A With-In Host Dengue Infection Model with Immune Response and Beddington-DeAngelis Incidence Rate

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ABSTRACT
A model of viral infection of monocytes population by dengue virus is formulated in a system of four ordinary differential equations. The model takes into account the immune response and the incidence rate of susceptible and free virus particle as Beddington-DeAngelis functional response. By constructing a block, the global stability of the uninfected steady state is investigated. This steady state always exists. If this is the only steady state, then it is globally asymptotically stable. If any infected steady state exists, then uninfected steady state is unstable and one of the infected steady states is locally asymptotically stable. These different cases depend on the values of the basic reproduction ratio and the other parameters.

Keywords: With-In Host Model; Dengue Viral Infection; Basic Reproduction Ratio; Beddington-DeAngelis Immune Response

1. Introduction
Dengue is an infectious mosquito-borne viral disease. It is estimated that about 50 million infections occur annually in over 100 countries [1]. There is no specific treatment for curing dengue patients. Hospital treatment in general is given as supportive care which includes bed rest, antipyretics, and analgesics. Most dengue infections are asymptomatic. Few of them suffer dengue fever and dengue haemorrhagic fever, which may end up in fatality.

Dengue virus is one of the most difficult arboviruses to isolate. There are four serotypes of the dengue virus and each of the serotype has numerous virus strains. Infection with one dengue serotype may provide lifelong immunity to that serotype, but there is no cross-protective immunity to other serotype, [2]. Identification of the primary target cells of dengue virus replication in infected human body has proven to be extremely difficult. It is generally believed that the target cells of dengue virus are monocytes or its differentiated cells the macrophages [3].

It is usually believed that dengue virus is quickly cleared in human body within approximately 7 days after the day of sudden onset of fever [1]. Naturally this clearing process is done by the immune system which is a result of complex dynamic reactions. Following [4], in this paper we try to understand the process using a mathematical model.

Mathematical modeling of dengue disease transmission in human and mosquito populations has been done since the beginning of last century. Some of the recent models could be seen in [2-5]. Several studies on infection model within human body have been done for various cases [2,3] and [5-11]. Meanwhile, mathematical modeling for with-in host dengue viral disease is quite new.

The model for with-in host dengue viral infection with Beddington-DeAngelis incidence rate and immune response is as following.

\[
\begin{align*}
\frac{dS}{dt} &= \mu - aS - \frac{aSV}{1 + \rho S + \omega V}, \\
\frac{dI}{dt} &= \frac{aSV}{1 + \rho S + \omega V} - \beta I - \nu IZ, \\
\frac{dV}{dt} &= kI - \gamma V - \frac{aSV}{1 + \rho S + \omega V}, \\
\frac{dZ}{dt} &= cI + dIZ - \delta Z,
\end{align*}
\]

where, \( \beta_i = \beta + \frac{\eta V}{\delta} \) and \( c_i = c + \frac{d\eta}{\delta} \).

The constant \( a > 0 \), is the rate constant characterizing infection of the cells. The constants \( \rho, \omega \) are positive.

In the above \( S(t), I(t), V(t) \) and \( Z(t) + \frac{\eta}{\delta} \) represent the density of susceptible monocytes, infected monocytes, free virus particles and immune cells in 1 μl

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blood at time $t$, respective. The production of susceptible monocytes by bone marrow is assumed at a constant rate $\mu$ and the life span of susceptible monocytes is $\frac{1}{\alpha}$. The flow from susceptible monocytes to the infected monocytes depends on the incidence rate of susceptible monocytes and free virus particle. This rate is shown by $\frac{\alpha SV}{1 + \rho S + \omega V}$, where $\frac{\alpha S}{1 + \rho S + \omega V}$ is the incidence response of susceptible monocytes to free virus particles. The period of infected monocytes is assumed constant as $\frac{1}{\beta}$. We assume virus multiplication is at constant rate $k$ and the virus clearance rate is at constant rate $\gamma$. We also assumed the immune cells are produced at constant rate $\eta$ and their life span is $\frac{1}{\delta}$. Moreover we assumed there is stimulation of immune cells production due to the increase of infected cell which is proportional to the density infected monocytes at a constant rate $c$ as well as from the contacts with infected cells at the rate $d$ and the immune cells will eliminate the infected monocytes at a constant rate $v$. Finally, the positive constants $\rho$ and $\omega$ have some biological meanings.

