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Theoretical analysis on the growth kinetics of SARS-CoV (within host)

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Abstract

A mathematical model is investigated to analyze the biological interactions between the immune system and SARS-CoV (within host). Homotopy Perturbation Method is executed to obtain an analytical solution to the non-linear system of ordinary differential equations. Graphical illustration to these solutions is also presented. The reliability and the simplicity of the aforementioned method is studied through the comparison between the numerical and graphical results. This comparison aids the better understanding of the disease dynamics and also the establishment of probable strategies for the treatment of COVID-19.

Keywords: Mathematical Modeling, COVID-19, Non -linear initial value problem, Homotopy Perturbation Method.
2020 AMS subject classifications: Find your subject classification at https://mathscinet.ams.org/msnhtml/msc2020.pdf. [1]

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1 Introduction

The World Health Organization declared the SARS-CoV as a potential threat to the human society Sharma et al. [2020]Ramadan and Shaib [2019]Ouassou et al. [2020]. Since then, researchers have been working really hard on various strategies to control the disease Ahmed et al. [2020]Nie et al. [2020]. A key factor to control the disease is by studying the disease severity and progression in the host. However, the quantitative analysis of the growth kinetics of the virus has not been able to study the severity in the host. It is therefore important to analyze the interactions within the host between SARS-CoV and the immune system Du and Yuan [2020]Hernandez-Vargas and Velasco-Hernandez [2020]Wang et al. [2020]. And this can be achieved by developing a mathematical model as they serve as a tool for characterizing the disease dynamics and in the forecast of severity of the disease. A mathematical model is therefore developed by S.M.E.K Chowdhury et.al Chowdhury et al. [2022]in the context of immune surveillance. We study this model analytically. The goal of our work is to derive a closed form analytical solution for the COVID-19 model for the susceptible, infected, recovered and exposed. This is done by implementing the technique of Homotopy Perturbation Method [HPM] He [1999]He [2004a]He [2004b]He [2004c] which is the coupling of homotopy and perturbation technique. The derived analytical results are beneficial in two fronts: first, it would contribute to a better comprehension of the disease dynamics which assist in designing effective treatment strategies and secondly, would enable the scientist in modifying the COVID-19 model to study the correlation between various model parameters and their impacts. This approach in its implementation is novel to this non-linear system of COVID-19 model.

2 Model formulation

The mathematical framework of the developed model is built on the interplay between the lymphocytes and virus particles within the host. Taking into account this interaction the model is proposed as Chowdhury et al. [2022]

$$\frac{\mathrm{d}E}{\mathrm{d}t} = a_1 - a_2E - a_3EV \tag{1}$$

$$\frac{\mathrm{d}E^i}{\mathrm{d}t} = a_3EV - b_1E^i \tag{2}$$

$$\frac{\mathrm{d}V}{\mathrm{d}t} = c_1E^i - c_2V - -c_3VL \tag{3}$$

$$\frac{\mathrm{d}N}{\mathrm{d}t} = d_1 - d_2N \tag{4}$$

Parameters	Physical Meaning
a_1	Regenration rate of epithelial cells
a_2	Rate at which epithelial cells die
a_3	Rate of infection of epithelial cells
b_1	Rate at which the infected epithelial cells die
c_1	Production rate of virus from infected epithelial cells
c_2	Rate at which the virus dies
e_1	Rate of proliferation of T-lymphocytes
e_2	Rate at which the T-lymphocytes die
e_3	Regeneration rate of T-lymphocytes
c_3	Rate at which the Natural Killer cells kills the virus
d_1	External influx rate of Natural Killer cells
d_2	Rate at which the Natural Killer cells die
c_4	Rate at which the T-lymphocytes kills the virus
n	Half saturation constant of T-lymphocytes

Table 1: Nomenclature

$$\frac{\mathrm{d}L}{\mathrm{d}t} = \frac{e_1 LV}{(n+V)} - e_2 L + e_3 \tag{5}$$

Where denotes the count of susceptible epithelial cells $E(t)$, infected epithelial cells $E^i(t)$, viral load $V(t)$, natural killer cells $N(t)$ and T-lymphocytes $L(t)$ respectively. The production rate of the virus is c_1 where as the infection rate is denoted by a_3 . the natural death rate of susceptible epithelial cells, infected epithelial cells, viral load , natural killer cells and T-lymphocytes are a_2, b_1,c_2,d_2,$e-2$ respectively. a_1 denotes the regeneration rate of the epithelial cells. The degeneration of virus particles occur when they are interacted with natural killer cells and T-lymphocytes at the rate d_1 and ${}_d3$ respectively. The NK cell's constant external source is denoted as a_2 . refers to the T-lymphocytes natural recruitment rate c_4 . In the presence of virus particles, the T-lymphocytes proliferate at a rate n.

