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ANALYTICAL AND NUMERICAL APPROACHES TO SOLVE A SYSTEM OF NONLINEAR ORDINARY DIFFERENTIAL EQUATIONS FOR THE SPREAD OF DENGUE FEVER OF WITH-IN-HOST MODEL

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Abstract

In recent years, many mathematical models have been developed and investigated based on real-life issues in engineering, medicine, agriculture, and many other fields. Moreover, the numerical approach was used to solve it due to its intricacy. However, in reality, this methodology merely offers an approximate solution, which is close to an exact solution but not exact. This article demonstrates how to find the analytical solutions of the system of nonlinear ordinary differential equations precisely by considering the mathematical model for the spread of dengue fever of the with-in-host model. Furthermore, stability analysis and numerical simulation were also provided. Finally, graphs from the analytical method and numerical simulation are compared to assess the solutions of the system's validity. This work may be helpful to many researchers in obtaining an analytical solution to the nonlinear dynamics.

1. Introduction

The Dengue Virus (DENV) causes several devastating vector-borne diseases, including Dengue Fever (DENF). One of the leading causes of death worldwide, DENF is spread to people through the bite of Aedes aegypti mosquitoes. One of the four virus serotypes with DENV:1-4 causes Dengue. These serotypes are parts of the Flavivirus genus including the viruses that cause yellow fever [1].

Currently, 50-100 million people in the world reside in areas where DENV transmission is possible. Once thought to be a summertime illness, DENF has now spread to other regions [2]. As a result, DENF cases have multiplied nearly five times in the last 30 years. This illness' signs and symptoms include a high fever, a headache in the front of the head, pain behind the eyes, joint problems, nausea, and vomiting, among others [3].

In most cases, the primary infection of DENF at the initial state causes asymptomatic or moderate illness and a lifelong immunity to that serotype after the virus clears from the body [4]. However, Dengue Hemorrhagic

Fever (DHF) is a severe illness brought on by secondary infections of DENF [5]. Uncertainty exists in the processes underlying the severity of subsequent dengue infections. According to a theory, a process known as "Antibody-Dependent Enhancement (ADE)" is how cross-reactive antibodies worsen the disease. Antibodies specific to that strain produce when a patient contracts the first dengue strain infection [6].

Even after treating the underlying infection, the body still has long-lived plasma cells that generate antibodies against the original virus strain [7]. When an illness with a second dengue serotype develops, antibodies from the initial infection attach to the secondary infection but do not neutralize it. However, phagocytic cells that release viral protein immune complexes absorb viruses that have not been destroyed and get ill. Due to the ADE, vaccination becomes problematic because if the population is not protected against all strains, they risk contracting more severe illnesses. Therefore, as a result, it is challenging to undertake a vaccine trial that intends to immunize against all four serotypes [8].

Proper care can manage DENF, which is usually a treatable infection. Patients who have feverish symptoms can use acetaminophen as a medication. It is preferable not to use antibiotics, corticosteroids, nonsteroidal anti-inflammatory medications, Aspirin, and Brufen in order to avoid bleeding and gastritis. Patients with DENF, whether proven or suspected, should have their platelets counted. Their hemoglobin levels should be routinely checked on the third day of symptoms, lasting one to two days after defervescence [9] and [10]. Unfortunately, immunization cannot stop dengue infection from occurring. Therefore, tetravalent vaccines have been created and are presently undergoing clinical research.

There have been numerous mathematical studies on DENF. However, only a few of those [11-16] address the dynamics within the host. Each also assumes that the production of target cells (monocytes) is constant. This presumption is true for healthy or non-infected people, although monocyte production can vary greatly, especially during an illness [17-19]. Typically, Macrophage Colony Stimulating Factor, a cytokine secreted by monocytes,

regulates manufacturing. Our model, therefore, also considers the platelet count during the interaction with the virus, in contrast to other research that specifically evaluated the involvement of cytokines and antibodies. Consequently, we recommend investigating the dynamics of the with-in-host epidemic model of DENF with platelet production capacity when extract of papaya leaves therapy is administered to the patients.

We considered the mathematical model on the effect of papaya leaves extracts as a DENF treatment by introducing a new set of differential equations. The innovative aspect of this work is that we solve the mathematical model on the effects of papaya leaf extracts as a DENF treatment using an analytical and numerical technique. The article is structured as follows. In Section 2, we develop a with-in-host mathematical model for immune response and papaya therapy for DENF and review the model in sufficient complexity. Then, in Sections 3 and 4, we investigate the analytical method and stability analysis of the mathematical model employed in Section 2. Next, the numerical simulation of the model is provided in Section 5. Finally, Section 6 provides the conclusion.

