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Global dynamics of SARS-CoV-2/cancer model with immune responses

A.M. Elaiw, A.D. Al Agha

Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia

Department of Mathematics, Faculty of Science, Al-Azhar University, Assiut Branch, Assiut, Egypt

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ABSTRACT

The world is going through a critical period due to a new respiratory disease called coronavirus disease 2019 (COVID-19). This disease is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Mathematical modeling is one of the most important tools that can speed up finding a drug or vaccine for COVID-19. COVID-19 can lead to death especially for patients having chronic diseases such as cancer, AIDS, etc. We construct a new within-host SARS-CoV-2/cancer model. The model describes the interactions between six compartments: nutrient, healthy epithelial cells, cancer cells, SARS-CoV-2 virus particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies. We verify the nonnegativity and boundedness of its solutions. We outline all possible equilibrium points of the proposed model. We prove the global stability of equilibria by constructing proper Lyapunov functions. We do some numerical simulations to visualize the obtained results. According to our model, lymphopenia in COVID-19 cancer patients may worsen the outcomes of the infection and lead to death. Understanding dysfunctions in immune responses during COVID-19 infection in cancer patients could have implications for the development of treatments for this high-risk group.

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1. Introduction

Coronavirus disease 2019 (COVID-19) is a new respiratory and highly infectious disease. It appeared in Wuhan, China in late 2019 and spread rapidly to a large number of countries around the world. On March 11, 2020, the World Health Organization (WHO) upgraded COVID-19 to a pandemic [1]. According to the WHO report of August 2020, over 1.7 million new COVID-19 cases and 39,000 new deaths were recorded in late August [2]. The total number of cases and deaths from the start of the pandemic to the date of this report reached over 23 million cases and 800,000 deaths [2]. Despite the tremendous effort and great competition between countries, no effective cure or vaccine has been proven yet. The WHO posted many guidelines to reduce the spread of COVID-19 such as wearing masks, washing hands, and monitoring a safe distance between you and others [3]. In response to these recommendations and to avoid the collapse of healthcare systems, countries imposed rules to follow in public places and workplaces.

COVID-19 is caused by a single-stranded RNA virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [4,5]. It belongs to the family Coronaviridae, which also involves SARS-CoV that emerged in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) that emerged in 2012 [6,7]. SARS-CoV-2 virus targets cells with angiotensin-

* Corresponding author.
E-mail address: a_m_elaiw@yahoo.com (A.M. Elaiw).

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converting enzyme 2 (ACE2) receptor, which makes these cells more susceptible to virus entry [8]. ACE2 is expressed in many cells such as myocardial epithelial cells, kidney tubular epithelial cells, and gastrointestinal epithelial cells [7]. However, type II alveolar epithelial cells have a higher expression rate of ACE2 and therefore are the main target for SARS-CoV-2 virus [7,9]. The most common symptoms of COVID-19 include fatigue, cough, fever, shortness of breath, sore throat, headache, and diarrhea [7,10]. Although a large percentage of patients show mild symptoms and do not need to stay in hospitals, about 20% of them develop pneumonia, multiple organ failure, and ultimately death [8,10]. Lymphopenia, which is defined as a lymphocyte count of less than 1.5 × 10^9/mm^3, was also reported in severe COVID-19 patients [4,11,12].

There are many risk factors that cause disease progression in COVID-19 patients and rise the need for intensive care unit (ICU) admission or using mechanical ventilation [4,13]. These factors include hypertension, older age, diabetes, chronic kidney disease, obesity, cardiovascular disease, and cancer [5,13,14]. Cancer patients are at higher risk of serious complications and death due to COVID-19 infection [15–17]. This risk increases further in patients with lymphopenia [1,10]. COVID-19/cancer patients with lymphopenia have a 10 times higher risk of death than the patients infected only by COVID-19 [7]. Therefore, several measures have been proposed to protect cancer patients during the pandemic [1]. In general, the role of immune dysregulation in COVID-19 cancer patients is being investigated [9,18].

