Numerical Modeling of Dengue Disease with Incubation Period of Virus

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Abstract

Now a days, Numerical models have great importance in epidemiology. It helps us to understand the transmission dynamics of infectious diseases in a very comprehensive way. In disease epidemiology, vector-host models are important because many diseases are spreading through vectors. Mosquitoes are vectors of dengue disease which spread the disease in a population. The infectious vectors infect the hosts while infectious hosts infect to vectors. Two main groups of dengue patients are Infected and Infectious. The susceptible mosquitoes can get dengue infection from infectious humans but not from infected ones. Humans can be categorized into Susceptible, infected, infectious and recovered ones while mosquitoes are susceptible, infected and infectious. Susceptible individual can transfer dengue infection from diseased mosquitoes only. The transmission dynamics of “Dengue Fever” with incubation period of virus has been analyzed in this paper. Using standard methods for analyzing a system, the stability of equilibrium points of the model has been determined. Finally a numerical model has been constructed for the same problem and numerical experiments are performed for different values of discretization parameter h. Results are compared with well-known numerical scheme i.e. Runge-Kutta method of order four (RK4). Unlike RK4 which fails for large time steps, the developed scheme gives results that converged to true steady states for any time step used.

Key Words: Dengue Virus; Incubation Period; Numerical Modeling; Stability

1. Introduction

Recently, diseases caused by Dengue virus have become major health problem in the world [1]. Most probably these diseases are found in tropical areas and also found in some sub-tropical areas [2]. These diseases are found in the following countries America, Africa, Western Pacific, South Asia and Eastern Mediterranean. Before 1970 there were only nine countries which were affected by the Dengue Disease but after 1995 it increased four times. Until 2001 there were 609,000 patients affected by this disease. This number of patients is double to the figure as in 1995. Now major population of the world is at risk due to this disease. World Health Organization estimated that 49M (Millions) patients can be affected each year by this disease. The attack rates of this disease is 40-50% can reach up to 80%-90% very soon. The dengue disease can be classified into three different types which are Dengue fever, Dengue hemorrhagic fever and Dengue shock syndrome. These types have different symptoms.

Dengue Fever symptoms are less in appearance in case of children’s while these appear in case of young and grown up children. Dengue hemorrhagic fever is one of the complex diseases which can turn into fatal condition. This type of disease occurs to the patient when a patient is prone to the dengue virus more than once. Dengue shock syndrome (DSS) is a severe type of which can lead the patient to the hospitalization.

1.1 Causes

It can be caused by following types of viruses: DEN (1 to 4)

1.2 Transmission

The main cause of Dengue disease is Aedes mosquito. After biting the infected human, it becomes infected with this disease and then that disease will be transmitted to other human beings. There are two types of Aedes mosquitoes which cause this disease. These types are: Aedes aegypti and Aedes albopictus. The transmission cycle of dengue virus by the mosquito Aedes aegypti begins
with a dengue infectious person. Most of these people will have virus circulating in the blood (viremia) that lasts for about four to seven days [3,4]. Dengue cannot be transmitted directly from one person to another person. It needs a mosquito as transmitter from one person to another. Mosquitoes are only infected by this disease by biting an infected person. Virus replicates within the mosquito during the incubation period of 8-12 days. After this, glands of mosquito become infected and then virus of this disease will be transmitted to other person after biting that person. Then virus replicates in this newly infected person during the incubation period [5].

1.3 Symptoms

Its Symptoms are 4 to 7 days fever after a person has been attacked by mosquito infected with virus. Symptoms are severe headache, retro-orbital pain nausea, muscle and joint pain, rashes, vomiting and high fever. DHF includes all symptoms of dengue fever with some additional symptoms which are bleeding from the nose, gums, or under the skin. It is severe form of dengue which can lead to death.

2. Model Formation

2.1 Assumption

- The number of human and mosquito remains same.
- DEN virus effete gets permanent protection from the particular virus but becomes sensitive for others.
- Death and birth rate of human and mosquito goes on side by side.

Variables for model are:

- $S_h(t)$: Susceptible individuals with in time $t$
- $X_h(t)$: Infected individuals with in time $t$
- $I_h(t)$: Infectious individuals with in time $t$
- $R_h(t)$: Recovered individuals with in time $t$
- $S_v(t)$: Susceptible mosquitoes with in time $t$
- $X_v(t)$: Infected mosquitoes with in time $t$
- $I_v(t)$: Infectious mosquitoes with in time $t$

2.2 Mathematical Model

The transmission of dengue virus is shown by following flow chart [6].