3 Homotopy perturbation method

Epidemiological modeling of the diseases using nonlinear dynamical equations gives deeper insights into the behavioral patterns and the transmission dynamics of the disease. As solutions to these non-linear problems are a bit more complex, a substantial amount of work has been dedicated by researchers in developing a solution method to these models. Such methods include ADM , VIM , HAM , HPM He [1999]He [2004c]He [2005]Abbasbandy [2006]Rafei and Ganji [2006]Yıldırım and Öziş [2007]Sivasamy and Kumar [2021] etc. In this paper,

we execute HPM in finding an analytical solution to the COVID-19 model. The advantage of HPM over other method is its ability to reduce a complex non-linear problem into a serious of linear equation and finding the solution the same.

3.1 Basic idea of homotopy perturbtion method [HPM]

Consider the following function

$$D_o(u) - f(r) = 0, r\epsilon\Omega \tag{6}$$

with the boundary conditions as

$$B_o(u, \frac{\partial u}{\partial n}) = 0, r\epsilon\Gamma \tag{7}$$

Where D_0 is a general differential operator, B_0 is a boundary operator, $f(r)$ is a known analytical function and Γ is the boundary of the domain Ω . In general, the operator D_0 can be divided into a linear part L and a non-linear part N. We can rewrite the eqn (6) as

$$L(u) + N(u) - f(r) = 0 \tag{8}$$

We now construct a homotopy as $v(r, p) :\rightarrow \Omega \times [0, 1] \times \Re$ by the homotopy technique which statisfies

$$H(v, p) = (1 - p)[L(v) - L(v_0)] + p[D_0 - f(r)] = 0 \tag{9}$$

$$H(v, p) = L(v) - L(v_0) + p[N(v) - f(r)] = 0 \tag{10}$$

Here p is the embedding parameter and belongs to the interval [0, 1] and the initial approximation of eqn.(6) is u_0 which satisfies the boundary condition. Now,eqn (9) and (10) leads to

$$H(v, 0) = L(v) - L(u_0) = 0 \tag{11}$$

$$H(v, 1) = D_0 - f(r) = 0 \tag{12}$$

Setting p=0 makes the eqns. (9) and (10) as linear and seeting p=1 makes them non-linear.. This process is presented as $L(v) - L(u_0) = 0$ to $D_0 - f(r) = 0$. We use p, the embedding parameter as a small parameter and assume that the solutions of eqns. (9) and (10) can be written as a power series in p:

$$v = v_0 + pv_1 + p^2v_2 + ... \tag{13}$$

Fixing p=1 leads to the approximation of eqn (6) as

$$v = v_0 + pv_1 + p^2v_2 + ... \tag{14}$$

This is the basic idea of the HPM.

4 Analytical solution to the COVID-19 model using homotopy perturbation method

$$(1-p)\left(\frac{\mathrm{d}E}{\mathrm{d}t} = a_1 - a_2E\right) + p\left(\frac{\mathrm{d}E}{\mathrm{d}t} = a_1 - a_2E - a_3EV\right) = 0 \tag{15}$$

$$(1-p)\left(\frac{\mathrm{d}E^i}{\mathrm{d}t} + b_1E^i\right) = p\left((\frac{\mathrm{d}E^i}{\mathrm{d}t} = a_3EV - b_1E^i\right) = \tag{16}$$

$$(1-p)\left(\frac{\mathrm{d}V}{\mathrm{d}t} + c_2V\right) + p\left((\frac{\mathrm{d}V}{\mathrm{d}t} = c_1E^i - c_2V - -c_3VL\right) = 0 \tag{17}$$

$$(1-p)\left(\frac{\mathrm{d}L}{\mathrm{d}t} + e_2L - e_3\right) + p\left((\frac{\mathrm{d}L}{\mathrm{d}t} = \frac{e_1LV}{(n+V)} - e_2L + e_3\right) = 0 \tag{18}$$