The above model is valid for only one serotype of dengue virus circulate in an infected host and dengue infects monocytes in blood stream. For more detail the reader is referred to [4] and references therein.

The local stability of the equilibrium points of the system (1) for Lotka-Voltera functional response i.e. $\phi(S) = aS$, has been discussed in [4]. The model (1) is a generalization of the self-regulating cytotoxic T lymphocytes (CTL) response model. The predator-prey like CTL response model and the linear immune response model in chapter 6 of [5].

In this paper, we will analyze the global stability of the viral free equilibrium for Beddington-DeAngelis incidence response, $\frac{\alpha S}{1 + \rho S + \omega V}$. In fact we will show that if this equilibrium is the only rest point of the system (1), then it is globally asymptotically stable. If there are some other equilibria, then the local stability of them depends on the values of the parameters.

2. Global Stability of the Uninfected Equilibrium

In this section, at first we will find the equilibrium points of the system (1) and the eigenvalues of this system at these points. This information leads us to prove the locally asymptotical stability of the equilibrium points.

At an equilibrium point of the system (1) we must have

$$ \begin{cases} \mu - \alpha S - \frac{\alpha SV}{1 + \rho S + \omega V} = 0, \\ \frac{\alpha SV}{1 + \rho S + \omega V} - \beta I - \nu IZ = 0, \\ kI - \gamma V - \frac{\alpha SV}{1 + \rho S + \omega V} = 0, \\ cI + dIZ - \delta Z = 0 \end{cases} \quad (2) $$

From the first equation we obtain, $\frac{\mu - \alpha S}{k} = \frac{\gamma (1 + \rho S)}{(a + \omega \alpha)S - \omega \mu + 1}$. From the fourth equation we obtain $Z = \frac{cI}{\delta - dl}$. Substituting these values of $V, I$ and $Z$ into the second equation yields,

$$ \left( \mu - \alpha S \right) \left[ 1 - \frac{\beta I}{k} \left( \frac{\gamma (1 + \rho S)}{aS - \omega (\mu - \alpha S)} + 1 \right) \right] + \frac{vc \beta I^2}{k^2} \left[ \frac{\mu - \alpha S}{\delta - \frac{d \beta I}{k}} \left( \frac{\gamma (1 + \rho S)}{aS - \omega (\mu - \alpha S)} + 1 \right) \right] = 0. $$

If, $\mu - \alpha S = 0$, then from this, we have $S = \frac{\mu}{\alpha}$. Thus $y_0 = \left( \frac{\mu}{\alpha}, 0, 0 \right)$ is one of the equilibrium points of the system (1). If,

$$ \left( \mu - \alpha S \right) \left[ 1 - \frac{\beta I}{k} \left( \frac{\gamma (1 + \rho S)}{aS - \omega (\mu - \alpha S)} + 1 \right) \right] + \frac{vc \beta I^2}{k^2} \left[ \frac{\mu - \alpha S}{\delta - \frac{d \beta I}{k}} \left( \frac{\gamma (1 + \rho S)}{aS - \omega (\mu - \alpha S)} + 1 \right) \right] = 0, $$

then

$$ q_3 S^3 + q_2 S^2 + q_1 S + q_0 = 0, \quad (3) $$

where,

$$ q_3 = -d \alpha \beta I \left( e \alpha + a \right) \left( y b + e \alpha + a \right), $$

$$ q_2 = -d \alpha \beta I \left( e \alpha + a \right), $$

$$ q_1 = -d \alpha \beta I, $$

$$ q_0 = d \alpha \beta I. $$
In the following we consider the stability property of the equilibrium point \( y_0 \). In order to do this we check the sign of the eigenvalues of Jacobi matrix of (1) at \( y_0 \). The Jacobi matrix is

\[
J = \begin{bmatrix}
-a - \frac{aV(1+\omega V)}{(1+\rho S+\omega V)^2} & 0 & \frac{-aS(1+\rho S)}{(1+\rho S+\omega V)^2} & 0 \\
\frac{aV(1+\omega V)}{(1+\rho S+\omega V)^2} & -\beta_1 - \gamma Z & \frac{aS(1+\rho S)}{(1+\rho S+\omega V)^2} & -\gamma t \\
\frac{-aV(1+\omega V)}{(1+\rho S+\omega V)^2} & k & \frac{-aS(1+\rho S)}{(1+\rho S+\omega V)^2} & 0 \\
0 & c_i + dZ & 0 & d_l - \delta
\end{bmatrix}
\]