2. The Mathematical Model of DENF with-in-host

The model described here considers the host's immune reaction and DENV with-in-host while papaya leaf extract is given to the patients. There are seven sets of first-order nonlinear ODEs explaining the Susceptible Monocytes Cell (SMC) (referred to as WBC), $A(t)$, Infected Monocytes Cells (IMC), $B(t)$, healthy platelets, $P(t)$, infected platelets, $Q(t)$, T immune reactivity, $S(t)$, dengue pathogens, $V(t)$, and papaya leaves extract (treatment), $T(t)$. Biology reveals that before infecting immune cells across the body and infecting humans, DENV targets the human immune system and is initially rejected by cells that are weak to infection. The SMC (η_A) is believed to be continually produced. So, a logical growth rate is used to evaluate it. The virus's success rate in penetrating it determines whether such a healthy SMC becomes infected, as expressed as β_1 per unit of time.

The parameter N, which represents the bloodstream's circulatory release of free virions, is measured. The other parameters involved in a set of equations (1) are described in detail in Table 1, together with their values, and α indicates how soon therapy-induced increases in immune production occur.

Table 1. List of symbols and abbreviations

s_1	10	Source term of SMC [22]
s_2	100	Source term of platelets [10]
$A_{\max}$	3×10^4	Maximum quantities of SMC [10]
$P_{\max}$	45×10^4	Maximum quantities of platelets [10]
η_A	0.1	Replacement of SMC [23]
η_P	0.1	Replacement of platelets [10]
N	500	Number of viruses produced by IMC [8]
β_1	0.0013	Lysing rate of monocyte [8]
β_2	0.5	Lysing rate of platelets [22]
β_3	0.9	Lysing rate of DV [22]
β_4	0.007	The rate at which antibodies destroy viral particles [23]
β_5	0.87	The rate at which papaya leaves destroy viral particles [18]
ξ_1	0.05	Transformation rate of healthy SMC to stronger [23]
ξ_2	0.5	Transformation rate of platelets cells to stronger [22]
μ_A	0.14	The natural death rate of SMC [21]
μ_B	0.14	The death rate of IMC [24]
μ_P	0.11	The natural death rate of platelets [21]
μ_Q	0.01	The death rate of viral platelets [8]
μ_V	3.48	The death rate of viral particles [23]
μ_S	0.009	The death rate of immunity cells [23]
μ_T	0.07	The death rate of papaya leaves [12]
α	2	The rate at which the production of immunity by therapy [10]
f	25	Quantity of papaya leaves per day [10]

The dynamic model of a DENF with papaya leaves therapy is an overview as follows:

$$\left.\begin{aligned}
\frac{dA}{dt} &= s_1 + \eta_A A\left(1 - \frac{A}{A_{\max}}\right) - \beta_1 VA - \mu_A A + \xi_1 TA \\
\frac{dB}{dt} &= \beta_1 AV - \mu_B B \\
\frac{dP}{dt} &= s_2 + \eta_P P\left(1 - \frac{P}{P_{\max}}\right) - \beta_2 VP - \mu_P P + \xi_2 TP \\
\frac{dQ}{dt} &= \beta_2 PV - \mu_Q Q \\
\frac{dS}{dt} &= \gamma P - \mu_S S - \beta_3 SV \\
\frac{dV}{dt} &= N\mu_B B - \beta_1 VA - \beta_2 VP - \beta_4 VS - \beta_5 VT - \mu_V V \\
\frac{dT}{dt} &= \alpha f - \mu_T T
\end{aligned}\right\}. \qquad (1)$$

3. Analytical Approach for the System of NLODE

3.1. Definition

Consider the general linear non-homogeneous system, $\frac{dZ}{dt} = J(t)Z + B$, $Z(t_0) = Z_0$, where both $J(t)$ and B are continuous on some interval I.

3.2. Theorem

Let $\Psi(t)$ *be a fundamental matrix of solution of* $\frac{dZ}{dt} = J(t)Z$. *Then the solution of* $\frac{dZ}{dt} = J(t)Z + B$, $Z(t_0) = Z_0$ *is*

$$Z(t) = \Psi(t)C + \Psi(t)\int_{t_0}^{t} \Psi^{-1}(s)B(s)ds.$$

The NLODE (1) transformed into a linearized system by considering the following steps to obtain an analytical solution:

(i) determine the fixed points of (1),

(ii) identifying the Jacobian matrix at the fixed points.