Supposing the approximate solutions of Eq. (1-5) have the form

$$E = E_0 + pE_1 + p^2E_2 + ... \tag{19}$$

$$E^i = E_0^i + pE_1^i + p^2E_2^i + ... \tag{20}$$

$$V = V_0 + pV_1 + p^2V_2 + ... \tag{21}$$

$$L = L_0 + pL_1 + p^2L_2 + ... \tag{22}$$

Substituting the Eq. (15-18) respectively into Eq. (1-5)

$$\begin{aligned}(1-p)\left(\frac{\mathrm{d}(E_0 + pE_1 + p^2E_2 + ...)}{\mathrm{d}t} - a_1 + a_2(E_0 + pE_1 + p^2E_2 + ...)\right) + \\ p\left(\frac{\mathrm{d}(E_0 + pE_1 + p^2E_2 + ...)}{\mathrm{d}t} - a_1 + a_2(E_0 + pE_1 + p^2E_2 + ...)\right. \\ \left. + a_3(E_0 + pE_1 + p^2E_2 + ...)(V_0 + pV_1 + p^2V_2 + ...) = 0\right.\end{aligned} \tag{23}$$

$$\begin{aligned}(1-p)\left(\frac{\mathrm{d}(E_0^i + pE_1^i + p^2E_2^i + ...)}{\mathrm{d}t} + b_1(E_0^i + pE_1^i + p^2E_2^i + ...)\right) + \\ p\left(\frac{\mathrm{d}(E_0^i + pE_1^i + p^2E_2^i + ...)}{\mathrm{d}t} - a_3(E_0 + pE_1 + p^2E_2 + ...)(V_0 + pV_1 + p^2V_2 + ...)\right. \\ \left. - b_1(E_0^i + pE_1^i + p^2E_2^i + ...) = 0\right.\end{aligned} \tag{24}$$

$$(1-p)\left(\frac{\mathrm{d}(V=V_0+pV_1+p^2V_2+...)}{\mathrm{d}t}+c_2(V=V_0+pV_1+p^2V_2+...)\right)+$$
$$p\left((\frac{\mathrm{d}(V=V_0+pV_1+p^2V_2+...)}{\mathrm{d}t}-c_1(E_0^i+pE_1^i+p^2E_2^i+...)\right.$$
$$-c_2(V=V_0+pV_1+p^2V_2+...)$$
$$\left.-c_3(V=V_0+pV_1+p^2V_2+...)(L_0+pL_1+p^2L_2+...)=0\right. \quad (25)$$

$$(1-p)\left(\frac{\mathrm{d}(L_0+pL_1+p^2L_2+...)}{\mathrm{d}t}+e_2(L_0+pL_1+p^2L_2+...)-e_3\right)+$$
$$p\left((\frac{\mathrm{d}L}{\mathrm{d}t}=\frac{e_1(L_0+pL_1+p^2L_2+...)(V_0+pV_1+p^2V_2+...)}{(n+(V_0+pV_1+p^2V_2+...))}\right.$$
$$\left.-e_2(L_0+pL_1+p^2L_2+...)+e_3=0\right. \quad (26)$$

Equating the terms of Eq (23-26) with the identical powers of p, we obtain

$$p^0:\frac{\mathrm{d}E_0}{\mathrm{d}t}+a_2E-a_1=0 \quad (27)$$

$$p^0:\frac{\mathrm{d}E_0^i}{\mathrm{d}t}+b_1E_0^i=0 \quad (28)$$

$$p^0:\frac{\mathrm{d}V_0}{\mathrm{d}t}+c_2V_0=0 \quad (29)$$

$$p^0:\frac{\mathrm{d}L_0}{\mathrm{d}t}+e_2L_0-e_3=0 \quad (30)$$

$$\frac{\mathrm{d}E_1}{\mathrm{d}t}+a_2E_1+a_3E_0V_0=0 \quad (31)$$

$$\frac{\mathrm{d}E_1^i}{\mathrm{d}t}-a_3E_0V_0+b_1E_0^i=0 \quad (32)$$

$$\frac{\mathrm{d}V_1}{\mathrm{d}t}-c_1E_0^i-c_2V_1+c_3V_0L_0=0 \quad (33)$$

$$\frac{\mathrm{d}L}{\mathrm{d}t}-\frac{e_1L_0V_0}{(n+V_i)}+e_2L_1=0 \quad (34)$$

Number of susceptible epithelial cells are given by

$$E(t)=\frac{a_1}{a_2}+(E_i-\frac{a_1}{a_2})e^{-a_2t}-\frac{a_3a_1V_ie^{-c_2t}}{a_2(a_2-c_2)}+\frac{a_3(E_i-\frac{a_1}{a_2})V_ie^{(-a_2+c_2)t}}{c_2}$$
$$+\frac{a_3a_1V_ie^{-a_2t}}{a_2(a_2-c_2)}-\frac{a_3(E_i-\frac{a_1}{a_2})V_ie^{-a_2t}}{c_2} \quad (35)$$

