Global Analysis of a HCV Model with CTL, Antibody Responses and Therapy

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Abstract

In this paper, the global analysis of a HCV model with CTLs, antibody responses and therapy is studied. We incorporate into our model two treatments; the aim of the first one is to reduce the infected cells, while the second is to block the virus. We prove that the solutions with positive initial conditions are all positive and bounded. Moreover, we establish by using some appropriate Lyapunov functions that with the therapy the model becomes more stable than the one without treatment.

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1 Introduction

Hepatitis C is a liver disease caused by the hepatitis C virus (HCV). Approximately, 130 – 150 million people globally have chronic hepatitis C infection. Therefore, HCV infection presents a significant global public health issue [6]. For this reason, many mathematical models have been developed in order to understand the HCV dynamics [1, 5, 9]. In this article, we will consider the basic model presented by Wodarz in [9] and we will continue the investigation by introducing therapy into the model. It is well known that the antiviral therapies combined with interferon and ribavirin are successful in 90% of persons with acute infection and in 50% cases of persons with chronic infection [2]. The model of the HCV dynamics that we consider is under the following form:

\[
\begin{align*}
\frac{dX}{dt} &= \lambda - dX - \beta (1 - u_1) VX, \\
\frac{dY}{dt} &= \beta (1 - u_1) VX - aY - pYZ, \\
\frac{dV}{dt} &= k(1 - u_2)Y - \delta V - qVW, \\
\frac{dW}{dt} &= gVW - hW, \\
\frac{dZ}{dt} &= cYZ - bZ,
\end{align*}
\]

(1)

the problem is supplemented by the initial conditions:

\[X(0) = X_0, Y(0) = Y_0, V(0) = V_0, Z(0) = Z_0, W(0) = W_0.\]

This model contains five variables, that is, uninfected cells (X), infected cells (Y), free virus (V), an antibody response (W) and a CTL response (Z). Susceptible host cells (X) are produced at a rate \(\lambda\), die at a rate \(dX\) and become infected by virus at a rate \(\beta XV\). Infected cells die at a rate \(aY\) and are killed by the CTL response at a rate \(pYZ\). Free virus is produced by infected cells at a rate \(kY\) and decays at a rate \(\delta V\) and is neutralized by antibodies at a rate \(qVW\). CTLs expand in response to viral antigen derived from infected cells at a rate \(cYZ\) and decay in the absence of antigenic stimulation at a rate \(bZ\). Antibodies develop in response to free virus at a rate \(gVW\) and decay at a rate \(hW\). The parameter \(u_1\) represents the efficiency of drug therapy in blocking new infection, so that infection rate in the presence of drug is \(\beta (1 - u_1)\), while the parameter \(u_2\) stands for the efficiency of drug therapy in inhibiting viral production, such that the virion production rate under therapy is \(k(1 - u_2)\).

Clearly, the system (1) has a basic infection reproductive number of
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\[ R_0 = \frac{\lambda \beta k(1 - u_1)(1 - u_2)}{da\delta}. \]

The present paper is organized as follows. In section 2, we study the global existence of solutions, followed in section 3 by the analysis of the model. We discuss and conclude in the last section.

2 The global existence of solutions

In order to prove the global existence of solutions, we study the positivity and boundedness of solutions of system (1) describing the evolution of the cell population. For biological reasons, we assume that the initial data for this model satisfy:

\[ X_0 \geq 0, \ Y_0 \geq 0, \ V_0 \geq 0, \ W_0 \geq 0, \ Z_0 \geq 0. \]

**Proposition 1.** All solutions with non-negative initial conditions exist for all \( t > 0 \) and remain bounded and non-negative. Moreover we have

i) \( X(t) \leq X_0 + \frac{\lambda}{\delta} \),

ii) \( Y(t) \leq Y_0 + \max(1, 2 - \frac{d}{a})X_0 + \max(\frac{\lambda}{a}, \frac{\lambda}{\delta}) \),

iii) \( V(t) \leq V_0 + \frac{k(1-u_2)}{\delta} \|Y\|_\infty \),

iv) \( W(t) \leq W_0 + \frac{g}{q} \left[ \max(1; 2 - \frac{\delta}{h})V_0 + \max(\frac{k(1-u_2)}{\delta}; \frac{k(1-u_2)}{h}) \|Y\|_\infty \right] \),

v) \( Z(t) \leq Z_0 + \frac{c}{p} \left[ \max(1; 2 - \frac{d}{b})X_0 + Y_0 + \max(\frac{\lambda}{b}, \frac{\lambda}{d}) + \max(0; 1 - \frac{a}{b}) \|Y\|_\infty \right] \).