Mathematical models have been used to understand the transmission of COVID-19 between individuals and provide useful insights into the development of control strategies [19]. Crucial and important decisions can be taken based on these models. Most of the recent COVID-19 models are epidemiological models based on SEIR models (see for example, [19–24]). These models depict the transmission dynamics of the virus between susceptible, exposed, infectious, and recovered individuals. Different computations were performed to estimate the basic reproductive number and to predict the impact of control measures on reducing the transmission rates of the disease [19–24].

Within-host models, which study the interactions between SARS-CoV-2 and human cells, have received less attention than epidemiological models. Most of within-host SARS-CoV-2 models are based on Nowak and Bangham’s model [25] that was extended to study the dynamics of several viruses such as human immunodeficiency virus (HIV) [26–28], hepatitis B virus (HBV) [29–31], chikungunya virus (CHIKV) [32], and other viruses. For example, Du and Yuan [8] studied a within-host model of COVID-19 infection. They explored the effect of the interaction between innate and adaptive immunity on the peak of viral load in COVID-19 patients. Li et al. [33] used a within-host viral model to study the dynamics of SARS-CoV-2 virus in host, and they estimated the values of model’s parameters. Ghosh [34] proposed a mathematical model to study the interaction between healthy cells, virus particles, and immune response in SARS-CoV-2 infection. He tested the efficacy of different antiviral drugs and estimated the parameters by fitting with real data. Hattaf and Yousfi [35] proposed a within-host model to study the interactions between host epithelial cells, SARS-CoV-2 virus, and cytotoxic T lymphocytes (CTLs) with virus-to-cell and cell-to-cell transmission modes. Pinky and Dobrovolny [36] used a mathematical model to investigate SARS-CoV-2 coinfections with many other respiratory viruses. They argued that SARS-CoV-2 virus replication is suppressed by other viruses when the infections occur simultaneously.

As mentioned above, cancer patients who get infected by SARS-CoV-2 are at increased risk of severe infection and death. To design effective treatments that can target both SARS-CoV-2 and cancer, we need to understand the interactions between healthy cells, cancer cells, virus particles, and immune responses. Mathematical modeling is a powerful tool that can help us understand the within-host interactions. To the best of our knowledge, no mathematical models have been developed so far to study the effect of COVID-19 on cancer patients. In this paper, we construct a new within-host SARS-CoV-2/cancer model. This model is different from other within-host models investigated before because it is an adjustment of the oncolytic virotherapy models studied in Wang et al. [37] and Elaiw et al. [38]. For our proposed model, we (i) show the nonnegativity and boundedness of model’s solutions; (ii) discuss all biologically acceptable equilibrium points of the suggested model; (iii) prove the global stability of equilibria; (iv) prove the theoretical results by performing some numerical simulations; (v) present the effect of lymphopenia on the growth of cancer cells and SARS-CoV-2 particles.

This paper is organized as follows. Section 2 provides a full description of the new model under study. Section 3 shows that the solutions of the developed model are nonnegative and bounded. In addition, it lists all possible equilibrium points. Section 4 proves the global asymptotic stability of equilibria considered in Section 3. Section 5 presents some numerical simulations to support the theoretical results of the previous section. Finally, Section 6 discusses the results and some possible future works.

2. SARS-CoV-2/cancer model with immune response

In this section, we investigate a SARS-CoV-2/cancer model with two types of immune responses: SARS-CoV-2-specific antibody immune response and cancer-specific CTL immune response. Thus, we propose the following ordinary differential equation model

