h(\lambda)$ on $\left(-\infty,\infty\right)$ that the equation $h(\lambda)=0$ =0 has minimum one non-negative root so $E_1$ is unstable.

For $R_0>1$the steady state $E_1$ behaves as unstable and the non-negative steady state $E_2$ ensue to be unique equilibrium in the interior of the feasible region.

**Theorem 3.2:** If $\tau=0$ and $R_{0}>1$ then the endemic equilibrium state $E_2$ is locally asymptotically stable.

Proof: $$\begin{vmatrix} -\mu-\frac{\beta v^{*}}{1+\alpha v^{*}}-\lambda & \delta & -\frac{\beta s_h^{*}}{(1+\alpha v^{*})2}e^{-\lambda\tau} \\ \frac{\beta v^{*}}{1+\alpha v^{*}} & -(c+\delta)e^{-\lambda\tau}-\lambda & \frac{\beta s_h^{*}}{(1+\alpha v^{*})2}e^{-\lambda\tau} \\ 0 & pe^{-\lambda\tau} & -\gamma-\lambda \end{vmatrix}=0$$

The related transcendental equation at $E_2$ is

$$P(\lambda,\tau)+Q(\lambda,\tau)e^{-\lambda\tau}=0 \quad (10)$$

$$P(\lambda,\tau)=\lambda^3+b_1(\tau)\lambda^2+b_2(\tau)\lambda+b_3(\tau)$$

$$Q(\lambda,\tau)=b_4(\tau)\lambda^2+b_5(\tau)\lambda+b_6(\tau);$$

Where

$$b_1(\tau)=\left[\gamma-\left(-\mu-\frac{\beta v^{*}}{1+\alpha v*}\right)\right]$$

$$b_2(\tau)=\left[\gamma\left(-\mu-\frac{\beta v^{*}}{1+\alpha v*}\right)+\frac{\beta v^{*}\delta}{1+\alpha v^{*}}\right]$$

$$b_3(\tau)=\frac{\beta\delta\gamma v^{*}}{1+\alpha v*}+\gamma(c+\delta)\left(-\mu-\frac{\beta v^{*}}{1+\alpha v*}\right)-\left(-\mu-\frac{\beta v^{*}}{1+\alpha v*}\right)\left(\frac{p\beta s_h^{*}}{1+\alpha v^{*}}e^{-\lambda\tau}\right)-\frac{p\beta^2 s_h^{*}v^{*}}{\left(1+\alpha v^{*}\right)^3}e^{-\lambda\tau}$$

$$,b_4(\tau)=(c+\delta),$$

$$b_5(\tau)=\left(\gamma(c+\delta)\left(-\mu-\frac{\beta v^{*}}{1+\alpha v*}\right)\right)$$

$$b_6(\tau)=\gamma\left(c+\delta\right)\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\text{-}\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\left(\frac{p\beta s_h^*}{1+\alpha v^*}e^{-\lambda\tau}\right)-\frac{p\beta^2 s_h^* v^*}{\left(1+\alpha v^*\right)^3}e^{-\lambda\tau}$$

when $\tau=0$ the equation (10) will have

$$\lambda^3+\lambda^2\left(b_1+b_4\right)+\lambda\left(b_2+b_5\right)+\left(b_3+b_6\right) \tag{11}$$

$$b_1+b_4=\left[\gamma-\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\right]+\left(c+\delta\right)$$

$$b_2+b_5=\left[\gamma\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)+\frac{\beta v^*\delta}{1+\alpha v^*}\right]+\left(\gamma\left(c+\delta\right)\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\right)$$

$$b_3+b_6=\frac{\beta\delta\gamma v^*}{1+\alpha v^*}+$$

$$\gamma\left(c+\delta\right)\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\text{-}\left(-\mu-\frac{\beta v^*}{1+\alpha v^*}\right)\left(\frac{p\beta s_h^*}{1+\alpha v^*}e^{-\lambda\tau}\right)-\frac{p\beta^2 s_h^* v^*}{\left(1+\alpha v^*\right)^3}e^{-\lambda\tau}$$

We can show that $b_1+b_4>0; b_2+b_5>0; b_3+b_6>0$ and
$\left(b_1+b_4\right)\left(b_2+b_5\right)-(b_3+b_6)>0$

Therefore using Routh- Hurwitz criteria we shown that when $\tau=0$ $E_2$ is locally asymptotically stable.