**Proof**

For positivity, we show that any solution starting in non negative orthant \( \mathbb{R}_+^5 = \{(X, Y, V, W, Z) \in \mathbb{R}^5 : X \geq 0, Y \geq 0, V \geq 0, W \geq 0, Z \geq 0\} \) remains there forever. In fact, \((X(t), Y(t), V(t), W(t), Z(t)) \in \mathbb{R}_+^5 \) we have

\[ \dot{X} \big|_{X=0} = \lambda \geq 0, \ \dot{Y} \big|_{Y=0} = \beta(1-u_1)VX \geq 0, \ \dot{V} \big|_{V=0} = k(1-u_2)Y \geq 0, \ \dot{W} \big|_{W=0} = 0 \geq 0, \ \dot{Z} \big|_{Z=0} = 0 \geq 0 \]

Hence, positivity of all solutions initiating in \( \mathbb{R}_+^5 \) is guaranteed [?].

From the first equation of the system (1), we deduce that \( \dot{X} + dX \leq \lambda \), then \( \frac{d}{dt}(Xe^{dt}) \leq \lambda e^{dt} \). Hence,

\[ X(t) \leq X_0e^{-dt} + \frac{\lambda}{d}(1 - e^{-dt}), \]
Since $0 \leq e^{-dt} \leq 1$, we deduce (i).

From the first and second equation of the system (1), we have

$$
\dot{Y} + aY \leq \lambda - dX - \dot{X}.
$$

Thus,

$$
Y(t)e^{at} - Y_0 \leq \frac{\lambda}{a}(e^{at} - 1) - \int_0^t e^{(a-d)s} \frac{d}{ds}(X(s)e^{ds})ds.
$$

Using the integration by parts, we get

$$
\int_0^t e^{(a-d)s} \frac{d}{ds}(X(s)e^{ds})ds = [X(s)e^{as}]_0^t - (a - d) \int_0^t X(s)e^{as}ds.
$$

Therefore,

$$
Y(t) \leq (X_0 + Y_0)e^{-at} + \frac{\lambda}{a}(1 - e^{-at}) - X(t) + (a - d) \int_0^t X(s)e^{a(s-t)}ds. \tag{2}
$$

If $a - d \leq 0$, then

$$
Y(t) \leq X_0 + Y_0 + \frac{\lambda}{a}. \tag{3}
$$

If $a - d \geq 0$, then

$$
Y(t) \leq X_0 + Y_0 + (a - d) \int_0^t X(s)e^{a(s-t)}ds.
$$

According to i), we have

$$
Y(t) \leq X_0 + Y_0 + \frac{\lambda}{a} + \frac{(a-d)}{a}(X_0 + \frac{\lambda}{d})(1 - e^{-at}),
$$

hence,

$$
Y(t) \leq Y_0 + (2 - \frac{d}{a})X_0 + \frac{\lambda}{a}. \tag{4}
$$

From (3) and (4), we deduce (ii).

Now, we prove iii). The third equation of system 1, and $(V(t), Z(t)) \in \mathbb{R}^2_+$, imply that

$$
V(t) \leq V_0e^{-\delta t} + k(1 - u_2) \int_0^t Y(s)e^{(s-t)}ds,
$$

then

$$
V(t) \leq V_0 + \frac{k(1-u_2)}{\delta} \|	ext{Y}\|_\infty (1 - e^{-t\delta}).
$$
Since $1 - e^{-t\delta} \leq 1$, we deduce (iii).
Using a same technique to show (2), we get

$$W(t) = W_0 e^{-ht} + \frac{g}{q} \left\{ \int_0^t [k(1 - u_2)Y(s) + (h - \delta)V(s)] e^{h(s-t)}ds - V(t) + V_0 e^{-ht} \right\}. \tag{5}$$

If $h - \delta \leq 0$, then

$$W(t) \leq W_0 + \frac{g}{q} \left( \frac{k(1 - u_2)}{h} \|Y\|_{\infty} + V_0 \right). \tag{6}$$

If $h - \delta \geq 0$, using (iii), we have

$$W(t) \leq W_0 + \frac{g}{q} \left[ \frac{k(1 - u_2)}{\delta} \|Y\|_{\infty} + (2 - \frac{\delta}{h})V_0 \right]. \tag{7}$$

From (6) and (7), we deduce (iv).