The following equations describe transmission dynamics of Dengue infection in human and vector populations:

$$
\begin{align*}
\frac{dS_h}{dt} &= \lambda N_T - \beta_h S_h I_v - \mu_S S_h \\
\frac{dX_h}{dt} &= \beta_h S_h I_v - \alpha_h X_h - \mu_X X_h \\
\frac{dI_h}{dt} &= \alpha_h X_h - r I_h - \mu_I I_h \\
\frac{dR_h}{dt} &= r I_h - \mu_R R_h \\
\frac{dS_v}{dt} &= C - \beta_v I_h S_v - \mu_S S_v \\
\frac{dX_v}{dt} &= \beta_v I_h S_v - \alpha_v X_v - \mu_X X_v \\
\frac{dI_v}{dt} &= \alpha_v X_v - \mu_I I_v \\
\end{align*}
$$

with conditions:

$$N_T = S_h + X_h + I_h + R_h$$

and

$$N_v = S_v + X_v + I_v$$

Where

- $N_T$: Total human population
- $\lambda$: Birth rate of human population
- $\beta_h$: Infectious rate of dengue virus from vector to human population
- $\alpha_h$: Rate of changing the infected human population to infectious human population
- $\beta_v$: Infectious rate of dengue virus from human to vector population
- $\mu_h$: Death rate of human population
- $R$: Recovery rate of human population
\[ C : \text{Constant recruitment rate of the vector population} \]
\[ \alpha_v : \text{Death rate of vector population} \]

As \( N_T \) and \( N_v \) are constant, so,
\[
\frac{dN_T}{dt} = 0 \quad \text{and} \quad \frac{dN_v}{dt} = 0
\]

which implies that \( \lambda = \mu_h \)

Now for vector population
\[
\frac{dN_v}{dt} = \frac{d}{dt}(S_v + X_v + I_v)
\]
\[
\frac{dN_v}{dt} = C - \mu_v S_v + \mu_v X_v - \mu_v I_v
\]
\[
0 = C - \mu_v S_v + \mu_v X_v - \mu_v I_v
\]
\[
0 = C - \mu_v S_v + \mu_v X_v - \mu_v I_v
\]
\[
0 = C - \mu_v S_v + \mu_v X_v - \mu_v I_v
\]

For normalization of system (1), we let
\[
S = \frac{S_h}{N_T}, X = \frac{X_h}{N_T}, I = \frac{I_h}{N_T}, R = \frac{R_h}{N_T}
\]
\[
S_v = \frac{S_v}{N_T}, X_v = \frac{X_v}{N_T}, I_v = \frac{I_v}{N_T}
\]

The system of differential equation for transmission dynamics of Dengue fever in normalized form is
\[
\frac{dS}{dt} = \mu_h - \beta_h S \frac{C}{\mu_v} - \mu_h S
\]
\[
\frac{dX}{dt} = \beta_h S \frac{C}{\mu_v} - \alpha_h X - \mu_h X
\]
\[
\frac{dI}{dt} = \alpha_h X - r_l - \mu_h I
\]
\[
\frac{dX_v}{dt} = \beta_h S \frac{C}{\mu_v} - \alpha_v X_v - \mu_v X_v - \mu_v I_v
\]
\[
\frac{dI_v}{dt} = \alpha_v X_v - \mu_v I_v
\]

With the conditions
\[ S + X + I + R = 1 \quad \text{and} \quad S_v + X_v + I_v = 1 \]

### 2.3 Equilibrium Points

The system has two possible equilibrium points i.e., the Disease Free Equilibrium (DFE) and Endemic Equilibrium (EE).