Infected epithelial cells are given by

$$E^i(t) = E^i(t)e^{b_1 t} + \frac{a_3 a_1 V_i e^{-c_2 t}}{a_2(b_1 - c_2)} + \frac{a_3(E_i - \frac{a_1}{a_2})V_i e^{(-a_2 - c_2)t}}{b_1 - a_2 - c_2} + \frac{a_3 a_1 V_i e^{-b_1 t}}{a_2(b_1 - c_2)} - \frac{a_3(E_i - \frac{a_1}{a_2})V_i e^{-b_1 t}}{b_1 - a_2 - c_2} \quad (36)$$

Viral load cells are given by

$$V(t) = V_i(t)e^{-c_2 t} + \frac{c_1 E_i e^{-b_1 t}}{c_2 b_1} + (\frac{c_3 d_1 V_i}{d_2} - \frac{c_4 e_3 V_i}{e_2})te^{-c_2 t} + \frac{c_3(N_i - \frac{d_1}{d_2})V_i e^{(-(d_2 + c_2)t}}{d_2} - \frac{c_1 E_i e^{-c_2 t}}{c_2(b_1 - c_2)} - \frac{c_3(N_i - \frac{d_1}{d_2})V_i e^{(-c_2)t}}{d_2} + \frac{c_3(N_i - \frac{d_1}{d_2})L_i e^{(-(e_2 + c_2)t}}{e_2} - \frac{c_3(N_i - \frac{d_1}{d_2})L_i e^{(-e_2)t}}{e_2} \quad (37)$$

Natural killer cells are given by

$$N(t) = \frac{d_1}{d_2} - \left(N_i - \frac{d_1}{d_2}\right)e^{-d_2 t} \quad (38)$$

T-lymphocytes cells are given by

$$L(t) = \frac{e_3}{e_2} + (L_i - \frac{e_3}{e_2})e^{-e_2 t} + \frac{e_3 e_1 V_i e^{-c_2 t}}{e_3(n + V_i)(-c_2 + e_2)} - \frac{e_1(L_i - \frac{e_3}{e_2})V_i e^{(-a_2 + e_2)t}}{c_2(n + V_i)} - \frac{e_3 e_1 V_i e^{-e_2 t}}{e_3(n + V_i)(-c_2 + e_2)} + \frac{e_1(L_i - \frac{e_3}{e_2})V_i e^{(-e_2 + e_2)t}}{c_2(n + V_i)} \quad (39)$$

5 Numerical simulation

An analytical expression for the time-dependent non-linear COVID-19 model is derived by executing the method of Homotopy Perturbation for the equations (1-6). The numerical solutions to these equations are obtained using MATLAB software. In order to check the efficiency of HPM in solving the COVID-19 model, comparison between the numerical and analytical results are carried out which is illustrated in the figures 1-12.

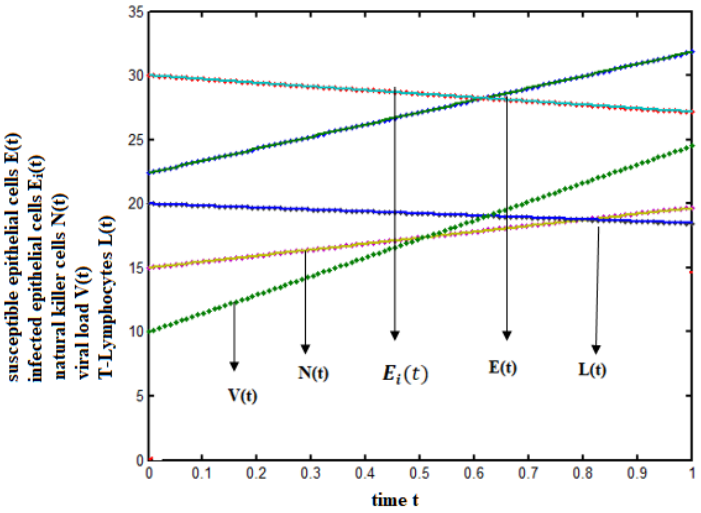

Figure 1: Illustration of numerical and analytical results for the populations of susceptible epithelial cells , infected epithelial cells , Viral Load , Natural Killer Cells and T-lymphocytes against time t.