Finally, we prove v). The fifth equation of system (1) implies that

$$\dot{Z} + bZ = cYZ = c \frac{p}{p} \left[ \lambda - (\dot{X} + dX) - (\dot{Y} + aY) \right].$$

Using the same techniques for the proof of (2) and (5), we get

$$Z(t) = \left[ \frac{c}{p} (X_0 + Y_0 - \frac{\lambda}{b}) + Z_0 \right] e^{-bt} + \frac{c}{p} \left\{ \frac{\lambda}{b} + \int_0^t [(b-d)X(s) + (b-a)Y(s)] e^{b(s-t)}ds - X(t) - Y(t) \right\}. \tag{8}$$

If $b - d \leq 0$ and $b - a \leq 0$, we have

$$Z(t) \leq Z_0 + \frac{c}{p} \left( \frac{\lambda}{b} + X_0 + Y_0 \right).$$

If $b - d \leq 0$ and $b - a \geq 0$, we have

$$Z(t) \leq Z_0 + \frac{c}{p} \left[ \frac{\lambda}{b} + X_0 + Y_0 + (1 - \frac{a}{b}) \|Y\|_{\infty} \right].$$

If $b - d \geq 0$ and $b - a \leq 0$, we have

$$Z(t) \leq Z_0 + \frac{c}{p} \left[ \frac{\lambda}{d} + (2 - \frac{d}{b})X_0 + Y_0 \right].$$

If $b - d \geq 0$ and $b - a \geq 0$, we have

$$Z(t) \leq Z_0 + \frac{c}{p} \left[ \frac{\lambda}{d} + (2 - \frac{d}{b})X_0 + Y_0 + (1 - \frac{a}{b}) \|Y\|_{\infty} \right]. \tag{9}$$

From (8) and (9), we deduce (v).
3 Analysis of the model

In this section, we will prove that there exist a disease free equilibrium point and four endemic equilibrium points. Next, we will study the global stability of these equilibrium points.

By a simple calculation, the system (1) has always one disease-free equilibrium:

\[ E_0 = \left( \frac{\lambda}{d}, 0, 0, 0, 0 \right) \]

and four endemic equilibrium points:

\[ E_1 = (X_1, Y_1, V_1, 0, 0) \]

where

\[ X_1 = \frac{a \delta}{k \beta (1 - u_1)(1 - u_2)}, Y_1 = \frac{\lambda k \beta (1 - u_1)(1 - u_2) - a \delta}{ak \beta (1 - u_1)(1 - u_2)}, V_1 = \frac{\lambda k \beta (1 - u_1)(1 - u_2) - a \delta}{\beta \delta a (1 - u_1)}. \]

\[ E_2 = (X_2, Y_2, V_2, 0, Z_2) \]

where

\[ X_2 = \frac{\lambda \delta c}{d \delta c + k \beta b (1 - u_1)(1 - u_2)}, Y_2 = \frac{b}{c}, V_2 = \frac{k (1 - u_2)b}{\delta c}, \]

\[ Z_2 = \frac{k \beta \lambda c (1 - u_1)(1 - u_2) - a (d \delta c + k \beta b (1 - u_1)(1 - u_2))}{p [d \delta c + k \beta b (1 - u_1)(1 - u_2)]}. \]

\[ E_3 = (X_3, Y_3, V_3, 0, Z_3) \]

where

\[ X_3 = \frac{\lambda g}{dg + \beta h (1 - u_1)}, Y_3 = \frac{\lambda \beta (1 - u_1) h}{a (dg + \beta h (1 - u_1))}, \]

\[ V_3 = \frac{h}{g}, W_3 = \frac{g k \lambda (1 - u_1)(1 - u_2) - \delta a (dg + \beta h (1 - u_1))}{a q (dg + \beta h (1 - u_1))}. \]

\[ E_4 = (X_4, Y_4, V_4, W_4, Z_4) \]

where

\[ X_4 = \frac{\lambda g}{dg + \beta (1 - u_1) h}, Y_4 = \frac{b}{c}, V_4 = \frac{h}{g}, \]

\[ W_4 = \frac{k b g (1 - u_2) - \delta h c}{c q h}, Z_4 = \frac{c \beta h \lambda (1 - u_1) - ab (dg + \beta (1 - u_1) h)}{(dg + \beta (1 - u_1) h) p b}. \]