**Disease Free Equilibrium:**
\[ V_0 (1,0,0,0,0) \]

**Endemic Equilibrium:**
\[ V_1 (S^*, X^*, I^*, X_v^*, I_v^*) \]

Where
\[
S^* = \frac{(\alpha_v + \mu_v)(MN\mu_2^2 \mu_v + \alpha_h \gamma_v \mu_h)}{\alpha_h \gamma_v \mu_h + \alpha_v \gamma_h}
\]
\[
X^* = \frac{M \mu_2^2 \mu_v (\alpha_v + \mu_v)(E_0 - 1)}{\alpha_h \mu_v (\alpha_v + \mu_v) + \alpha_v \gamma_h}
\]
\[
I^* = \frac{\mu_h \mu_v (\alpha_v + \mu_v)(E_0 - 1)}{\alpha_h \mu_v (\alpha_v + \mu_v) + \alpha_v \gamma_h}
\]
\[
X_v^* = \frac{\mu_v (MN \mu_3^2 \mu_v)(E_0 - 1)}{\gamma_h \alpha_v (\alpha_h \gamma_v \mu_h + MN \mu_2^2 \mu_v)}
\]
\[
l_v^* = \frac{MN \mu_3^2 \mu_v}{\gamma_h (\alpha_h \gamma_v \mu_h + MN \mu_2^2 \mu_v)} (E_0 - 1)
\]

Where
\[
E_0 = \frac{\alpha_h \alpha_v \gamma_h \gamma_v}{(r + \mu_h)(\alpha_h + \mu_h)(\mu_v (\alpha_v + \mu_v))}
\]
\[
\gamma_h = \beta_h \left( \frac{C}{\mu_v} \right), \quad \gamma_v = \beta_v \frac{N_T}{\mu_h}
\]

### 3. RK4 Scheme

\[ k_1 = h \left\{ \mu_h - \beta_h S^n v^n \left( \frac{C}{\mu_v} \right) - \mu_h S^n \right\} \]
\[ P_1 = h \left\{ \beta_h S^n v^n \left( \frac{C}{\mu_v} \right) - \alpha_h X^n - \mu_h X^n \right\} \]
\[ m_1 = h (\alpha_h X^n - r_l^n - \mu_h X^n) \]
\[ n_1 = h (\beta_h l^n T(1 - X_v^n - I_v^n) - \alpha_v X_v^n - \mu_v X_v^n) \]
\[ O_1 = h (\alpha_v X_v^n - \mu_v I_v^n) \]
Numerical Experiments

Numerical experiments are performed using values of parameters given in Table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value (day⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N_r )</td>
<td>5,000</td>
</tr>
<tr>
<td>( \alpha_k )</td>
<td>1/5</td>
</tr>
<tr>
<td>( \beta_k )</td>
<td>0.00005</td>
</tr>
<tr>
<td>( \mu_k )</td>
<td>0.0000391</td>
</tr>
<tr>
<td>( \alpha_v )</td>
<td>1/10</td>
</tr>
<tr>
<td>( \beta_v )</td>
<td>0.00008</td>
</tr>
<tr>
<td>( \mu_v )</td>
<td>1/14</td>
</tr>
<tr>
<td>( r )</td>
<td>1/14</td>
</tr>
<tr>
<td>( C ) (DFE)</td>
<td>3.00</td>
</tr>
<tr>
<td>( C ) (EE)</td>
<td>300</td>
</tr>
</tbody>
</table>

Fig. 2 DFE (Susceptible Human Fraction)

Fig. 3 DFE (Infected Human Fraction)
Numerical Modeling of Dengue Disease with Incubation Period of Virus

Fig. 4  DFE (Infectious Human Fraction)

Fig. 5  DFE (Infected Vector Fraction)

Fig. 6  DFE (Infectious Vector Fraction)

Fig. 7  DFE (h=10 days)

Fig. 8  DFE (h=13 days)

Fig. 9  DFE (h=15 days)

Fig. 10 EE (Susceptible Human Fraction)

Fig. 11 EE (Infected Human Fraction)
In this section we shall construct Non-Standard Finite Difference scheme (NSFD) for the normalized continuous dynamical system (2)-(6). First order time derivatives are described by using forward difference approximation [7,8]: $f(t)$ can be approximated as:

$$\frac{df(t)}{dt} = \frac{f(t + l) - f(t)}{l} + O(l) \quad \text{as} \quad l \to 0$$

where $S^n, I^n$ and $R^n$ are the approximations of $S(nl), I(nl)$ and $R(nl)$, for $n = 0, 1, 2, \ldots$ and where ‘$l$’ is step size of time. For satisfying biological nature of the continuous time model, $S^n, I^n$ and $R^n$ should be non-negative. The numerical method which has been developed to solve the system must hold Conservation law proposed by Mickens [9, 10]. Thus the NSFD scheme for system (1) will become

$$\frac{S^{n+1} - S^n}{l} = \mu_h - \beta_h S^n I^n T \left( \frac{C}{\mu_c} \right) - \mu_h S^{n+1} \quad (7)$$

$$\frac{X^{n+1} - X^n}{l} = \beta_h S^n I^n T \left( \frac{C}{\mu_c} \right) - \alpha_h X^n + \mu_h X^{n+1} \quad (8)$$

$$\frac{[I^{n+1} - I^n]}{l} = \alpha_h X^n - \mu_h I^{n+1} \quad (9)$$

$$\frac{[X^{n+1} - X^n]}{l} = \beta_h N_T I^n T (1 - X^n - I^n) - \alpha_h X^n I^n T \left( \frac{C}{\mu_c} \right) - \mu_h X^{n+1} \quad (10)$$