## 4. Permanence

The system, (1) is said to, be- uniformly incessant if there, is a $\xi>0$, autonomous of elementary data ∍_ every solution of S (t.), I (t.), V (t.), with the initial-conditions of the (1) system satisfying $\lim\inf_{t\to+\infty} s(t)\geq\xi, \lim\inf_{t\to+\infty} I(t)\geq\xi, \lim\inf_{t\to+\infty} V(t)\geq\xi$.

**Theorem 4.1**. System (1) supposed to be, permanent if - $R_0$ >1.

So as to show the - permanence of the, system we introduce the Permanence- theory for, infinite dimensional -system using the theorem 4.1 in Hale- et- al [4].

The semi- group 'Y(t)' is known to be point ,dissipative in X if there is-bounded non-empty set, B in X ∋ for any $x \in X$, there ,is $y_0 = y_0(x, B)$ such that $y_0 = y_0(x, B)$ for $t \geq t_0$.

Let X be a, complete metric-space .Assuming $X^O$ is-open and dense, in X, $X^0 \subset X$, $X^0 \subset X$, $X^0 \cap X_0 = \varnothing$. Presuming that- Y (t) is a $C^0$ – semi group, on X satisfying

$$\begin{Bmatrix} Y(t): X^0 \rightarrow X^0 \\ Y(t): X_0 \rightarrow X_0 \end{Bmatrix} - (12)$$

Let $\{y_b(t) = y(t)|X_0\}$ and $A_b$ be the- global attractor, of $y_b(t)$

! **Lemma 4.1** Suppose that (t) -satisfies (12) and the following, we have

(i) There is a $t_0 \geq 0$ å -Y(t) is compact for -$t > t_0$

(ii) oY (t) is point -dissipative in .X.

(iii) $\overline{A_b} = \cup_{x \grave{o} A_b} \omega(x)$ is isolated, and, has an acyclic-covering $\bar{M}$ ,where $\bar{M} = \{M_1, M_2, M_{3,} \ldots . M_n\}$.

$(iv) W^S(M_i) \cap X_0 = \varnothing$ for0i=.1,.2,.3,....n

'Then' $X_0$ is a uniform-repellor with , respect to $X^0$ i.e. there is, an $\varepsilon > 0$,such that\ for any $X \in X^0$ $\lim_{t \rightarrow +\infty} \inf d(Y(t)x, X_0 \geq \varepsilon \geq \varepsilon$ where d is a distance of $Y(t)x$ from $X_0$

**Proof:** Let us start by proving that the, boundary -planes of $R_+^3$ repulse the non-negative solution for the system (1) uniformly. Let us define

$C_0 = \{(\varphi_1, \varphi_2, \varphi_3) \in C([-\tau, 0], R_+^3): \varphi_1(\theta) \neq 0, \varphi_2(\theta) = \varphi_3(\theta) = 0, (0 \in [-\tau, 0])\}$. If $C^0 = \operatorname{int} C([-\tau, 0], R_+^3)$ , it's sufficient to prove ∃ an $\varepsilon_0 > 0$ ∋ for any solution $u_t$ of the system (1) instigating from- $C^0$ $\lim \inf_{t \rightarrow \infty} d(u_t, c^0) \geq \varepsilon_0$. Therefore we prove, that the below constraints of lemma 4.1 are satisfied. Effortlessly we see that $C^0$ and $C_0$ are non-negative constant. In addition (i) and (ii),conditions of lemma 4.1 satisfies evidently. Hence we, only need, verify (iii) and (IV) conditions. There- is a constant solution $E_1$ in $C_0$ that equate with S(.t)=$\hat{S}$,I(.t)=V(.t)=0, If (S(t.),V(t.),I(t.)) is solution for the system (1) instigating from $C_0$, then $S(t) \to \hat{S}, I(t) \to 0, V(t) \to 0$, as t→ ∞. It is clear that $E_1$ is an isolated constant .Now we prove that $W^s(E_1) \cap C^0 = \varnothing$.Presuming the contrary that ∃ a -positive solution $(\bar{S}(t), \bar{I}(t), \bar{V}(t))$ of the system (1) ∃$(\bar{s}(t), \bar{I}(t), \bar{V}(t)) \to (\hat{S}, \mathrm{I}(t), \mathrm{V}(t))$ as $t \to +\infty$ .Let us select $\psi > 0$ small enough such that $\hat{S}(t) - \psi > \bar{s}$ .

Let $t_0$>0 be adequately large such as $Sh - \psi < Sh(t) < Sh + \psi$ *for* t >$t_0 - \tau$.