3.3. Determination of the fixed points for system of equations

The equilibrium values must first be determined to properly comprehend the seven-component model's dynamics. System (1) has some points of equilibrium $E(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T})$ which are obtained by solving the system of equations $\dot{A} = 0, \dot{B} = 0, \dot{P} = 0, \dot{Q} = 0, \dot{S} = 0, \dot{V} = 0, \dot{T} = 0,$ i.e.,

$$s_1 + \eta_A A\left(1 - \frac{A}{A_{\max}}\right) - \beta_1 VA - \mu_A A + \xi_1 TA = 0, \tag{2}$$

$$\beta_1 AV - \mu_B B = 0, \tag{3}$$

$$s_2 + \eta_P P\left(1 - \frac{P}{P_{\max}}\right) - \beta_2 VP - \mu_P P + \xi_2 TP = 0, \tag{4}$$

$$\beta_2 PV - \mu_Q Q = 0, \tag{5}$$

$$\gamma P - \mu_S S - \beta_3 SV = 0, \tag{6}$$

$$N\mu_B B - \beta_1 VA - \beta_2 VP - \beta_4 VS - \beta_5 VT - \mu_V V = 0, \tag{7}$$

$$\alpha f - \mu_T T = 0. \tag{8}$$

On solving the above system of equations, we get the positive equilibrium point of the system (1) as

$$E = (\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T})$$

$$= (1.07023 \times 10^7, 0, 1.35255 \times 10^9, 0, 1.4285 \times 10^{11}, 0, 714.2816).$$

3.4. Identification of the Jacobian matrix at the fixed points

The nonlinear system (1) can be written as:

$$\begin{cases} \dfrac{dA}{dt} = s_1 + \eta_A A\left(1 - \dfrac{A}{A_{\max}}\right) - \beta_1 VA - \mu_A A + \xi_1 TA = f_1(A, B, P, Q, S, V, T), \\ \dfrac{dB}{dt} = \beta_1 AV - \mu_B B = f_2(A, B, P, Q, S, V, T), \\ \dfrac{dP}{dt} = s_2 + \eta_P P\left(1 - \dfrac{P}{P_{\max}}\right) - \beta_2 VP - \mu_P P + \xi_2 TP = f_3(A, B, P, Q, S, V, T), \\ \dfrac{dQ}{dt} = \beta_2 PV - \mu_Q Q = f_4(A, B, P, Q, S, V, T), \\ \dfrac{dS}{dt} = \gamma P - \mu_S S - \beta_3 SV = f_5(A, B, P, Q, S, V, T), \\ \dfrac{dV}{dt} = N\mu_B B - \beta_1 VA - \beta_2 VP - \beta_4 VS - \beta_5 VT - \mu_V V \\ \qquad = f_6(A, B, P, Q, S, V, T), \\ \dfrac{dT}{dt} = \alpha f - \mu_T T = f_7(A, B, P, Q, S, V, T). \end{cases} \tag{9}$$

The nonlinear system (1) can be approximated into a linear system as follows:

$$\begin{cases} \dfrac{dA}{dt} = f_1(A, B, P, Q, S, V, T) \approx f_1(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\ \qquad + \dfrac{\partial f_1}{\partial A}(A - \overline{A}) + \dfrac{\partial f_1}{\partial B}(B - \overline{B}) + \dfrac{\partial f_1}{\partial P}(P - \overline{P}) + \dfrac{\partial f_1}{\partial Q}(Q - \overline{Q}) \\ \qquad + \dfrac{\partial f_1}{\partial S}(S - \overline{S}) + \dfrac{\partial f_1}{\partial V}(V - \overline{V}) + \dfrac{\partial f_1}{\partial T}(T - \overline{T}), \\ \dfrac{dB}{dt} = f_2(A, B, P, Q, S, V, T) \approx f_2(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\ \qquad + \dfrac{\partial f_2}{\partial A}(A - \overline{A}) + \dfrac{\partial f_2}{\partial B}(B - \overline{B}) + \dfrac{\partial f_2}{\partial P}(P - \overline{P}) + \dfrac{\partial f_2}{\partial Q}(Q - \overline{Q}) \\ \qquad + \dfrac{\partial f_2}{\partial S}(S - \overline{S}) + \dfrac{\partial f_2}{\partial V}(V - \overline{V}) + \dfrac{\partial f_2}{\partial T}(T - \overline{T}), \\ \dfrac{dP}{dt} = f_3(A, B, P, Q, S, V, T) \approx f_3(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\ \qquad + \dfrac{\partial f_3}{\partial A}(A - \overline{A}) + \dfrac{\partial f_3}{\partial B}(B - \overline{B}) + \dfrac{\partial f_3}{\partial P}(P - \overline{P}) + \dfrac{\partial f_3}{\partial Q}(Q - \overline{Q}) \\ \qquad + \dfrac{\partial f_3}{\partial S}(S - \overline{S}) + \dfrac{\partial f_3}{\partial V}(V - \overline{V}) + \dfrac{\partial f_3}{\partial T}(T - \overline{T}), \end{cases}$$