From (7)

$$S^{n+1} = [\mu_h + \beta_h S^n I^n T \left( \frac{C}{\mu_c} \right)] S^n - \mu_h S^{n+1}$$

$$I^{n+1} = \alpha_h X^n - \mu_h I^{n+1}$$

$$X^{n+1} = \beta_h N_T I^n T (1 - X^n - I^n) - \alpha_h X^n I^n T \left( \frac{C}{\mu_c} \right) - \mu_h X^{n+1}$$
\[ S^{n+1} = \frac{l \mu_h + S^n}{1 + l[\beta_h (V/c + \mu) l^n + \mu_h]} \]  

From (8)

\[ X^{n+1} = \frac{l \beta_h S^{n+1} l^n \left( \frac{C}{\mu} \right) - l \alpha_h X^{n+1} - l \mu_h X^{n+1} + X^n}{1 + l[\alpha_h + \mu_h]} \]  

\[ X^{n+1} = \]  

Form (9)

\[ l^{n+1} - l \alpha_h X^{n+1} - l \mu_l^{n+1} + l^n \]

\[ l^{n+1} = \frac{l \alpha_h X^{n+1} + l^n}{1 + l[l + \mu_h]} \]  

Form (10)

\[ X_{n+1} = l \beta_v N_T l^{n+1} (1 - X_{n+1} - l X_{n+1} + l X_{n+1} - l \mu_v X_{n+1} - X^n + X_v^n) \]

\[ X_{n+1} = \]  

Form (11)

\[ l_{n+1} = l X_{n+1} + l l_{n+1} + l^n \]

\[ l_{n+1} = \frac{l \alpha X_{n+1} + l^n}{1 + l[l + \mu_v]} \]  

4.1 Convergence Analysis:

The stability and convergence of the proposed NSFD scheme about disease free equilibrium point \( V_0 (1,0,0,0,0) \) are discussed here. Let

\[ F_1 = S^{n+1} = \frac{l \mu_h + S^n}{1 + l[\beta_h \left( \frac{C}{\mu} \right) l^n + \mu_h]} \]

\[ F_2 = X^{n+1} = \frac{l \beta_h S^{n+1} l^n \left( \frac{C}{\mu} \right) - l \alpha_h X^{n+1} - l \mu_h X^{n+1} + X^n}{1 + l[\alpha_h + \mu_h]} \]

\[ F_3 = l^{n+1} = \frac{l \alpha_h X^{n+1} + l^n}{1 + l[l + \mu_h]} \]

\[ F_4 = X_{n+1} = \frac{l \beta_v N_T l^{n+1} (1 - l_{n+1} + X^n)}{1 + l[\beta_v N_T l^n + \alpha_v + \mu_h]} \]

\[ F_5 = l_{n+1} = \frac{l \alpha X_{n+1} + l^n}{1 + l[l + \mu_v]} \]

And the Jacobian matrix is

\[ j(F^*) = \begin{bmatrix} \frac{\partial F_1}{\partial S} & \frac{\partial F_1}{\partial X} & \frac{\partial F_1}{\partial l} & \frac{\partial F_1}{\partial X_v} & \frac{\partial F_1}{\partial l_v} \\ \frac{\partial F_2}{\partial S} & \frac{\partial F_2}{\partial X} & \frac{\partial F_2}{\partial l} & \frac{\partial F_2}{\partial X_v} & \frac{\partial F_2}{\partial l_v} \\ \frac{\partial F_3}{\partial S} & \frac{\partial F_3}{\partial X} & \frac{\partial F_3}{\partial l} & \frac{\partial F_3}{\partial X_v} & \frac{\partial F_3}{\partial l_v} \\ \frac{\partial F_4}{\partial S} & \frac{\partial F_4}{\partial X} & \frac{\partial F_4}{\partial l} & \frac{\partial F_4}{\partial X_v} & \frac{\partial F_4}{\partial l_v} \\ \frac{\partial F_5}{\partial S} & \frac{\partial F_5}{\partial X} & \frac{\partial F_5}{\partial l} & \frac{\partial F_5}{\partial X_v} & \frac{\partial F_5}{\partial l_v} \end{bmatrix} \]