Then, we have for $t > t_0$

$$\begin{cases} \dot{\tilde{I}}(t) \geq \beta(Sh - \psi)V(t-\tau) - (c+\delta)\tilde{I}(t-\tau) \\ \dot{V}(t) = p\tilde{I}(t-\tau) - \gamma V(t) \end{cases} \tag{13}$$

Let's contemplate the matrix defined by

$$B_\psi = \begin{pmatrix} -(c+\delta)e^{-\lambda\tau} & \beta(Sh - \psi) \\ pe^{-\lambda\tau} & -\gamma \end{pmatrix}$$

Since $B_\psi$ composes non-negative off-diagonal elements from the theorem of Perron –Frobenius,

We could say there in a non-negative latent vector V for the maximum latent value $\lambda_1$ of $B_\psi$ .

Let us consider

$$\begin{cases} \dot{I}(t) = \beta(Sh - \psi)V(t-\tau) - (c+\delta)\tilde{I}(t-\tau) \\ \dot{V}(t) = p\tilde{I}(t-\tau) - \gamma V(t) \end{cases} \tag{14}$$

Let $\upsilon = (\upsilon_1, \upsilon_2)$ and l>0 be small enough such that

$l\upsilon_1 < \tilde{I}(t_0 + \theta)$ ; $l\upsilon_2 < V(t_0 + \theta)$

For $\theta \in [-\tau, 0]$, if $(I(t), V(t))$ is a result of the system (14) satisfying

$I(t) = l\upsilon_1, V(t) = l\upsilon_2$ for $t_0 - \tau \le t \le t_0$.

As the semi-flow of the system (14) is monotone upon $A_\psi \upsilon > 0$,it is evident that

$I(t) \to +\infty, V(t) \to +\infty$ as $t \to +\infty$ and $B_\psi \upsilon > 0$. Let $t_0 > 0$ be adequate thus and so

$\tilde{I}(t) \ge I(t), V(t) \ge V(t).\tilde{I}(t) \to +\infty, V(t) \to +\infty,$ as $t \to +\infty$.

Therefore we come to conclusion that $C_0$ repels the non-negative solutions of the system (1) uniformly from lemma4.1 then the conclusion of theorem 4.1 follows and the system (1) is permanent.

## 5. HOPF Bifurcation from E2

Let us treat τ as a bifurcation variable and the criterion for Hopf bifurcation is specified from the, endemic- equilibrium $E_2$.

The characteristic-equation of, the linearization, of the system (1) nearly the –endemic-equilibrium $E_2$ is given, by

$$P(\lambda, \tau) + Q(\lambda, \tau)e^{-\lambda\tau} = 0 \tag{15}$$

Where $\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = p(\lambda,\tau)\,; b_4\lambda^2 + b_5\lambda + b_6 = Q(\lambda,\tau)$

$$i.e\ \lambda^3 + b_1(\tau)\lambda^2 + b_2(\tau)\lambda + b_3(\tau) + e^{-\lambda\tau}\left(b_4(\tau)\lambda^2 + b_5(\tau)\lambda + b_6(\tau)\right) \tag{16}$$

As $\tau = 0$ equation (16) takes the form

$\lambda^3 + \lambda^2(b_1 + b_4) + \lambda(b_2 + b_5) + (b_3 + b_6) = 0$ and all roots contain negative real parts which is same as proving 3.2

Weighing the continuity in $\tau$ and the Rouche's theorem yielded in 'Foundations of Modern Analysis' the transcendental equation (16) roots has positive real part iff ithas purely imaginary roots. Let us authenticate the existence of purely imaginary roots for theequation (16) therefore we acquire the constraints for all latent values to hold negative real parts.

Indicate $\lambda(\tau) = \sigma(\tau) + i\omega(\tau), \omega > 0$ be the latent root for (16) where $\sigma(\tau), \omega(\tau)$ subjected to time-lag $\tau$, when $\tau = 0$ the endemic equilibrium is stable using (3.2) theorem hence

$\sigma(0) < 0$. When, $\tau > 0$ is, adequately small, by the, continuity in' $\tau$ we still have o $\sigma(\tau) < 0$ and still we have $_oE_2$ is stable." If $\sigma(\tau_0) = 0$ evidently for $\tau_0 > 0$ value (such that $\lambda = i\omega(\tau_0)$), is a 'purely- imaginary- root' for the 'equation' (16), and when $\sigma(\tau)$ becomes positive the endemic equilibrium loses stability and in due course turn into unstable when $\sigma(\tau)$ become non-negative. So we can say that while such an $\omega(\tau_0)$ doesn't exist or to mean that (16) equation will not hold any purely imaginary root for all time –lag, the $E_2$ is stable always. Let us prove that is palpably for the characteristic equation (16)