\[
\begin{align*}
\frac{dA(t)}{dt} &= \mu - \theta A(t) - \eta_1 A(t) N(t) - \eta_2 A(t) C(t), \\
\frac{dN(t)}{dt} &= \sigma_1 \eta_1 A(t) N(t) - \eta_3 N(t) V(t) - (\theta + \theta_1) N(t), \\
\frac{dC(t)}{dt} &= \sigma_2 \eta_2 A(t) C(t) - \eta_4 C(t) W(t) - (\theta + \theta_2) C(t), \\
\frac{dV(t)}{dt} &= \sigma_3 \eta_3 N(t) V(t) - \eta_5 V(t) Z(t) - (\theta + \theta_3) V(t), \\
\frac{dW(t)}{dt} &= \sigma_4 \eta_4 (1 - \rho_1) C(t) W(t) - (\theta + \theta_4) W(t), \\
\frac{dZ(t)}{dt} &= \sigma_5 \eta_5 (1 - \rho_2) V(t) Z(t) - (\theta + \theta_5) Z(t),
\end{align*}
\]
where $A(t), N(t), C(t), V(t), W(t)$, and $Z(t)$ denote the concentrations of nutrient, healthy epithelial cells, cancer cells, SARS-CoV-2 virus particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies at time $t$, respectively. The model is considered in the chemostat in which there is a competition between healthy epithelial cells and cancer cells on a restricted nutrient source [37]. The nutrient is recruited from a source at rate $\mu$ and decays at rate $\theta A$. It is consumed by healthy epithelial cells at rate $\eta_1 AN$, while it is consumed by cancer cells at rate $\eta_2 AC$. The healthy epithelial cells and cancer cells grow after consuming the nutrient at rates $\sigma_1 \eta_1 AN$ and $\sigma_2 \eta_2 AC$, respectively. SARS-CoV-2 virus infects epithelial cells at rate $\eta_3 NV$, while it replicates at rate $\sigma_3 \eta_3 NV$. The natural death rates of epithelial cells, cancer cells, virus particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies are given by $\delta_1, \delta_2, \delta_3, \delta_4$, and $\delta_5$, respectively. The parameter $\rho_1$ measures the effect of lymphopenia on reducing the stimulation rate of cancer-specific CTL immune response, where $0 \leq \rho_1 < 1$. On the other hand, the parameter $\rho_2$ measures the effect of lymphopenia on the production rate of SARS-CoV-2-specific antibodies, where $0 \leq \rho_2 < 1$. All parameters of model (1) are assumed to be positive. The description of all parameters is provided in Table 2. For simplicity, we will use the following notations in the next sections:

$$\Theta_1 \equiv \theta + \theta_1, \quad \Theta_2 \equiv \theta + \theta_2, \quad \Theta_3 \equiv \theta + \theta_3, \quad \Theta_4 \equiv \theta + \theta_4, \quad \Theta_5 \equiv \theta + \theta_5.$$ 

### 3. Basic properties

In this section, we establish the existence, nonnegativity, and boundedness of the solutions of model (1). In addition, we determine all biologically acceptable equilibrium points of system (1) and identify the conditions needed for their existence.
Theorem 1. Let \( \pi_i > 0, \ i = 1, 2, \ldots, 6 \), and define the compact set \( \Pi = \left\{ (A, N, C, V, W, Z) \in \mathbb{R}_+^6 : 0 \leq A(t) \leq \pi_1, 0 \leq N(t) \leq \pi_2, 0 \leq C(t) \leq \pi_3, 0 \leq V(t) \leq \pi_4, 0 \leq W(t) \leq \pi_5, 0 \leq Z(t) \leq \pi_6 \right\} \). Then, the set \( \Pi \) is positively invariant for model (1).

Proof. From model (1), we have

\[
\frac{dA}{dt} \bigg|_{A=0} = \mu > 0, \quad \frac{dN}{dt} \bigg|_{N=0} = 0, \quad \frac{dC}{dt} \bigg|_{C=0} = 0, \quad \frac{dV}{dt} \bigg|_{V=0} = 0, \quad \frac{dW}{dt} \bigg|_{W=0} = 0, \quad \frac{dZ}{dt} \bigg|_{Z=0} = 0.
\]

This guarantees that \( (A(t), N(t), C(t), V(t), W(t), Z(t)) \in \mathbb{R}_+^6 \) for all \( t \geq 0 \) when the initial conditions \( (A(0), N(0), C(0), V(0), W(0), Z(0)) \in \mathbb{R}_+^6 \). To show the boundedness, we define

\[
\Omega(t) = A(t) + \frac{1}{\sigma_1} N(t) + \frac{1}{\sigma_2} C(t) + \frac{1}{\sigma_1 \sigma_3} V(t) + \frac{1}{\sigma_2 \sigma_4} (1 - \rho_1) W(t) + \frac{1}{\sigma_1 \sigma_3 \sigma_5} (1 - \rho_2) Z(t).
\]