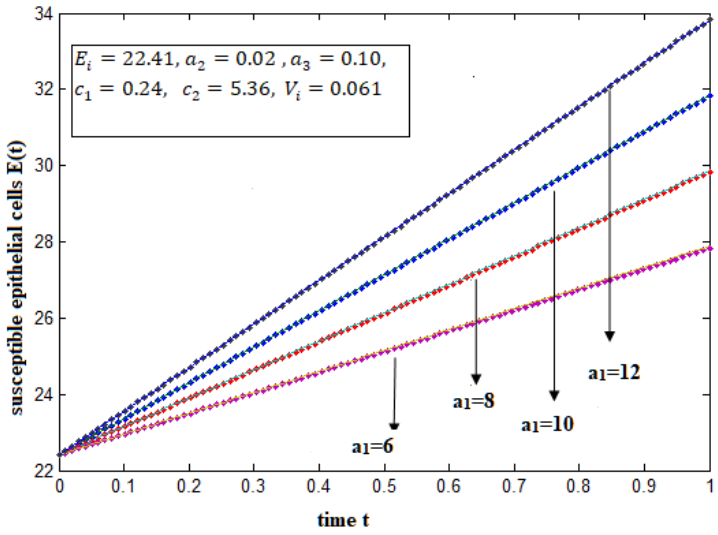

Figure 2: Illustration of analytical and graphical results for the population of susceptible against time t.

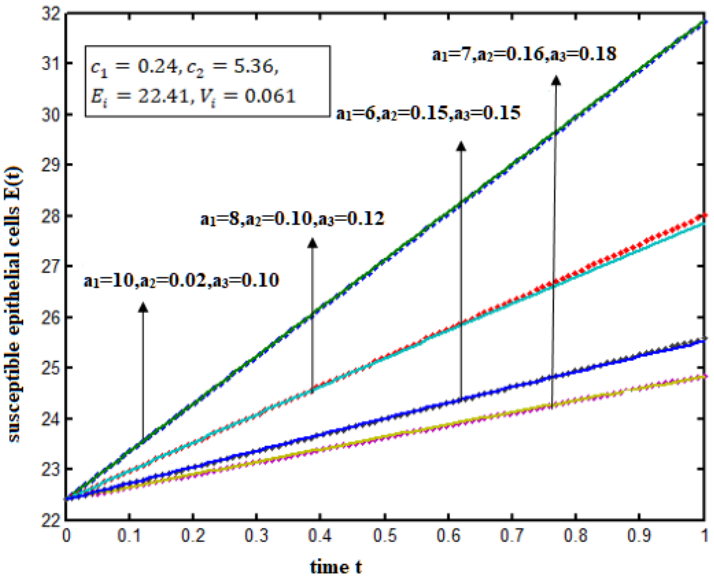

Figure 3: Illustration of analytical and graphical results for the population of susceptible against time t.

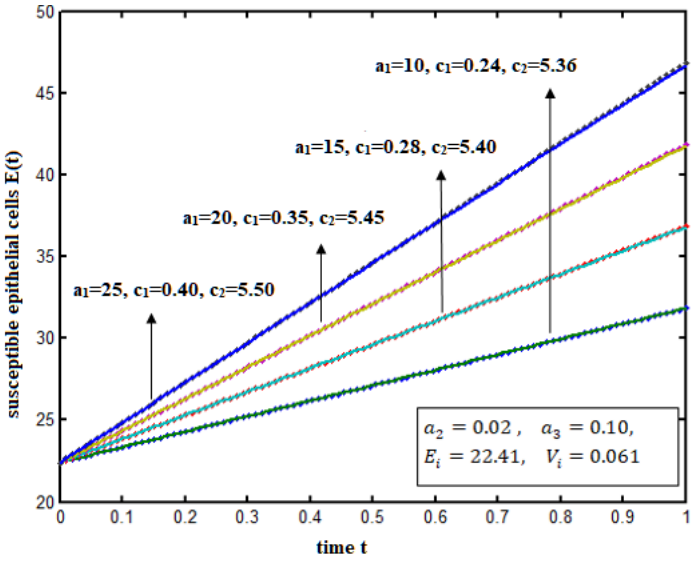

Figure 4: Illustration of analytical and graphical results for the population of susceptible against time t.