So the value of \( J \) at \( y_0 \) is

\[
J(y_0) = \begin{bmatrix}
-a & 0 & 0 & 0 \\
0 & -\beta_1 & 0 & 0 \\
0 & k & -\gamma & 0 \\
0 & c_i & 0 & -\delta
\end{bmatrix}
\]

The eigenvalues of \( J(y_0) \) are the roots of the characteristic polynomial

\[
(x + \alpha)(x + \delta) \left( x^2 + \left( \beta_1 + \gamma + \frac{a\mu}{1+\rho\alpha} \right) x - \beta_1 \gamma \right) + \beta_1 \gamma = 0.
\]

These roots are

\[
x_1 = \frac{-\beta_1 + \gamma + \frac{a\mu}{1+\rho\alpha}}{2},
\]

\[
x_2 = \frac{-\beta_1 + \gamma + \frac{a\mu}{1+\rho\alpha}}{2}.
\]

where, \( \Delta = \left( \beta_1 - \gamma + \frac{a\mu}{1+\rho\alpha} \right)^2 + 4k \frac{a\mu}{1+\rho\alpha} \).

Clearly, \( x_1 \), \( x_2 \), and \( x_3 \) have negative real part. If \( x_3 \) has negative real part, then the equilibrium \( y_0 \) is locally asymptotically stable. But \( x_3 \) is negative if and only if, \( \sqrt{\Delta} < \left( \beta_1 + \gamma + \frac{a\mu}{1+\rho\alpha} \right) \). This condition equals
to, 
\[ \frac{k a \mu}{\alpha} \frac{\mu}{\alpha} \beta_1 (\gamma + (\gamma p + a) \mu) \alpha < 1. \]

Set, \( R_0 = \frac{k a \mu}{\beta_1 (\gamma + (\gamma p + a) \mu) \alpha} \). This number is called the basic reproduction ratio [7].

Therefore we have the following theorem.

**Theorem 2.1.** If, \( R_0 < 1 \), the equilibrium point \( y_0 \) is locally asymptotically stable and if \( R_0 > 1 \), the equilibrium \( y_0 \) is unstable.

Now we will show that if, \( R_0 < 1 \), then the equilibrium, \( y_0 \) is globally asymptotically stable. In order to see this, first of all consider the following domain in the \((S, I, V, Z)\) space.

\[ D_a = \{(S, I, V, Z) : 0 < S < a, I > 0, V > 0, Z > 0 \}, a \geq \frac{\mu}{\alpha}. \]

It follows that the flow generated by that system (1.1) gets into \( D_a \) on the boundary of \( D_a \). Let \( D = D_a \) for, \( a = \frac{\mu}{\alpha}. \) Thus \( \overline{D} \) is a global attractor. Now in \( \overline{D} \) consider the following set for \( C > 0 \):

\[ Q_c = \{(S, I, V, Z) : 0 < S < \frac{\mu}{\alpha}, I > 0, V > 0, Z > 0 \text{ and } K(S, I, V, Z) \leq C \}, \]

where, \( K(S, I, V, Z) = A_1 \left( \frac{\mu}{\alpha} - S \right) + A_2 I + A_3 V + A_4 Z \)

and

\[ A_1 = -\beta_1 (\gamma + \varphi^*) \left( 1 - R_c^2 \right) \]
\[ A_2 = \left( \gamma + \varphi^* + 1 \right) \left( \beta d - vc \right) - d \varphi^* \]
\[ A_3 = \phi^* \left( \beta d - vc \right) A_1 \]
\[ A_4 = \left( \gamma + \varphi^* + 1 \right) \left( \beta d - vc \right) - d \varphi^* \]

and \( \varphi^* = \frac{a \mu}{1 + \rho \frac{\mu}{\alpha}}. \)