$$
\begin{cases}
\dfrac{dQ}{dt} = f_4(A, B, P, Q, S, V, T) \approx f_4(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\
\quad + \dfrac{\partial f_4}{\partial A}(A - \overline{A}) + \dfrac{\partial f_4}{\partial B}(B - \overline{B}) + \dfrac{\partial f_4}{\partial P}(P - \overline{P}) + \dfrac{\partial f_4}{\partial Q}(Q - \overline{Q}) \\
\quad + \dfrac{\partial f_4}{\partial S}(S - \overline{S}) + \dfrac{\partial f_4}{\partial V}(V - \overline{V}) + \dfrac{\partial f_4}{\partial T}(T - \overline{T}), \\
\dfrac{dS}{dt} = f_5(A, B, P, Q, S, V, T) \approx f_5(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\
\quad + \dfrac{\partial f_5}{\partial A}(A - \overline{A}) + \dfrac{\partial f_5}{\partial B}(B - \overline{B}) + \dfrac{\partial f_5}{\partial P}(P - \overline{P}) + \dfrac{\partial f_5}{\partial Q}(Q - \overline{Q}) \\
\quad + \dfrac{\partial f_5}{\partial S}(S - \overline{S}) + \dfrac{\partial f_5}{\partial V}(V - \overline{V}) + \dfrac{\partial f_5}{\partial T}(T - \overline{T}), \\
\dfrac{dV}{dt} = f_6(A, B, P, Q, S, V, T) \approx f_6(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\
\quad + \dfrac{\partial f_6}{\partial A}(A - \overline{A}) + \dfrac{\partial f_6}{\partial B}(B - \overline{B}) + \dfrac{\partial f_6}{\partial P}(P - \overline{P}) + \dfrac{\partial f_6}{\partial Q}(Q - \overline{Q}) \\
\quad + \dfrac{\partial f_6}{\partial S}(S - \overline{S}) + \dfrac{\partial f_6}{\partial V}(V - \overline{V}) + \dfrac{\partial f_6}{\partial T}(T - \overline{T}), \\
\dfrac{dT}{dt} = f_7(A, B, P, Q, S, V, T) \approx f_7(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) \\
\quad + \dfrac{\partial f_7}{\partial A}(A - \overline{A}) + \dfrac{\partial f_7}{\partial B}(B - \overline{B}) + \dfrac{\partial f_7}{\partial P}(P - \overline{P}) + \dfrac{\partial f_7}{\partial Q}(Q - \overline{Q}) \\
\quad + \dfrac{\partial f_7}{\partial S}(S - \overline{S}) + \dfrac{\partial f_7}{\partial V}(V - \overline{V}) + \dfrac{\partial f_7}{\partial T}(T - \overline{T}).
\end{cases}
\tag{10}
$$

At the fixed points,

$$f_i(\overline{A}, \overline{B}, \overline{P}, \overline{Q}, \overline{S}, \overline{V}, \overline{T}) = 0, \text{ where } i = 1, 2, 3, 4, 5, 6, 7.$$

Thus the system (10) can be written as

$$\begin{cases} A' = a_{11}(A-\overline{A}) - \beta_1 A(V-\overline{V}) + \xi_1 A(T-\overline{T}), \\ B' = \beta_1(A-\overline{A}) - \mu_B(B-\overline{B}) + \beta_1 A(V-\overline{V}), \\ P' = a_{33}(P-\overline{P}) - \beta_2 P(V-\overline{V}), \\ Q' = \beta_2 V(P-\overline{P}) - \mu_Q(Q-\overline{Q}) + \beta_2 P(V-\overline{V}), \\ S' = \gamma(P-\overline{P}) - \mu_S - \beta_3(S-\overline{S}) - \beta_3 S(V-\overline{V}), \\ V' = -\beta_1 V(A-\overline{A}) + N\mu_B(B-\overline{B}) - \beta_2 V(P-\overline{P}) \\ \qquad - \beta_4 V(S-\overline{S}) + a_{66}(V-\overline{V}) - \beta_5 V(T-\overline{T}), \\ T' = -\mu_T(T-\overline{T}), \end{cases} \tag{11}$$

where

$$a_{11} = \eta_A - \frac{2A\eta_A}{A_{\max}} - \mu_A + \xi_1 T, \quad a_{33} = \eta_P - \frac{2P\eta_P}{P_{\max}} - \mu_P + \xi_2 T,$$