In order to study the global stability of the points \( E_1, E_2, E_3 \) and \( E_4 \), we define the following numbers:

\[ \begin{align*}
D_0^W &= \frac{\lambda k (1 - u_2) g}{a \delta h}, \\
H_0^W &= \frac{1}{R_0 + \frac{1}{D_0}}.
\end{align*} \]
\[
\begin{aligned}
D_0^Z &= \frac{\lambda_c}{ab}, \\
H_0^Z &= \frac{1}{R_0 + \frac{1}{D_0^Z}},
\end{aligned}
\]

(11)

Then, these equilibria can be written as follows:

\[
E_i = \left( \frac{\lambda}{a} Q_i^X, \frac{\lambda}{a} Q_i^Y, \frac{\delta}{a} Q_i^V, \frac{\delta}{a} Q_i^W, \frac{\alpha}{p} Q_i^Z \right),
\]

where \(0 \leq i \leq 4\),

\[
\begin{array}{l}
Q_0^X = 1, Q_0^Y = Q_0^Y = Q_0^W = Q_0^Z = 0, \\
Q_1^X = \frac{1}{R_0}, Q_1^Y = 1 - \frac{1}{R_0}, Q_1^Y = R_0 - 1, Q_1^W = Q_1^Z = 0, \\
Q_2^X = \frac{H_0^Z}{R_0}, Q_2^Y = \frac{1}{D_0^Z}, Q_2^Y = \frac{R_0}{D_0^Z}, Q_2^W = Q_2^Z = 0, Q_2^Z = H_0^Z - 1, \\
Q_3^X = \frac{H_0^W}{R_0}, Q_3^Y = \frac{H_0^W}{D_0^Z}, Q_3^Y = \frac{R_0}{D_0^Z}, Q_3^W = H_0^W - 1, Q_3^Z = 0, \\
Q_4^X = \frac{H_0^W}{R_0}, Q_4^Y = \frac{1}{D_0^Z}, Q_4^Y = \frac{R_0}{D_0^Z}, Q_4^W = \frac{D_0^W}{D_0^Z} - 1, Q_4^Z = \frac{D_0^W}{D_0^Z} H_0^W - 1.
\end{array}
\]

It is easy to remark that

**Remark 2.**

1. If \(R_0 < 1\), then the point \(E_1\) does not exist and \(E_1 = E_f\) when \(R_0 = 1\).
2. If \(H_0^Z < 1\), then \(E_2\) does not exist and \(E_2 = E_1\) when \(H_0^Z = 1\).
3. If \(H_0^W < 1\), then \(E_3\) does not exist and \(E_3 = E_1\) when \(H_0^W = 1\).
4. If \(D_0^W < D_0^Z\) or \(\frac{D_0^W}{D_0^Z} H_0^W < 1\), then \(E_4\) does not exist. Moreover \(E_4 = E_2\) when \(D_0^W = D_0^Z\) and \(E_4 = E_3\) when \(\frac{D_0^W}{D_0^Z} H_0^W = 1\).

The number \(D_0^W\) represents the basic defence number by antibody response, \(D_0^Z\) represents the basic defence number by CTL response. \(H_0^W\) is the half harmonic mean of \(R_0\) and \(D_0^W\) and \(H_0^Z\) is the half harmonic mean of \(R_0\) and \(D_0^Z\).

We put

\[
H_0^{W,Z} = \frac{H_0^W D_0^Z}{D_0^Z}
\]
We remark that $H_0^W = H_0^{W,W}$ and $H_0^Z = H_0^{Z,Z}$. The importance of these parameters is related to the following result:

**Proposition 3.**

1. If $R_0 \leq 1$, then the point $E_0$ is globally asymptotically stable.

2. If $R_0 > 1$, $H_0^W \leq 1$ and $H_0^Z \leq 1$, then $E_1$ is globally asymptotically stable.

3. If $H_0^Z > 1$ and $D_0^Z > D_0^W$, then the point $E_2$ is globally asymptotically stable.

4. If $H_0^W > 1$ and $H_0^{W,Z} \leq 1$, then the point $E_3$ is globally asymptotically stable.

5. If $D_0^W > D_0^Z$ and $H_0^{W,Z} > 1$, then the point $E_4$ is globally asymptotically stable.

**Proof.** For the proof, we will use the same techniques given in [3, 7, 10]. We consider the following Lyapunov function defined in $\mathbb{R}_+^5$ by:

$$V(X, Y, V, W, Z) = x^*\left(\frac{X}{X^*} - \ln \frac{X}{X^*}\right) + y^*\left(\frac{Y}{Y^*} - \ln \frac{Y}{Y^*}\right) +$$

$$\frac{\beta(1-u_1)X^*}{u + qW^*}[v^*\left(\frac{V}{V^*} - \ln \frac{V}{V^*}\right) + \frac{q}{g}w^*\left(\frac{W}{W^*} - \ln \frac{W}{W^*}\right)] + \frac{p}{c}z^*\left(\frac{Z}{Z^*} - \ln \frac{Z}{Z^*}\right),$$

where $E^* = (X^*, Y^*, V^*, W^*, Z^*)$ is an equilibrium of the system.