If we differentiate \( K(S, I, V, Z) \) along the orbits of the system (1), we obtain:

\[ \frac{dK}{dr} = -A_1 S + A_2 I + A_3 V + A_4 Z \]
\[ = -A_2 \left( \mu - \alpha S - V \varphi(S, V) \right) \]
\[ + A_3 \left( V \varphi(S, V) - \beta_1 I - \gamma V \right) \]
\[ + A_4 \left( \beta_1 I + dIZ - \delta Z \right) \]
\[ = -A_4 \left( \mu - \alpha S \right) + (-\beta_1 A_3 + kA_3 + cA_4) I \]
\[ + (\phi A_1 + \phi A_2 - (\gamma + \varphi) A_3) V \]
\[ - \delta A_1 Z + (dA_4 - \gamma A_4) IZ \]

Here, \( \varphi := \varphi(S, V) = \frac{aS}{1 + \rho S + \omega V}. \) Since on the surface \( K(S, I, Z, V) = C \) of the boundary of \( Q_c \), we have \( \mu - \alpha S > 0 \) and \( \varphi < 0 \) and \( \beta_1 (\gamma + \varphi^*) \left( 1 - R_c^2 \right) > 0 \), therefore \( \frac{dK}{dr} < 0. \) Thus the flow gets into \( Q_c \) on, \( K(S, I, Z, V) = C \). Hence the flow gets into \( Q_c \) from its boundary. Therefore \( Q_c \) is an attractor in \( \overline{D} \) for all \( C > 0. \) Thus \( y_0 \) is a global attractor. Thus we have proved the following theorem.

**Theorem 2.2.** If, \( R_0 < 1 \), then \( y_0 \) the uninfected equilibrium is the only equilibrium of the system (1). Moreover this equilibrium is globally asymptotically stable.

Since \( y_0 \) is globally asymptotically stable for \( R_0 < 1 \), any other equilibrium points of the system (1) cannot exist for \( R_0 < 1 \). Therefore, \( y_0 \) is the unique equilibrium point for \( R_0 < 1 \).

### 3. Stability of the Other Equilibrium Points

In this section, we consider the stability of the other rest point of the system (1). In order to this, we consider the Equation (3). First, we consider this equation for \( c_1 = 0 \) and then for \( c_2 = 0 \) .

There are two cases for \( c_1 = 0 \) as follows.

**Case 1.** \( c = d = 0 \)

In this case, the system (1) has two equilibrium points, \( y_0 \) and another one. To see this, from the first equation of (2) we obtain, \( -\alpha S = \frac{aSV}{1 + \rho S + \omega V}. \) Since \( c = d = 0 \) from the fourth equation we get \( Z = 0. \) Substituting these values of \( V \) and \( Z \) into the second equation yields, \( I = \frac{\mu - \alpha S}{\beta_1}. \) By using the value of \( I \) and the third equation we get \( V = \frac{(k - \beta_1) \mu - \alpha S}{\beta_1 \gamma}. \) Using these values into the Equation (3), we obtain,
Thus one of the roots is  \( x = -\delta \). The other roots are given by

\[
x^3 + q_3x^2 + q_1x + q_0 = 0.
\]

Here  \( q_2 = \alpha + \gamma + \beta + A + B \),

\[
q_1 = \beta_1\gamma + (\beta - k + A)B + (\beta_1 + \gamma)(\alpha + A)
\]

and  \( q_0 = \beta\alpha\gamma + (\beta_1\alpha - k\alpha)B + \beta\gamma A \).

By substituting the value of \( A, B \) and \( V_o \) in \( q_2, q_1 \) and \( q_0 \) we see that \( q_2, q_1 \) and \( q_0 \) are positive. Moreover, it is easy to check that, \( q_2, q_1 > q_0 \). By the Rouths Hurwitz Criteria, all roots of the cubic polynomial have negative real part. Therefore we have the following theorem.

**Theorem 3.1.** If, \( R_0 > 1 \), then the equilibrium point \( y_i \) exists and is locally asymptotically stable. Moreover the equilibrium \( y_0 \) exists and is unstable.