$$a_{66} = -\beta_1 A - \beta_2 P - \beta_4 S - \beta_5 T - \mu_V.$$

As a result, the system (11) is linear. In matrix form, it can be shown as

$$\begin{pmatrix} A' \\ B' \\ P' \\ Q' \\ S' \\ V' \\ T' \end{pmatrix} = \begin{pmatrix} a_{11} & 0 & 0 & 0 & 0 & -\beta_1 A & \xi_1 A \\ \beta_1 V & -\mu_B & 0 & 0 & 0 & \beta_1 A & 0 \\ 0 & 0 & a_{33} & 0 & 0 & -\beta_2 P & \xi_2 P \\ 0 & 0 & \beta_2 V & -\mu_Q & 0 & \beta_2 P & 0 \\ 0 & 0 & \gamma & 0 & -\mu_S - \beta_3 V & -\beta_3 S & 0 \\ -\beta_1 V & N\mu_B & -\beta_2 V & 0 & -\beta_4 V & a_{66} & -\beta_5 V \\ 0 & 0 & 0 & 0 & 0 & 0 & -\mu_T \end{pmatrix} \begin{pmatrix} A-\overline{A} \\ B-\overline{B} \\ P-\overline{P} \\ Q-\overline{Q} \\ S-\overline{S} \\ V-\overline{V} \\ T-\overline{T} \end{pmatrix}. \tag{12}$$

Around the equilibrium point

$$(1.07023\times10^7,\ 0,\ 1.35255\times10^9,\ 0,\ 1.4285\times10^{11},\ 0,\ 714.2816),$$

the linear system (12) can be written using the input variables listed in Table 1.

$$\begin{pmatrix} A' \\ B' \\ P' \\ Q' \\ S' \\ V' \\ T' \end{pmatrix} = \begin{pmatrix} r_{11} & 0 & 0 & 0 & 0 & r_{16} & r_{17} \\ r_{21} & r_{22} & 0 & 0 & 0 & r_{26} & 0 \\ 0 & 0 & r_{33} & 0 & 0 & r_{36} & r_{37} \\ 0 & 0 & r_{43} & r_{44} & 0 & r_{46} & 0 \\ 0 & 0 & r_{53} & 0 & r_{55} & r_{56} & 0 \\ r_{61} & r_{62} & r_{63} & 0 & r_{65} & r_{66} & r_{67} \\ 0 & 0 & 0 & 0 & 0 & 0 & r_{77} \end{pmatrix} \begin{pmatrix} A \\ B \\ P \\ Q \\ S \\ V \\ T \end{pmatrix} + \begin{pmatrix} b_{11} \\ b_{21} \\ b_{31} \\ b_{41} \\ b_{51} \\ b_{61} \\ b_{71} \end{pmatrix}, \tag{13}$$

where

$$b_{11} = -422669, \quad b_{21} = 0, \quad b_{31} = 1.72132 \times 10^{11},$$

$$b_{41} = 0, \quad b_{51} = 2.0361 \times 10^{8}, \quad b_{61} = 0, \quad b_{71} = 49.9997.$$

The fundamental matrix of the system (12) is given by

$$\phi(t) = \begin{pmatrix} v_{11}e^{\lambda_1 t} & v_{12}e^{\lambda_2 t} & v_{13}e^{\lambda_3 t} & v_{14}e^{\lambda_4 t} & v_{15}e^{\lambda_5 t} & v_{16}e^{\lambda_6 t} & v_{17}e^{\lambda_7 t} \\ v_{21}e^{\lambda_1 t} & v_{22}e^{\lambda_2 t} & v_{23}e^{\lambda_3 t} & v_{24}e^{\lambda_4 t} & v_{25}e^{\lambda_5 t} & v_{26}e^{\lambda_6 t} & v_{27}e^{\lambda_7 t} \\ v_{31}e^{\lambda_1 t} & v_{32}e^{\lambda_2 t} & v_{33}e^{\lambda_3 t} & v_{34}e^{\lambda_4 t} & v_{35}e^{\lambda_5 t} & v_{36}e^{\lambda_6 t} & v_{37}e^{\lambda_7 t} \\ v_{41}e^{\lambda_1 t} & v_{42}e^{\lambda_2 t} & v_{43}e^{\lambda_3 t} & v_{44}e^{\lambda_4 t} & v_{45}e^{\lambda_5 t} & v_{46}e^{\lambda_6 t} & v_{47}e^{\lambda_7 t} \\ v_{51}e^{\lambda_1 t} & v_{52}e^{\lambda_2 t} & v_{53}e^{\lambda_3 t} & v_{54}e^{\lambda_4 t} & v_{55}e^{\lambda_5 t} & v_{56}e^{\lambda_6 t} & v_{57}e^{\lambda_7 t} \\ v_{61}e^{\lambda_1 t} & v_{62}e^{\lambda_2 t} & v_{63}e^{\lambda_3 t} & v_{64}e^{\lambda_4 t} & v_{65}e^{\lambda_5 t} & v_{66}e^{\lambda_6 t} & v_{67}e^{\lambda_7 t} \\ v_{71}e^{\lambda_1 t} & v_{72}e^{\lambda_2 t} & v_{73}e^{\lambda_3 t} & v_{74}e^{\lambda_4 t} & v_{75}e^{\lambda_5 t} & v_{76}e^{\lambda_6 t} & v_{77}e^{\lambda_7 t} \end{pmatrix}, \tag{14}$$