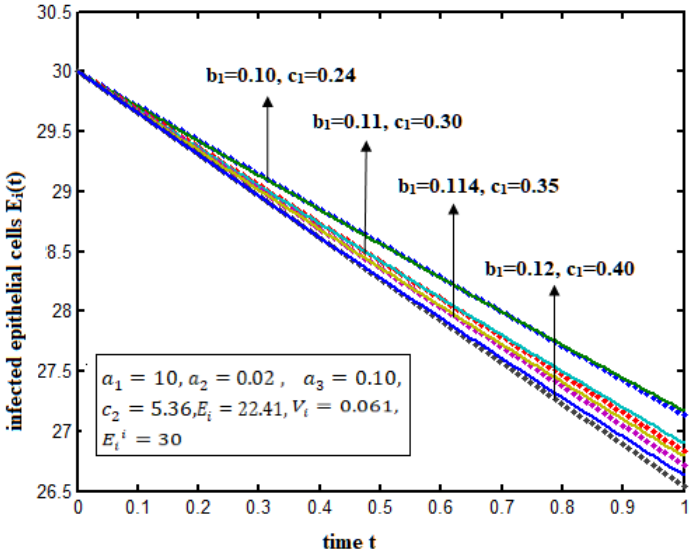

Figure 5: Illustration of analytical and graphical results for the population of susceptible against time t.

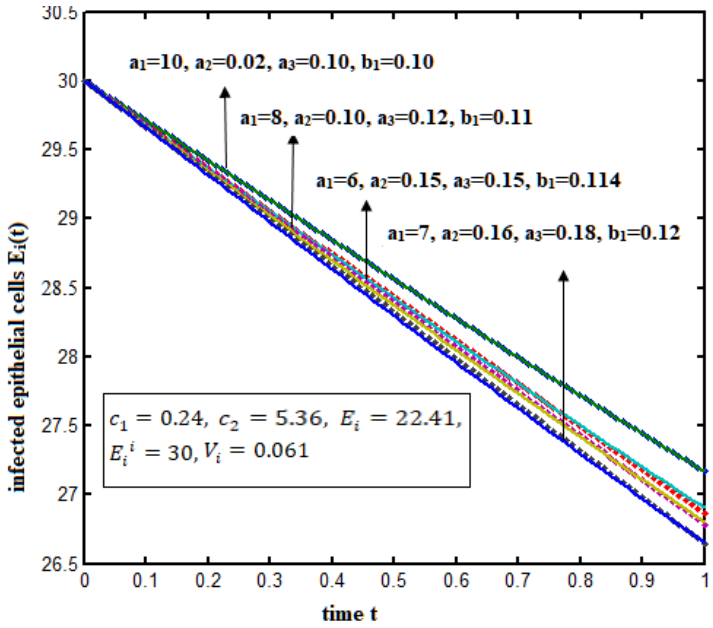

Figure 6: Illustration of analytical and graphical results for the population of infected epithelial against time t.

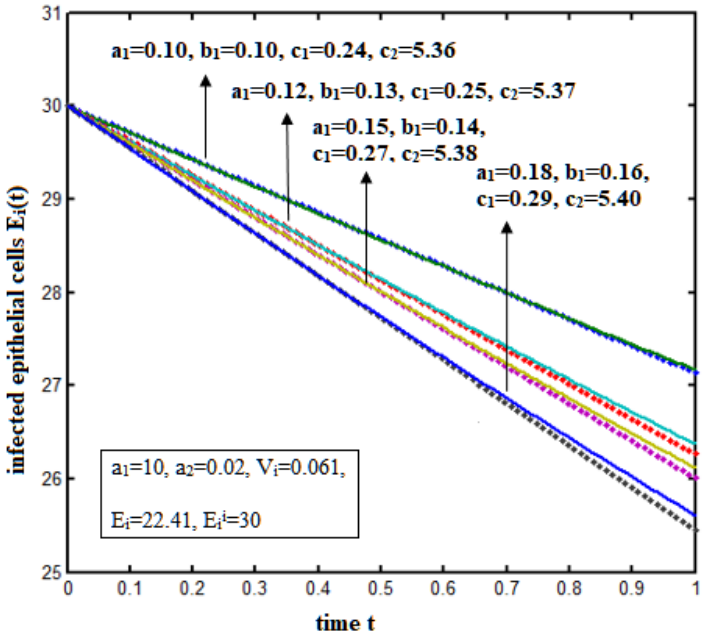

Figure 7: Illustration of analytical and graphical results for the population of infected epithelial against time t.