Clearly $i\omega(\omega > 0)$ is root of an equation (16) if,

$$-i\omega^3 - b_1\omega^2 + ib_2\omega + b_3 - b_4\omega^2.\cos\omega + ib_5\omega.\cos\omega + b_6.\cos\omega + ib_4\omega^2.\sin\omega + b_5\omega.\sin\omega - ib_6\sin\omega \tag{17}$$

Squaring real and imaginary parts

$$(b_1\omega^2 - b_3)^2 = (-b_4\omega^2.\cos\omega + b_6.\cos\omega + b_5\omega.\sin\omega)^2 \tag{18}$$

$$(\omega^3 - b_2\omega)^2 = (b_5\omega.\cos\omega + b_4\omega^2.\sin\omega - b_6\sin\omega)^2 \tag{19}$$

Which is equivalent to

$$\omega^6 + \omega^4(b_1^2 - 2b_2 - b_4^2) + \omega^2(b_2^2 - 2b_1b_3 + 2b_4b_6 - b_5^2) + b_3^2 - b_6^2 \tag{20}$$

Let

$$G(\omega,\tau) = \omega^6 + B_1\omega^4 + B_2\omega^2 + B_3 = 0 \tag{21}$$

where $B_1 = b_1^2 - 2b_2 - b_4^2$; $B_2 = b_2^2 - 2b_1b_3 + 2b_4b_6 - b_5^2$; $B_3 = b_3^2 - b_6^2$

The polynomial G can be given as $G(\omega,\tau) = j(\omega^2,\tau)$, as the third degree polynomial is denoted by'j' and defined as

$$j(z,\tau) = z^3 + B_1z^2 + B_2z + B_3$$

For the, equation

$$j(z,\tau) = z^3 + B_1z^2 + B_2z + B_3 = 0 \tag{22}$$

Let us suppose that $B_3 \geq 0$ for $B_3 = b_3^2 - b_6^2 > 0$ and $B_2 > 0$ then (22) have negative real roots.

Perceiving that

$$\frac{dj(z)}{dz} = 3z^2 + 2B_1 z + B_2$$

say

$$3z^2 + 2B_1 z + B_2 = 0 \tag{23}$$

$$\text{then } z = \frac{-2B_1 \pm \sqrt{4B_1^2 - 12B_2}}{6}$$

$$z_{1,2} = \frac{-B_1 \pm \sqrt{B_1^2 - 3B_2}}{3}$$

If $B_2 > 0$ then $\sqrt{B_1^2 - 3B_2} < B_1$. thus both $z_1$ , $z_2$ are negatives. Therefore (23) have negative roots .As $j(0) = B_3 \geq 0$, shows that equation (22) has negative roots.

So ,if $B_3 \geq 0$ and $B_2 > 0$ then there is no $\omega$ so that $i\omega$ is a latent root of the (16) equation that is $\lambda$ will not be purely imaginary root of (16).Thus the, real parts--of all latent- roots of (16) ,are non- positive $\forall$ time-lag $\tau \geq 0$. Hence $E_2$ is asymptotically stable for each $\tau$ if the following constraints carry

(i) $b_1 > 0, b_3 + b_5 > 0, b_1 (b_2 + b_4) - (b_3 + b_5) > 0$

(ii) $B_3 \geq 0$ , $B_2 > 0$.

The' stability of steady- state rely on lag value that may cause oscillations, if either $B_3 or B_2$ is non-positive. Let us consider if $B_3 < 0$ then from ($22_0$) we, have j.(0)< 0 and $\lim_{z \to \infty} j(z) = \infty$ .And so equation (22) contains minimum one positive root be $z_0$ and hence (20) has at least one root given by $\omega_0$ which is appositive root.

And if $B_2 < 0$ then $\sqrt{(B_1^2 - 3B_2)} > B_1$ and $Z_1 = \frac{1}{3}\left(-B_1 + \sqrt{B_1^2 - 3B_2}\right) > 0$ hence equation- (22) and- equation (20) has a, non-negative root $\omega_0$. which implicit that there exist a sole pair of purely imaginary roots to equation (16).