**Remark 3.1.** Since, the rest points and the eigenvalues depend continuously on the parameters, thus for small values of \( c > 0 \) and \( d > 0 \), \( y_i \) exists and is locally asymptotically stable.

**Case 2.** \( c = \eta = 0, d \neq 0 \)

In this case, the system (1) has three equilibrium points and \( y_0 \) is one of them. Since \( c = \eta = 0 \), the fourth equation of the system (1) gives \( dZ - \delta Z = 0 \). Therefore, \( Z = 0 \) or \( I = \frac{\delta}{d} \). For \( Z = 0 \), substituting the value of \( Z \) into the second equation yields, \( I = \frac{\mu - \alpha S}{\beta} \). By using the value of \( I \) and the third equation we get,

\[
V = \frac{k - \beta)(\mu - \alpha S)}{\beta_1\gamma}.
\]

Substituting values of \( c \) and \( \eta \) into the Equation (3), we obtain,

\[
S = \frac{\gamma\beta + \alpha\alpha(k - \beta)}{(k - \beta)(\alpha + \omega) - \rho\beta}.
\]

Thus we get

\[
y_i' = \left( S, \frac{\gamma\beta + \alpha\alpha(k - \beta)}{(k - \beta)(\alpha + \omega) - \rho\beta}, \frac{0}{0}, 0 \right) \text{ as another rest point of the system (1).}
\]

For \( I = \frac{\delta}{d} \), by substituting this value of \( I \) in the second equation of the system (1), we obtain

\[
Z = \frac{d(\mu - \alpha S)}{n\delta} - \frac{\beta}{\nu} = \frac{d(\mu - \alpha S)}{n\delta} - \frac{\beta\delta}{\nu}. \text{ Then from the third equation we get, } V = \frac{k\delta - d(\mu - \alpha S)}{\nu}. \]

By using this value of \( V \) into the first equation of the system (1), we obtain the following quadratic equation.

\[
\left( ar\gamma + \alpha a + \omega a \right) S^2 + \left( k\delta + (a +\alpha \omega) + \alpha \gamma - \rho \gamma - \alpha\mu - 2\mu\omega \right) S + \left( \omega \mu^2 - \gamma \mu - \frac{\mu\omega k\delta}{d} \right) = 0.
\]
If \( k \delta - d (\mu - \alpha S) > 0 \) and \( d (\mu - \alpha S) - \beta \delta > 0 \), then \( y_2 = \left( S_s, \frac{\delta}{y}, \frac{k \delta - d (\mu - \alpha S_s)}{\beta \delta - d}, \frac{d (\mu - \alpha S_s) - \beta \delta}{\beta \delta} \right) \) is another equilibrium point of the system (1) where \( S_s \) is the positive root of the above quadratic equation.

In the following, we consider the stability property of these points.

At first consider it for \( y_1^* \). Here we check the sign of the eigenvalues of Jacobi matrix of the system (1) at \( y_1^* \).

From the formula (4) we have

\[
J(y_1^*) = \begin{bmatrix}
-\alpha - A & 0 & -B & 0 \\
A & -\beta - B & -vI_s \\
-A & k & -\gamma - B & 0 \\
0 & 0 & 0 & dI_s - \delta
\end{bmatrix}
\]

where \( I_s = \frac{\mu - \alpha S_s}{\beta} \), \( A = aV_s (1+\omega V_s) \)

\[
(1+\rho S_s + \omega V_s)^2, \quad B = \frac{aS_s (1+\rho S_s)}{(1+\rho S_s + \omega V_s)^2} \quad \text{and} \quad V_s = \frac{1}{(1+\rho S_s + \omega V_s)^2}.
\]

We calculate the eigenvalues of \( J(y_1^*) \) as follows:

\[
\det(xI_{4 \times 4} - J(y_1^*)) = \begin{vmatrix}
x + \alpha + A & 0 & B & 0 \\
-A & x + \beta - B & -vI_s \\
A & -k & x + \gamma + B & 0 \\
0 & 0 & 0 & x + \delta - dI_s
\end{vmatrix} = (x + \delta - dI_s)[x^3 + (\alpha + \gamma + \beta + A + B)x^2 + \beta \gamma ((\beta - k + \alpha)B + (\beta + \gamma)(\alpha + A)]x + (\beta \alpha \gamma (\beta - k \alpha)B + (\beta + \gamma)A)] = 0.
\]