$$\begin{cases}
\lambda_1 = -1.67624\times10^{9},\ v_{11} = 1.08205\times10^{-7},\ v_{21} = -1.08205\times10^{-7},\\
v_{31} = 0.00525959,\ v_{41} = -0.00525959,\ v_{51} = 0.999887,\\
v_{61} = 0.0130366,\ v_{71} = 0,\\
\lambda_2 = -484.406,\ v_{12} = 0,\ v_{22} = 0,\ v_{32} = -484.406,\ v_{42} = 0,\\
v_{52} = -0.00165154,\ v_{62} = 0,\ v_{72} = 0,\\
\lambda_3 = -35.6746,\ v_{13} = 1,\ v_{23} = 0,\ v_{33} = 0,\ v_{43} = 0,\ v_{53} = 0,\\
v_{63} = 0,\ v_{73} = 0,\\
\lambda_4 = -0.139419,\ v_{14} = -3.97165\times10^{-10},\ v_{24} = 0.0000242911,\\
v_{34} = -1.4166\times10^{-6},\ v_{44} = -0.0053007,\\
v_{54} = 0.999986,\ v_{64} = 1.0144\times10^{-12},\ v_{74} = 0,\\
\lambda_5 = -0.07,\ v_{15} = 0.000818362,\ v_{25} = 0,\ v_{35} = 0.0760293,\\
v_{45} = 0,\ v_{55} = -0.997105,\ v_{65} = 0,\ v_{75} = 5.44508\times10^{-8},\\
\lambda_6 = -0.01,\ v_{16} = 0,\ v_{26} = 0,\ v_{36} = 0,\ v_{46} = 1,\ v_{56} = 0,\ v_{66} = 0,\ v_{76} = 0,\\
\lambda_7 = -0.009,\ v_{17} = 0,\ v_{27} = 0,\ v_{37} = 0,\ v_{47} = 0,\ v_{57} = 1,\ v_{67} = 0,\ v_{77} = 0.
\end{cases}$$

By variation of constant formula, the analytical solution of the linear system (12) is given by

$$\begin{cases}
A(t) = a_{11} + a_{12}e^{\lambda_1 t} + a_{13}e^{\lambda_3 t} + a_{14}e^{\lambda_4 t} + a_{15}e^{\lambda_5 t},\\
B(t) = a_{21}e^{\lambda_1 t} + a_{22}e^{\lambda_4 t},\\
P(t) = a_{31} + a_{32}e^{\lambda_1 t} + a_{33}e^{\lambda_2 t} + a_{34}e^{\lambda_4 t} + a_{35}e^{\lambda_5 t},\\
Q(t) = a_{41}e^{\lambda_1 t} + a_{42}e^{\lambda_3 t} + a_{43}e^{\lambda_6 t},\\
S(t) = a_{51} + a_{22}e^{\lambda_1 t} + a_{53}e^{\lambda_2 t} + a_{54}e^{\lambda_4 t} + a_{55}e^{\lambda_5 t} + a_{56}e^{\lambda_6 t},\\
V(t) = a_{61}e^{\lambda_1 t} + a_{62}e^{\lambda_4 t},\\
T(t) = a_{71}e^{\lambda_5 t}(e^{\lambda_7 t} - 1),
\end{cases}$$

$$a_{11} = 1.07023\times10^{7},\quad a_{12} = 0.0029,\quad a_{13} = 432912,$$

$a_{14} = -5.33532 \times 10^{-8}$, $a_{15} = -1.07352 \times 10^{7}$, $a_{21} = -0.00296$,

$a_{22} = 0.00326$, $a_{31} = 1.35255 \times 10^{9}$, $a_{32} = 144.031$,

$a_{33} = -1.79202 \times 10^{8}$, $a_{34} = -0.00019$, $a_{35} = -9.97345 \times 10^{8}$,

$a_{41} = -144.031$, $a_{42} = -0.71207$, $a_{43} = 5.50001 \times 10^{7}$,

$a_{51} = 1.42851 \times 10^{11}$, $a_{22} = 27381.3$, $a_{53} = 295959$,

$a_{54} = 134.333$, $a_{55} = 1.30799 \times 10^{10}$, $a_{56} = -1.55932 \times 10^{11}$,

$a_{61} = 356.999$, $a_{62} = 1.36269 \times 10^{-10}$, $a_{71} = -714.28$.