Let $\lambda(\tau) = \sigma(\tau) + i\ \omega(\tau)$ be the, latent--root of, the, equation (16) so as to $\sigma(\tau_0) = 0, \omega(\tau_0) = \omega_0$

from the equations (18) and (19)

$$\tau_k = \cos^{-1}\left(\frac{\omega_0^4\left(2b_5 - 2b_1b_4\right) + \omega_0{}^2\left(2b_1b_6 - 2b_2b_5 + 2b_3b_4\right) - 2b_3b_6}{\left(b_4\omega_0^2 - b_6\right)^2 + b_5^2\omega_0^2}\right) + \frac{2k\pi}{\omega_0} \quad k=0,1,2 \tag{24}$$

for $\tau = 0$ $E_2$ is stable, and endure to be, stable for, $\tau < \tau_0$ if $\left.\frac{d\ \mathrm{Re}(\lambda)}{dt}\right|_{\tau=\tau_0} > 0$ that is the

transverse constraints carry. Which states that $\exists$ least way one latent value with non-negative real parts for $\tau > \tau_0$ i.e. –to-

prove $\wedge = sign\left\{\frac{d\ \ (\mathrm{Re}\,\lambda)}{d\tau}\right\}\Bigg|_{\tau=\tau_0} = sign\left\{\ \mathrm{Re}\left(\frac{d\lambda}{d\tau}\right)^{-1}\ \right\}\Bigg|_{\tau=\tau_0}$

Taking in to consideration

$$\lambda^3 + b_1(\tau)\lambda^2 + b_2(\tau)\lambda + b_3(\tau) + e^{-\lambda\tau}\left(b_4(\tau)\lambda^2 + b_5(\tau)\lambda + b_6(\tau)\right) \tag{25}$$

Differentiating (25) with respect to $\tau$ we get

$$\left[\frac{d\lambda}{dt}\right]^{-1} = \frac{3\lambda^2 + 2b_1\lambda + b_2 - \tau e^{-\lambda\tau}(b_4\lambda^2 + b_5\lambda + b_6) + e^{-\lambda\tau}\left(2b_4\lambda + b_5\right)}{g(\lambda,\tau) + \lambda e^{-\lambda\tau}\left(b_4\lambda^2 + b_5\lambda + b_6\right)}$$

$$\frac{3\lambda^2 + 2b_1\lambda + b_2 + \tau(\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3) + e^{-\lambda\tau}\left(2b_4\lambda + b_5\right)}{-\lambda(\lambda^3 + b_1\lambda^2 + b_2\lambda + b_3) + g(\lambda,\tau)}$$

where $g(\lambda,\tau)=-b_1'\lambda^2-b_2'\lambda-b_3'-e^{-\lambda\tau}\left(b_4'\lambda^2+b_5'\lambda+b_6'\right)$

Therefore

$$\wedge = sign\left\{\operatorname{Re}\left(\frac{3\lambda^2+2b_1\lambda+b_2+\tau(\lambda^3+b_1\lambda^2+b_2\lambda+b_3)+e^{-\lambda\tau}\left(2b_4\lambda+b_5\right)}{-\lambda(\lambda^3+b_1\lambda^2+b_2\lambda+b_3)+g(\lambda,\tau)}\right)\right\}\Bigg|_{\lambda=i\omega_0} = Sign\left\{\operatorname{Re}\left(\frac{p_1+iq_1}{p_2+iq_2}\right)\right\}$$

$$p_1=-3\omega_0^2+b_2-b_1\omega_0^2\tau_0+b_3\tau_0+b_5\cos\omega_0\tau_0+2b_4\omega_0\sin\omega_0\tau_0$$

$$q_1=2b_1\omega_0-\omega_0^3\tau_0+b_2\omega_0\tau_0+2b_4\omega_0\cos\omega_0\tau_0-b_5\sin\omega_0\tau_0$$

$$p_2=-\omega_0^4+b_2\omega_0+b_1'\omega_0^2-b_3'+b_4'\omega_0^2\cos\omega_0-b_6'\cos\omega_0-b_5'\omega_0\sin\omega_0$$

$$q_2=b_1\omega_0^3-b_3\omega_0-b_2'\omega_0-b_5'\omega_0\cos\omega_0-b_4'\omega_0^2\sin\omega_0+b_6'\sin\omega_0$$

$$sign\left\{\operatorname{Re}\left(\frac{p_1p_2+q_1q_2}{p_2^2+q_2^2}\right)\right\}$$