Thus one of the roots is \( x = dh_0 - \delta \). The other roots are given by

\[
x^3 + q_2x^2 + q_1x + q_0 = 0.
\]

Here \( q_2 = \alpha + \gamma + \beta + A + B \),

\( q_1 = \beta \gamma ((\beta - k + \alpha)B + (\beta + \gamma)(\alpha + A) \) and \( q_0 = \beta \alpha \gamma (\beta - k \alpha)B + (\beta + \gamma)A \).

By substituting the value of \( A, B \) and \( V_s \) in \( q_2, q_1 \) and \( q_0 \), we will see that \( q_2, q_1 \) and \( q_0 \) are positive. Moreover, it is easy to see that, \( q_2, q_1, q_0 > 0 \). By the Routh Hurwitz Criteria, all roots of the cubic polynomial have negative real part. If \( I_s < \frac{\delta}{d} \) or

\[
(d \mu - \beta \delta) - \alpha d S < 0, \quad \text{then real part of all of the eigenvalues are negative. Therefore the point} \ y_1^* \ \text{is locally asymptotically stable.}
\]

Now we consider the stability property of the other equilibrium point, \( y_2 \). From the formula (4) we have

\[
J(y_2) = \begin{bmatrix}
-\alpha - A & 0 & -B & 0 \\
A & -\beta - vZ_s & B & -\frac{\delta}{d} \\
-A & k & -\gamma - B & 0 \\
0 & dZ_s & 0 & 0
\end{bmatrix},
\]

where \( I_s = \frac{\delta}{d}, \quad Z_s = \frac{d (\mu - \alpha S_s) - \beta \delta}{\beta \delta} \), \( A = aV_s (1+\omega V_s) \)

\[
(1+\rho S_s + \omega V_s)^2, \quad V_s = \frac{1}{(1+\rho S_s + \omega V_s)^2} \quad \text{and} \quad B = \frac{aS_s (1+\rho S_s)}{(1+\rho S_s + \omega V_s)^2}.
\]

The eigenvalues of the matrix \( J(y_2) \) are given by the algebraic equation,

\[
\det(xI_{4 \times 4} - J(y_2)) = \begin{vmatrix}
x + \alpha + A & 0 & B & 0 \\
-A & x + \beta + vZ_s & -B & -\frac{\delta}{d} \\
A & -k & x + \gamma + B & 0 \\
0 & -dZ_s & 0 & x
\end{vmatrix} = 0,
\]

or

\[
x[(x + \alpha + A)((x + \beta + vZ_s)(x + \gamma + B) - kB) + B(kA - A(x + \beta + vZ_s))] - dZ_s[\frac{\delta}{d}AB - \frac{\delta}{d}(x + \alpha + A)(x + \gamma + B)] = 0.
\]

Then from the above equation we get

\[
x^3 + (\alpha + \beta + \gamma + B + vZ_s + A)x^2 + (\beta(\alpha + \gamma + \alpha + \gamma + \beta + \gamma)(\alpha + A)]x + (\beta \alpha \gamma (\beta - k \alpha)B + (\beta + \gamma)A)] = 0.
\]

By considering the value of \( Z_s \), it follows that all of the coefficients of the above equation are positive, then from Routh Hurwitz Criteria we see that all of the roots have negative real parts. Therefore we have the following theorem.

**Theorem 3.2.** For \( \eta = 0, d \neq 0 \) and \( R_0 > 1 \), we have the following results.

1) If \( d \mu - \beta \delta \leq 0 \), the equilibrium points \( y_0 \) and \( y_1^* \) are the only rest points of the system (1), then \( y_0 \) is unstable and \( y_1^* \) is locally asymptotically stable.

2) If \( d \mu - \beta \delta > 0 \), then for \( S_s > \frac{d \mu - \beta \delta}{\alpha d} \), the equi-
librium \( y_1' \), is locally asymptotically stable and for
\[ S < \frac{d \mu - \beta \delta}{\alpha d} \]
then it becomes unstable. If \( k \delta - d \mu < 0 \),
y\(_0\) and \( y_1' \) are the only two rest points of the system (1) and \( y_2 \) does not exist.