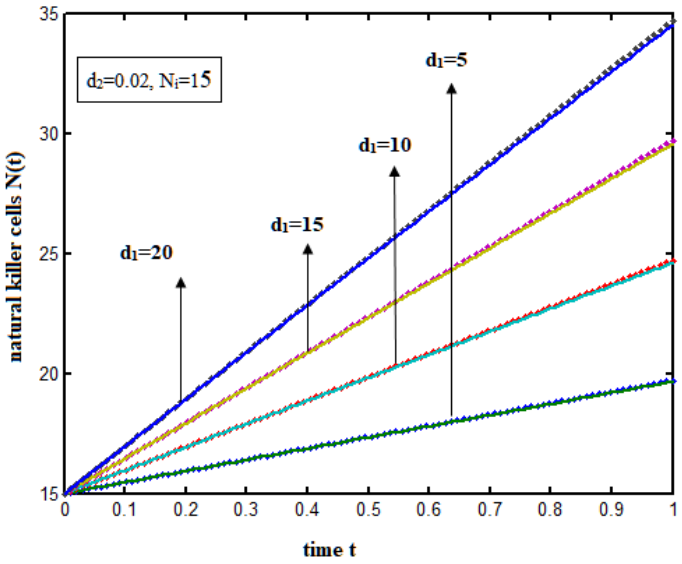

Figure 8: Illustration of analytical and graphical results for the population of natural killer cells against time t.

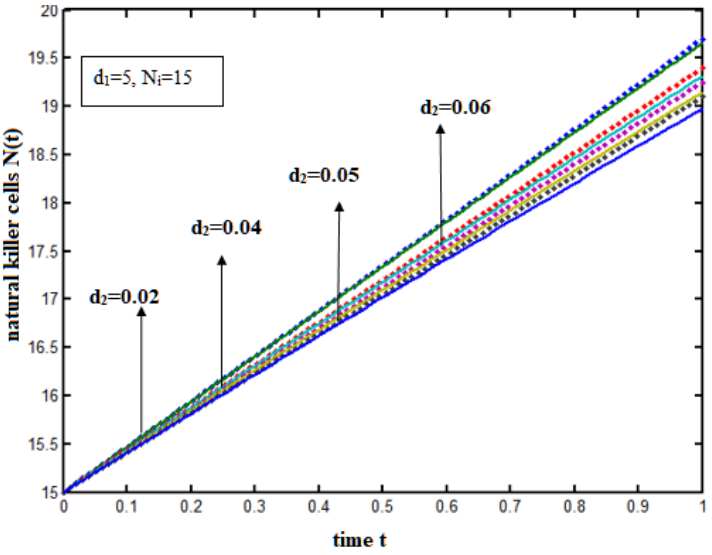

Figure 9: Illustration of analytical and graphical results for the population of natural killer cells against time t.

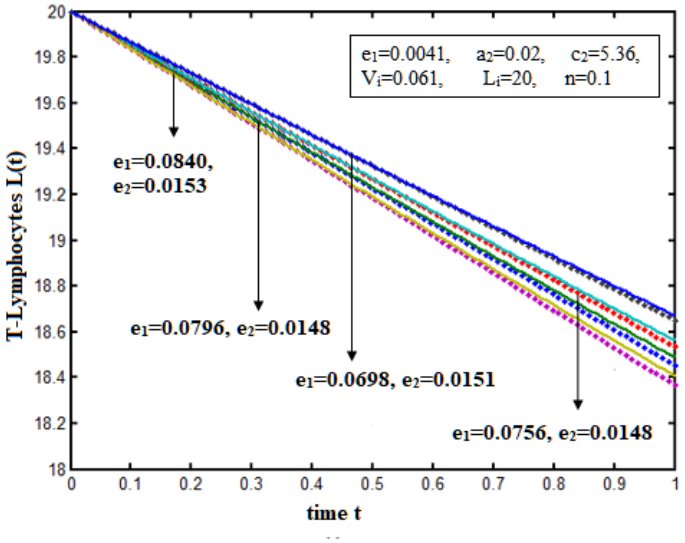

Figure 10: Illustration of analytical and graphical results for the population of T-lymphocytes against time t.