$as\ i=\ 1,\ 2,\ 3,\ 4,\ 5$ and $B_1>0, B_2>0, B_3>0,$

andit can be derived that $p_1\ p_2+q_1\ q_2>0$

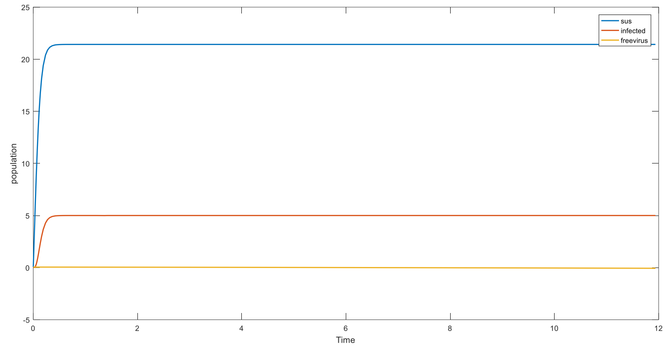
$$\text{therefore sign}\left\{\operatorname{Re}\left(\frac{d\lambda}{d\tau}\right)^{-1}\right\}\Bigg|_{\tau=\tau_0}>0$$

This shows, that the traverse constraint holds, and hopf" bifurcation "occurs is proved.

## Numerical Simulation

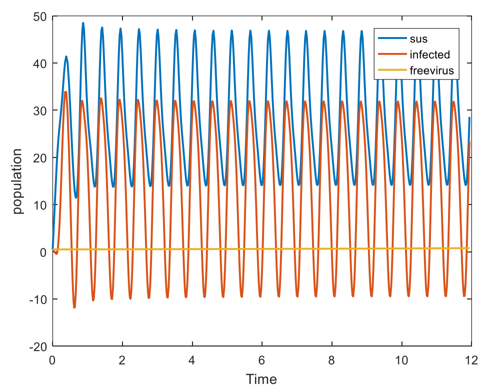
Let us learn about numerical simulations to demonstrate the analytic solutions for disease free equilibrium and endemic equilibrium points. For the system (1),we choose the parameter values;$A=160;\mu=.0003;\beta=.35;\alpha=.00009;\delta=.05;\gamma=.0002;p=.08;c=16;$shows that the infected equilibrium state is locally asymptotically stable $\forall\tau>0$ when $R_0>1$.

To illustrate analytical method when $R_0 < 1$ for population dynamics we choose the parameter values $A = 160; \mu = .0003; \beta = .35; \alpha = .00009 \delta = .05; \gamma = .002; p = .08; c = 12;$ demonstrating the system has DFE and is locally asymptotically stable as illustrated

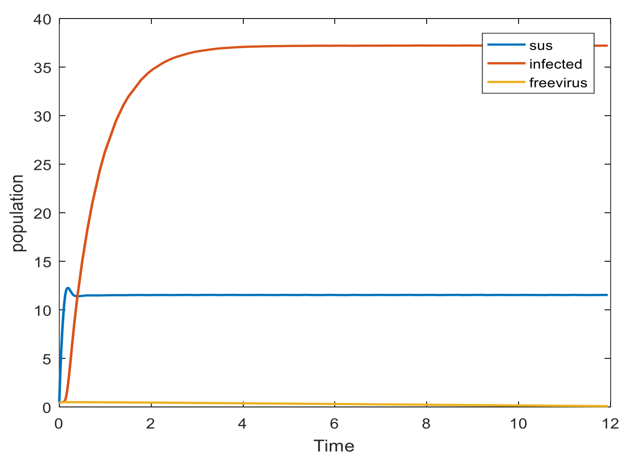



$$A = 160; \mu = .0003; \beta = .35; \alpha = .0009; \delta = 10; \gamma = .002; p = .08; c = 12;$$

The infection gets diverges




$$A = 160; \mu = 10; \beta = .35; \alpha = .00009; \delta = .05; \gamma = .001; p = .0001; c = 1.2;$$



## Conclusion

We have constructed an HBV model with cure term and saturated response. A delay term is incorporated into the model which describes the delay in the emission of virus particles and actively infected hepatocytes. It is evident that as delay escalates in number of virus particles and a time lag in. We obtain the constraints for the stability infected states with delay .The constraints for perseverance are given. We observe that as the delay accrued oscillation occurred and further increases in $\tau$ restitutes the dynamics to the stable form. Numerical simulations encapsulatethe results.

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