Where as:

\[ \frac{\partial F_1}{\partial S} = \frac{1}{1 + l \mu_h}, \frac{\partial F_1}{\partial X} = 0, \frac{\partial F_1}{\partial l} = 0, \frac{\partial F_1}{\partial X_v} = 0 \]

\[ \frac{\partial F_2}{\partial S} = \frac{-l (l \mu_h + l)}{(1 + l \mu_h)^2} \]

\[ \frac{\partial F_3}{\partial S} = \frac{l \beta_h \left( \frac{C}{\mu} \right)}{1 + l \mu_h}, \frac{\partial F_3}{\partial X} = 0, \frac{\partial F_3}{\partial l} = 0, \frac{\partial F_3}{\partial X_v} = 0 \]

\[ \frac{\partial F_4}{\partial S} = \frac{l \beta_v N_T}{1 + l \mu_v}, \frac{\partial F_4}{\partial X} = 0, \frac{\partial F_4}{\partial l} = 0, \frac{\partial F_4}{\partial X_v} = 0 \]

\[ \frac{\partial F_5}{\partial S} = \frac{l \mu_v}{1 + l \mu_v}, \frac{\partial F_5}{\partial X} = 0, \frac{\partial F_5}{\partial l} = 0, \frac{\partial F_5}{\partial X_v} = 0 \]

We have computed the largest Eigen value of Jacobian matrix for each time step and plotted as follows:
4.2 Numerical Experiments

Numerical experiments are performed using values of parameters given in Table 1.
The Numerical Modelling of transmission dynamics of Dengue Disease with incubation period of virus has been analysed in this paper. The model has two equilibrium points, i.e. Disease Free Equilibrium (DFE) and Endemic equilibrium (EE). An unconditionally convergent non-standard finite difference numerical model has been constructed and numerical experiments are performed for different values of discretization parameter ‘h’. Results are compared with well known numerical method i.e. Runge-Kutta method of order four (RK4). Table 2 shows the effect of different time step, h for both numerical schemes.

Table 2 Comparison of NSFD and RK-4

<table>
<thead>
<tr>
<th>h(\ell)</th>
<th>RK4</th>
<th>Numerical Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Convergence</td>
<td>Convergence</td>
</tr>
<tr>
<td>10</td>
<td>Convergence</td>
<td>Convergence</td>
</tr>
<tr>
<td>100</td>
<td>Divergence(method failed)</td>
<td>Convergence</td>
</tr>
<tr>
<td>1000</td>
<td>Divergence</td>
<td>Convergence</td>
</tr>
</tbody>
</table>

Table shows that the RK-4 method converge for small values of parameter h and it diverges for the large values but our numerical model will remain convergent even for a very large value of discretization parameter i.e., $h = 1000$. 

4. Results and Discussion

Figures 34 and 35 shows the comparison of Non-Standard Finite Difference (NSFD) scheme with Runge-Kutta method of order 4. It can been observed that when step size has been increased upto 13 days, the RK-4 scheme give negative values of infected human fraction and by increasing step size to 15 days the scheme diverges, while the proposed Non-Standard Finite Difference (NSFD) scheme preserves positivity and convergence of the solution for these values of step size. Unlike RK-4 which fails for large time steps, the developed NSFD scheme gives results that converged to true steady states for any time step used. The proposed scheme is easy to implement, numerically stable and shows a good agreement with analytic results produced by P. Pongsumpun et al.[6].

6. Conclusion

Figures 32, 33, 34 and 35 shows the comparison of transmission dynamics of Dengue Disease with incubation period of virus has been analysed in this paper. The model has two equilibrium points, i.e. Disease Free Equilibrium (DFE) and Endemic equilibrium (EE). An unconditionally convergent non-standard finite difference numerical model has been constructed and numerical experiments are performed for different values of discretization parameter ‘h’. Results are compared with well known numerical method i.e. Runge-Kutta method of order four (RK4). Table 2 shows the effect of different time step, h for both numerical schemes.
7. References