It easy to verifies that

$$\dot{V}(X, Y, V, W, Z) = \lambda[1 + Q_i^X + Q_i^Y + \frac{R_0 Q_i^X}{1 + Q_i^W}(\frac{Q_i^Y}{R_0} + \frac{Q_i^W}{D_0}) + \frac{Q_i^Z}{D_0}] - (dX +$$

$$\frac{\lambda^2}{dX}Q_i^X) - \beta(1-u_1)\lambda XV Q_i^Y - \frac{\lambda (1-u_2)kY}{1+Q_i^W}Q_i^XQ_i^Y + \frac{R_0 Q_i^X}{1+Q_i^W} - 1 -$$

$$\frac{Wq\lambda}{\delta}Q_i^X + \frac{Q_i^W}{1+Q_i^W}(Q_i^Y - \frac{R_0}{D_0}) + \frac{p\lambda z}{a}Q_i^Y - \frac{1}{D_0} + \frac{p\lambda z}{a}Q_i^Y - \frac{1}{D_0}.$$
then $\dot{V} < 0$ and $E_0$ is globally asymptotically stable, if $R_0 \leq 1$.

For $i = 1$ we have that

$$
\dot{V} = \lambda(3 - \frac{1}{R_0}) - (dX + \frac{\lambda^2}{R_0}dX) - \frac{\beta(1 - u_1)\lambda XV}{aY}(1 - \frac{1}{R_0}) - \frac{\lambda k(1 - u_2)Y}{uV}(1 - \frac{1}{R_0}) \\
+ \frac{\lambda qW}{\delta}(1 - \frac{1}{H_0^W}) + \frac{p\lambda Z}{a}(1 - \frac{1}{H_0^Z})
$$

$$
\dot{V} = \lambda\left[3(1 - \frac{1}{R_0}) + \frac{2}{R_0}\right] - (dX + \frac{\lambda^2}{R_0}dX) - \lambda^2 \frac{dX}{R_0}(1 - \frac{1}{R_0}) - \frac{\beta(1 - u_1)\lambda XV}{aY}(1 - \frac{1}{R_0}) \\
- \frac{\lambda k(1 - u_2)Y}{\delta V}(1 - \frac{1}{R_0}) + \frac{\lambda qW}{\delta}(1 - \frac{1}{H_0^W}) + \frac{p\lambda Z}{a}(1 - \frac{1}{H_0^Z}).
$$

Using the arithmetic-geometric inequality, if $R_0 > 1$, we have

$$
-\frac{\lambda^2}{R_0}dX(1 - \frac{1}{R_0}) - \frac{\beta(1 - u_1)\lambda XV}{aY}(1 - \frac{1}{R_0}) - \frac{\lambda k(1 - u_2)Y}{\delta V}(1 - \frac{1}{R_0}) \leq -3\lambda(1 - \frac{1}{R_0}).
$$

Since

$$
dX + \frac{\lambda^2}{R_0}dX \geq \frac{2\lambda}{R_0},
$$

then $\dot{V} < 0$ and $E_1$ is globally asymptotically stable, if $R_0 > 1$, $H_0^W \leq 1$ and $H_0^Z \leq 1$.

For $i = 2$ we have

$$
\dot{V} = \lambda(3 - \frac{H_0^Z}{R_0}) - (dX + \frac{\lambda^2}{dX}H_0^Z)(1 - \frac{1}{R_0}) - \frac{\beta(1 - u_1)\lambda XV}{aY} \frac{1}{D_0^Z} - \frac{\lambda k(1 - u_2)Y H_0^Z}{\delta V} \frac{1}{D_0^Z} \\
+ \frac{\lambda qW}{\delta} H_0^Z(1 - \frac{1}{D_0^W}) - \frac{\lambda k(1 - u_2)Y}{H_0^Z} \frac{1}{D_0^Z} - \frac{\lambda qW}{\delta} H_0^Z(1 - \frac{1}{D_0^W})
$$