4. Stability Analysis

The linearized system (11) has the following characteristic equation:

$$| J - \lambda I | = \lambda^7 + a_1\lambda^6 + a_2\lambda^5 + a_3\lambda^4 + a_4\lambda^3 + a_5\lambda^2 + a_6\lambda + a_7 = 0, \quad (15)$$

where

$a_1 = 1.67624 \times 10^{9}$, $a_2 = 8.72162 \times 10^{11}$, $a_3 = 2.91662 \times 10^{13}$,

$a_4 = 6.62868 \times 10^{12}$, $a_5 = 4.00743 \times 10^{11}$, $a_6 = 5.91801 \times 10^{9}$,

and $a_7 = 2.54429 \times 10^{7}$.

The eigenvalues of the matrix J are

$\lambda_1 = -1.67624 \times 10^{9}$, $\lambda_2 = -484.406$, $\lambda_3 = -35.6746$,

$\lambda_4 = -0.13$, $\lambda_5 = -0.07$, $\lambda_6 = -0.01$, $\lambda_7 = -0.009$.

In this case, every eigenvalue is negative. It follows that the system is asymptotically stable. The evidence analytical solution of the DENF model's effectiveness is presented in Figures 1-6.

5. Numerical Simulation

This article examined the quantitative performance of the papaya-based antiviral treatment model of (1), and the numerical simulations supporting the analytical results were done using computational tools. All of the biological parameters used to execute the numerical simulation are listed in Table 1. Many of the parameter values were obtained from earlier literature. However, some were estimated. Figure 1 shows that after the administration of papaya leaf extract, the rate of WBC cells gradually increased from the starting point until stabilizing after 20 days. Figure 2 shows that starting on day one, the proportion of infected WBC cells gradually reduced. After that, however, it reached a plateau and did not even appreciably increase after 30 days. Figure 3 depicts how dengue suppresses the bone marrow, which produces platelets. Therefore, the rate of platelets losing their count began to rise on the fourth day and stabilized after 20 days. Figure 4 illustrates how healthy persons' platelet counts drop after contracting the dengue virus and may potentially fall below 1×10^{8} platelets per liter. The platelet reduction typically happens three to four days into a fever, during the peak of the infection. In addition, it takes five days to reach a stable state. After contracting the DENV at the initial stage, Figure 5 unequivocally demonstrates that the immune cells lack the strength to combat them. The immune cell count, however, began to rise after just five days and returned to normal after 20 days. After 5-6 days, as patients made progress against their illness, the viral load gradually decreased. Patients' dengue viral loads showed that the first day of symptoms often resulted in the highest viral load. The viral burden then gradually reduced over the following few days. The infection rate finally decreased to 0 copies/ml on the fifth day following the fever, as illustrated in Figure 6.

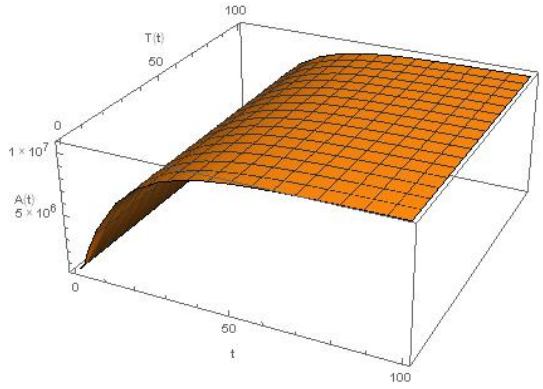

Figure 1. Effect of WBC healthy cells with papaya therapy.

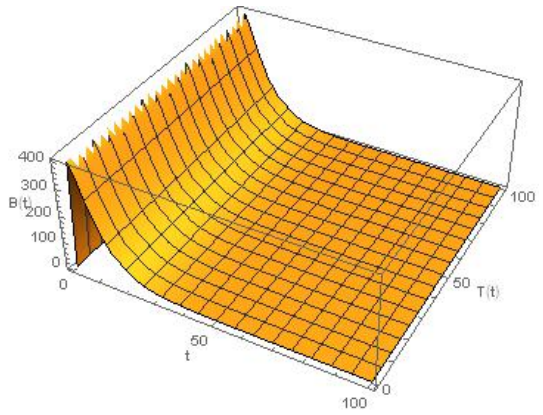

Figure 2. Effect of infected WBC with papaya therapy.