3) If \( d \mu - \beta \delta > 0 \) and \( \frac{d \mu - k \delta}{\alpha d} < S < \frac{d \mu - \beta \delta}{\alpha d} \),
then the equilibrium \( y_2 \) exists and is locally asymptotically stable. Moreover the equilibrium points \( y_0 \) and \( y_1' \) are unstable.

**Remark 3.2.** If \( d \mu - \beta \delta \leq 0 \), the point \( y_2 \) does not exist, therefore the point \( y_1' \) is the only endemic equilibrium point of the system (1). Also, for \( d \mu - \beta \delta > 0 \) and \( S > \frac{d \mu - \beta \delta}{\alpha d} \), the point \( y_1' \) is the only endemic equilibrium point.

**Remark 3.3.** 1) From continuous dependent of the equilibrium points and eigenvalues to the parameters, Theorem 3.1 and 3.2 must be valued for \( c_i > 0 \) and small.

2) For the case, \( c_i \neq 0 \) and large, if \( R_0 < 1 \), the point
\[ y_0 = \left( \frac{c_i}{\alpha}, 0, 0, 0 \right) \]
is the unique equilibrium of the system (1) which is globally asymptotically stable. If \( R_0 > 1 \), the system (1) has a unique endemic equilibrium point, \((S', I', V', Z')\) satisfying in the equations
\[ V = \left( \mu - \alpha S \right) \left( 1 + \rho S \right) \]
\[ I = \left( \frac{\mu - \alpha S}{k} \right) \left( \frac{\gamma (1 + \rho S)}{(a + \omega \alpha) s - \omega \mu} + 1 \right) \]
and the last equation of the upper table. Here stability property of this point is not shown.

### 4. Numerical Simulation

For the following numerical simulations, we use parameters of T-cells as the parameters of immune cells, those are \( \mu = 80 \text{ cell/(day \cdot ml)} \), \( \alpha = \frac{1}{3} \) days. The estimated value of \( \eta \) is obtained by assuming that the equilibrium value of the density of immune cells in the absence of infection is 2000 cells.

In this model the endemic status of the disease depends on the individual response toward incoming viruses. The larger the invasion rate \( \alpha \), the chance is higher to catch the disease. On the contrary the increase of the elimination rate \( \nu \) of infected cell, the risk of infection is lower.

For \( \rho = \omega = 1, \frac{1}{\delta} = 1 \gamma, \eta = 0.265 \text{ cell/(day \cdot ml)} \), \( \beta = 0.5, \gamma = 0.8, c = 0.01, k = 20, \nu = 0.001, d = 0.03 \), we have

For \( \rho = 1, \omega = 0 \) we obtain the same result in the above table.

If \( \rho = 0, \omega = 1 \) then for the same value of parameters we have the following table.

### 5. Conclusions

In order to understand the main characteristic of Dengue mystery, the author in [4] assumed that this virus can be eliminated by immune response which is described by the last equation of the system (1).

By using linear incidence rate of susceptible and free virus particle, they analyzed the existence of the endemic virus equilibria.

In this paper, from the analysis of the endemic equilibria it is found that, for Beddington DeAngelis incidence rate of susceptible and free virus particle, the same results are valid.

The reason for this correspondence is that in both models, the feature of the immune response is described by the term \( \eta + cI + dIZ \). However, the parameter \( \rho \) in Beddington Deangles makes the elimination of dengue virus by immune response in a shorter time. This fact can be seen by comparing Tables 1 and 2.