Using the arithmetico-geometric inequality, we have

$$
-\frac{\lambda^2}{dX} \frac{H_0^Z}{R_0}(1 - \frac{H_0^Z}{R_0}) - \frac{\beta(1 - u_1)\lambda XV}{aY} \frac{1}{D_0^Z} - \frac{\lambda k(1 - u_2)Y H_0^Z}{\delta V} \frac{1}{D_0^Z} \leq -3\lambda \frac{H_0^Z}{D_0^Z}.
$$

Since

$$
dx + \frac{\lambda^2}{dX} \left(\frac{H_0^Z}{R_0}\right)^2 \geq 2\lambda \frac{H_0^Z}{R_0},
$$
then $\dot{V} < 0$ and $E_2$ is globally asymptotically stable, if $H_0^W > 1$ and $D_0^Z > D_0^W$.

For $i = 3$ we have

$$
\dot{V} = \lambda(3 - \frac{H_0^W}{R_0}) - (dX + \frac{\lambda^2}{dX} \left( \frac{H_0^W}{R_0} \right)^2) - \frac{\beta(1 - u_1)\lambda XV}{aY} \frac{1}{D_0^Z} - \frac{\lambda k(1 - u_2)Y}{\delta V} \frac{H_0^W}{D_0^Z},
$$

Using the arithmetico-geometric inequality, we have

$$
-\frac{\lambda^2}{dX} \left( \frac{H_0^W}{R_0} \right)^2 \leq -3\lambda \frac{H_0^W}{D_0^W},
$$

then $\dot{V} < 0$ and $E_3$ is globally asymptotically stable, if $H_0^W \geq 1$ and $H_0^W < 1$.

For $i = 4$ we have

$$
\dot{V} = \lambda(3 - \frac{H_0^W}{R_0}) - (dX + \frac{\lambda^2}{dX} \left( \frac{H_0^W}{R_0} \right)^2) - \frac{\beta(1 - u_1)\lambda XV}{aY} \frac{1}{D_0^Z} - \frac{\lambda k(1 - u_2)Y}{\delta V} \frac{H_0^W}{D_0^Z} - \frac{\lambda k(1 - u_2)Y H_0^W}{\delta V} \frac{1}{D_0^Z}.
$$

Using the arithmetico-geometric inequality, we have

$$
-\frac{\lambda^2}{dX} \left( \frac{H_0^W}{R_0} \right)^2 \leq -3\lambda \frac{H_0^W}{D_0^W},
$$

then $\dot{V} \leq 0$.

The equality holds if and only if

$$
X = X^* \quad \text{and} \quad \frac{V}{V^*} = k(1 - u_2) \frac{D_0^Z}{D_0^W} = \frac{\eta^*}{\eta^*}.
$$

Let

$$
S = \{(X, Y, V, W, Z) \in \mathbb{R}_+^5 : \dot{V}(X, Y, V, W, Z) = 0\}.
$$

The trajectory $(X(t), Y(t), V(t), W(t), Z(t)) \in S$ implies that

$$
Y = Y^*, \quad V = V^*, \quad W = W^* \quad \text{and} \quad Z = Z^*.
$$

From LaSalle’s invariance principle [??], we conclude that $E_4$ is globally asymptotically stable, if $D_0^W > D_0^Z$ and $H_0^W > 1$. 
Figure 1: The basic reproduction number $R_0$ as function of the drug efficacy $\theta$ for $\lambda = 2 \cdot 10^5$, $\beta = 2 \cdot 10^{-7}$, $k = 20$, $d = 0.1$, $a = 0.5$ and $\delta = 4$.

4 Discussion and conclusion

In this work, we gave the global analysis of a HCV with CTL, antibody responses and therapy. The disease free equilibrium is globally asymptotically stable if the basic infection reproduction number satisfies $R_0 \leq 1$. For $R_0 > 1$, the global stability of the four endemic equilibrium points depends on both the basic defence rate by antibody response and the basic defence rate by CTL response. In addition, the goal of the therapy is to better control the concentrations of the virus and infected cells in order to reduce the value of the number of basic reproduction to a number below one. Indeed, if we put $\theta = u_1 + u_2 - u_1 u_2$ which represents the combined efficacy of the two drugs, we will have $1 - \theta = (1 - u_1)(1 - u_2)$ which means that each drug acts independently. Hence, $R_0$ becomes

$$R_0 = \frac{\lambda \beta (1 - \theta) k}{da \delta}.$$ 

Then from the above formula of $R_0$, we see that $R_0$ can be decreased by increasing the efficacy of therapy, i.e. increasing $u_1$ and $u_2$ (see Fig. 1).
References


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