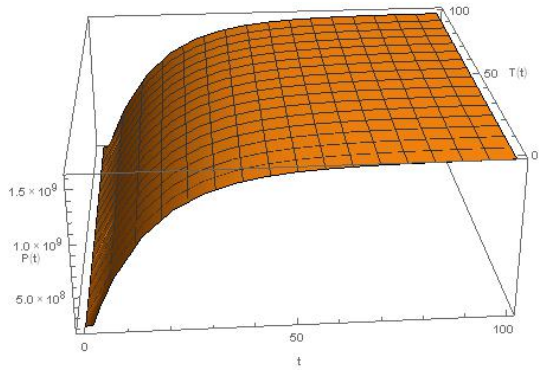

Figure 3. Effect of healthy platelets with papaya therapy.

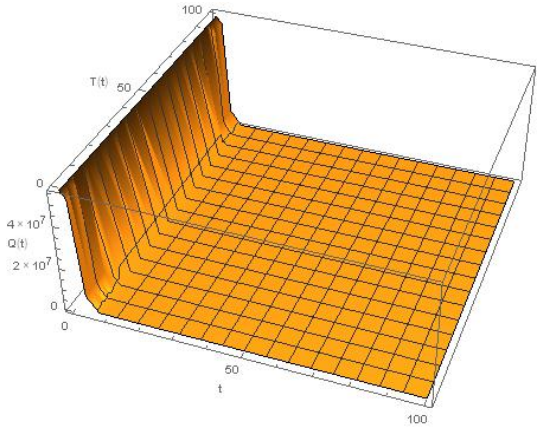

Figure 4. Effect of infected platelets with papaya therapy.

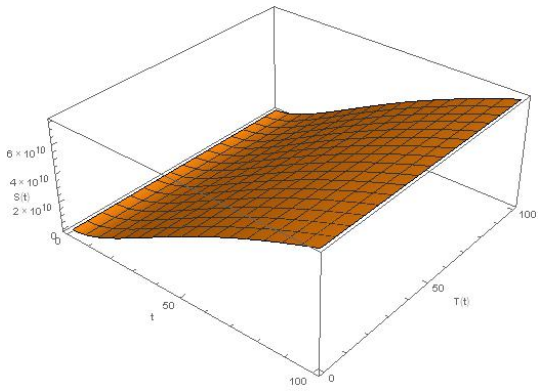

Figure 5. Effect of *T* immune reactivity with papaya therapy.

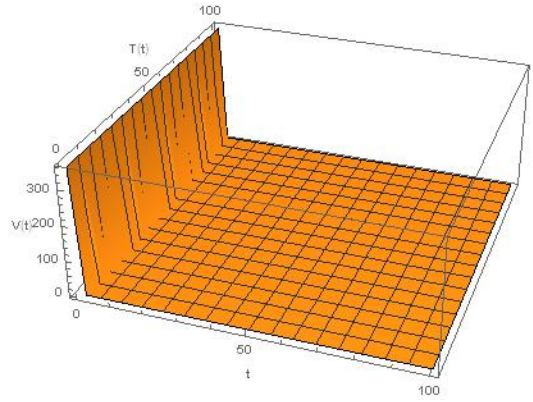

Figure 6. Effect of dengue pathogens with papaya therapy.

6. Conclusion

This study looked at the analytical solutions to a set of nonlinear differential equations that specifies the immune response to DENF within a host model where the patient receives treatment with an extract of papaya leaves. Seven sets of nonlinear differential equations are considered to determine the solutions to each equation using an analytical approach. Finding solutions to NLODEs is also very challenging. Applying the linearization technique to the systems can break them into linear components to balance such a situation. They were, furthermore, applying the method of variation of the parameter to the linear system with constant coefficients to reach the solutions. Finally, the system's stability was identified and discussed using solutions of NLODE obtained from analytical. We occasionally could not find exact solutions for some systems of nonlinear differential equations. In light of this, the solution of the governing equation was carried out through numerical simulation. Figures 1 and 2 demonstrate that the system solutions for the novel technique and the numerical simulation are the same. In our estimation, determining the performance of papaya leaves extracts against the dengue viral load is a vital component of the proposed method since it will help develop the techniques for treating the malignant DENV.

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