**Table 1. Status of equilibrium points of system (1) in the case \( \rho = \omega = 1 \).**

<table>
<thead>
<tr>
<th>( a )</th>
<th>( R_0 )</th>
<th>Equilibria points</th>
<th>Status of stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.001</td>
<td>0.2041</td>
<td>( y_0 = (240,0,0,0) )</td>
<td>Globally stable</td>
</tr>
<tr>
<td>0.002</td>
<td>0.2885</td>
<td>( y_0 = (240,0,0,0) )</td>
<td>Globally stable</td>
</tr>
<tr>
<td>0.003</td>
<td>0.3531</td>
<td>( y_0 = (240,0,0,0) )</td>
<td>Globally stable</td>
</tr>
</tbody>
</table>

**Table 2. Status of equilibrium points of system (1) in the case \( \rho = 0, \omega = 1 \).**

<table>
<thead>
<tr>
<th>( a )</th>
<th>( R_0 )</th>
<th>Equilibria points</th>
<th>Status of stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.001</td>
<td>2.7811</td>
<td>( y_0 = (239.3557,0.3599,0.7292,0) )</td>
<td>Unstable</td>
</tr>
<tr>
<td>&amp;</td>
<td></td>
<td>( y_1 = (239.3557,0.3599,0.7292,0) )</td>
<td>Not exist</td>
</tr>
<tr>
<td>&amp;</td>
<td></td>
<td>( y_2 = (240,0,0,0) )</td>
<td>Un stable</td>
</tr>
<tr>
<td>0.002</td>
<td>3.5452</td>
<td>( y_0 = (238,6419,0.7586,18.400,0) )</td>
<td>Unstable</td>
</tr>
<tr>
<td>&amp;</td>
<td></td>
<td>( y_1 = (238,6419,0.7586,18.400,0) )</td>
<td>Not exist</td>
</tr>
<tr>
<td>&amp;</td>
<td></td>
<td>( y_2 = (240,0,0,0) )</td>
<td>Un stable</td>
</tr>
<tr>
<td>0.003</td>
<td>3.9844</td>
<td>( y_0 = (237.9324,1.1549,28.0127,0) )</td>
<td>Unstable</td>
</tr>
<tr>
<td>&amp;</td>
<td></td>
<td>( y_1 = (237.9324,1.1549,28.0127,0) )</td>
<td>Not exist</td>
</tr>
</tbody>
</table>
By Theorem 2.2, if the basic reproduction number, $R_0$ is less than one, then uninfected equilibrium point, $y_0$ is the only steady state point of system (1) and it is globally asymptotically state. This means that the virus is eliminated by immune response. For larger values of $\eta$ and $\rho$, $R_0$ is more attractor and the virus is cleared much faster.

If the basic reproduction number, $R_0$ is more than one; for $c_i = 0$, besides of the uninfected steady state $y_0$, which is uninfected, there are some infected steady state. Here we consider two cases of endemic virus.

First, for $c = d = 0$, we have only one infected endemic $y_1$. If $\eta = 0$, there is no immune response, so the density of susceptible monocytes equal zero. In $\eta \neq 0$, this density equals $\frac{\eta}{\delta}$, so it does not depend on the other parameters for virus load of infected cell. For larger values of $\beta$ and $\rho$, the infected endemic $y_1$ is closer to the uninfected endemic $y_0$ and it is more controllable.

Second, for $c = \eta \neq 0$ and $d \neq 0$, from Theorem 3.2 we see that if $d \mu - \beta \delta$ is negative or positive small, then there is only one infected endemic equilibrium $y'_1$ which is stable. However if $d \mu - \beta \delta$ is positive and large, then the endemic virus equilibrium $y_2$ exists and is stable. This means that we found a new threshold $R_0$. For condition $R_0$ is less than this threshold the dynamic of the model is qualitatively same as the case $c = d = 0$. When $R_0$ is greater than this threshold, we have a new endemic virus equilibrium, $y_2$ which is stable and the equilibrium points $y_0$ and $y'_1$ are unstable. From the components of the endemic equilibrium $y_2$ we see that after the onset of the symptom, if $d$ increases, the $V$ and $I$ components of equilibria decrease and the $S$ and $Z$-components of equilibria will increase. Conversely, if $a$ and $\rho$ increase, the $V$ and $I$-components of equilibria will decrease but the virus load increases at the initial viral infection.

For case $c_i \neq 0$ and large and $R_0 > 1$, the model has a unique endemic virus. The $V$ and $I$ components of this equilibrium point decrease as $a$ increases and the $S$ and $Z$-components of it increase as $d$ increases.

Therefore, $d,a$ and $\rho$ are the important parameters to capture the phenomena that dengue virus is quickly cleared in a shorter time.

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REFERENCES