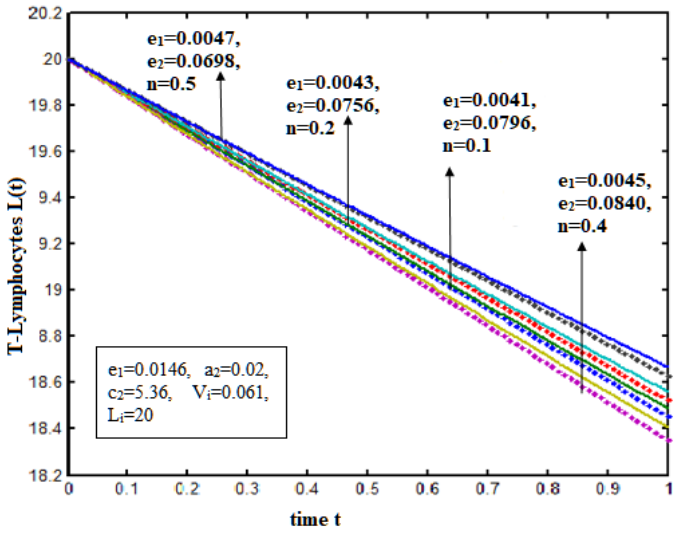

Figure 11: Illustration of analytical and graphical results for the population of T-lymphocytes against time t.

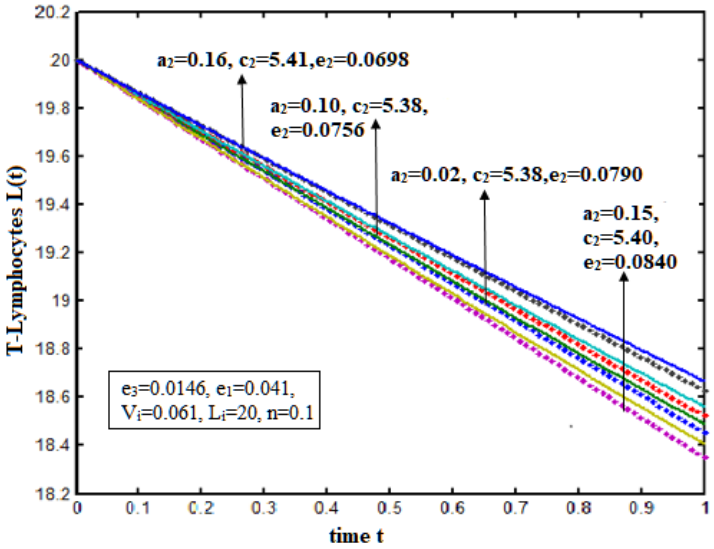

Figure 12: Illustration of analytical and graphical results for the population of T-lymphocytes against time t.

5.1 Results and discussion

Figure 1 illustrates the comparison between the analytical and numerical results for the populations of susceptible epithelial cells , infected epithelial cells , Viral Load , Natural Killer Cells and T-lymphocytes against time t for the parameter values $n = 0.1, d_1 = 5, a_1 = 10, a_2 = 0.02, a_3 = 0.10, b_1 = 0.10, c_1 = 0.24, c_2 = 5.36, c_3 = 0.231, c_4 = 0.431, e_1 = 0.0041, e_2 = 0.0796, e_3 = 0.0146, d_2 = 0.02$. Figure 2-4 presents the plot of susceptible epithelial cells against time t. Figure 5-7 presents the plot of infected epithelial cells against time t. Figure 8-9 indicated the plot of Natural Killer Cells against time t. Figure 10-12 represents the plot of T-lymphocytes against time t. Figure 2 depicts that the ratio of susceptible cells increases with time as the regeneration rate increases. Figure 3 indicates that the growth of epithelial cells is exponential when the rate of infection is higher. Figure 4 presents that even when the death of the infected cells is higher the growth of susceptible cells increases as there is an increase in the production rate of infected cells. Figure 5 depicts that the there is a steady decline in the rate of infected cells as the death rate of the infected cells increases. Figure 6 presents that the rate of growth of infected cells decreases when the rate of infection of the epithelial cells is lower and also a steady decline in the death rate of infected epithelial cells. Figure 7 indicates that the growth rate of the infected epithelial cells also depends on the death rate of the virus. Figure 8 and 9 represents that rate of natural killer cells increases in spite of the infection when there is an increase in external influx. Figure 10-12 presents that proliferation rate, regeneration are and the death rate of the T-lymphocytes has an impact on the growth of T-lymphocytes.

6 Conclusions

A theoretical model outling the interactions between the SARS-Cov and the immune system within the host has been investigated by combining the functions of NK cells and T-lymphocytes. Homotopy Perturbation method is executed to solve the non-linear equations and a closed form analytical solution is obtained.. Graphical illustration of the analyical and numerical solution is performed. A sound agreement between these results is noted. This comparison shows that HPM is an effective approach for solving such models.

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