Then, we get

\[
\frac{d\Omega(t)}{dt} = \mu - \theta A(t) - \frac{\Theta_1}{\sigma_1} N(t) - \frac{\Theta_2}{\sigma_2} C(t) - \frac{\Theta_3}{\sigma_1 \sigma_3} V(t) - \frac{\Theta_4}{\sigma_2 \sigma_4} (1 - \rho_1) W(t) - \frac{\Theta_5}{\sigma_1 \sigma_3 \sigma_5} (1 - \rho_2) Z(t)
\]

\[
\leq \mu - \varphi \left[ A(t) + \frac{1}{\sigma_1} N(t) + \frac{1}{\sigma_2} C(t) + \frac{1}{\sigma_1 \sigma_3} V(t) + \frac{1}{\sigma_2 \sigma_4} (1 - \rho_1) W(t) + \frac{1}{\sigma_1 \sigma_3 \sigma_5} (1 - \rho_2) Z(t) \right]
\]

\[
= \mu - \varphi \Omega(t),
\]

where \( \varphi = \min \{\theta, \Theta_1, \Theta_2, \Theta_3, \Theta_4, \Theta_5\} = \theta \). This implies that

\[
0 \leq \Omega(t) \leq \pi_1 \quad \text{if} \quad \Omega(0) \leq \pi_1, \quad \text{for} \quad t \geq 0,
\]

where \( \pi_1 = \frac{\mu}{\theta} \). As \( A(t), N(t), C(t), V(t), W(t), \) and \( Z(t) \) are nonnegative, we have

\[
0 \leq A(t) \leq \pi_1, \quad 0 \leq N(t) \leq \pi_2, \quad 0 \leq C(t) \leq \pi_3, \quad 0 \leq V(t) \leq \pi_4, \quad 0 \leq W(t) \leq \pi_5, \quad 0 \leq Z(t) \leq \pi_6
\]

if

\[
A(0) + \frac{1}{\sigma_1} N(0) + \frac{1}{\sigma_2} C(0) + \frac{1}{\sigma_1 \sigma_3} V(0) + \frac{1}{\sigma_2 \sigma_4} (1 - \rho_1) W(0) + \frac{1}{\sigma_1 \sigma_3 \sigma_5} (1 - \rho_2) Z(0) \leq \pi_1.
\]

where \( \pi_2 = \sigma_1 \pi_1, \pi_3 = \sigma_2 \pi_1, \pi_4 = \sigma_1 \sigma_3 \pi_1, \pi_5 = \sigma_2 \sigma_4 (1 - \rho_1) \pi_1, \) and \( \pi_6 = \sigma_1 \sigma_3 \sigma_5 (1 - \rho_2) \pi_1 \). This proves that the set \( \Pi \) is positively invariant. \( \square \)

Theorem 2. There exist \( R_N > 0, \ R_C > 0, \ R_{NW} > 0, \ R_{CW} > 0, \ R > 0, \ \psi_1 > 0, \ \psi_2 > 0, \) and \( \psi_3 > 0 \) such that model (1) has ten equilibrium points under the following conditions:

1. The trivial equilibrium \( E_0 = (A_0, 0, 0, 0, 0, 0) \) always exists;
2. The healthy-cell equilibrium \( E_1 = (A_1, N_1, 0, 0, 0, 0) \) exists if \( R_N > 1 \);
3. The cancer-cell equilibrium \( E_2 = (A_2, 0, C_2, 0, 0, 0) \) exists if \( R_C > 1 \);
4. The infection cancer-immune-free equilibrium \( E_3 = (A_3, N_3, 0, V_3, 0, 0) \) exists if \( R_N > R_{NW} \);
5. The cancer-CTL equilibrium \( E_4 = (A_4, 0, C_4, 0, W_4, 0) \) exists if \( R_C > R_{CW} \);
6. The virus-free equilibrium \( E_5 = (A_5, N_5, C_5, 0, W_5, 0) \) exists if \( \frac{R_N}{R_C} > 1 \) and \( R_N > R_{CW} \);
7. The immune-free equilibrium \( E_6 = (A_6, N_6, C_6, V_6, 0, 0) \) exists if \( \frac{R_N}{R_C} > 1 \) and \( R_C > R_{NW} \);
8. The cancer-free equilibrium \( E_7 = (A_7, N_7, 0, V_7, 0, Z_7) \) exists if \( R_N > R_C \) and \( R_N > R_{NW} + \frac{\psi_1 \psi_5}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \);\)
9. The antibodies-free equilibrium \( E_8 = (A_8, N_8, C_8, V_8, W_8, 0) \) exists if \( R_N > R_{CW} + \frac{R_N}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \) and \( R_C > R_{NW} + \frac{R_N}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \);\)
10. The coexistence equilibrium \( E_9 = (A_9, N_9, C_9, V_9, W_9, Z_9) \) exists if \( R_C > R_N + \frac{R_N}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \) and \( R_N > R_{NW} + \frac{R_N}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \) and \( R_C > R_{NW} + \frac{R_N}{\psi_2} \frac{\psi_3}{\psi_4} (1 - \rho_2) \).

Proof. Any equilibrium point \( E = (A, N, C, V, W, Z) \) of system (1) satisfies the following system of equations:

\[
\begin{align*}
\mu - \theta A - \eta_1 AN - \eta_2 AC &= 0, \\
\sigma_1 \eta_1 AN - \eta_3 NV - \Theta_1 N &= 0, \\
\sigma_2 \eta_2 AC - \eta_4 CW - \Theta_2 C &= 0, \\
\sigma_3 \eta_3 NV - \eta_5 VZ - \Theta_3 V &= 0, \\
\sigma_4 \eta_4 (1 - \rho_1) CW - \Theta_4 W &= 0, \\
\sigma_5 \eta_5 (1 - \rho_2) VZ - \Theta_5 Z &= 0.
\end{align*}
\]

(2)

By finding the solutions of algebraic system (2), we get the following equilibrium points:

1. The trivial equilibrium is given by \( E_0 = (A_0, 0, 0, 0, 0, 0) \), where \( A_0 = \frac{\mu}{\theta} > 0 \). Thus, \( E_0 \) always exists.
(2) The healthy-cell equilibrium takes the form $E_1 = (A_1, N_1, 0, 0, 0, 0)$, where

$$A_1 = \frac{\Theta_1}{\sigma_1 \eta_1}, \quad N_1 = \frac{\theta}{\eta_1} \left( \mathcal{R}_N - 1 \right).$$

where $\mathcal{R}_N = \frac{\mu \eta_1}{\sigma_1 \eta_1}$. As $A_1 > 0$, the equilibrium $E_1$ exists when $N_1 > 0$ and this holds if $\mathcal{R}_N > 1$. Hence, $\mathcal{R}_N$ is a threshold number needed for the persistence of only healthy epithelial cells in the presence of nutrient.

(3) The cancer-cell equilibrium takes the form $E_2 = (A_2, 0, C_2, 0, 0, 0)$, where

$$A_2 = \frac{\Theta_2}{\sigma_2 \eta_2}, \quad C_2 = \frac{\theta}{\eta_2} \left( \mathcal{R}_C - 1 \right),$$

where $\mathcal{R}_C = \frac{\mu \eta_2}{\sigma_2 \eta_2}$. As $A_2 > 0$, the equilibrium point $E_2$ is defined when $C_2 > 0$ which corresponds to the condition $\mathcal{R}_C > 1$. Hence, $\mathcal{R}_C$ is a threshold number needed for the persistence of only cancer cells in the presence of nutrient.

(4) The infection equilibrium is given by $E_3 = (A_3, N_3, 0, V_3, 0, 0)$, where

$$A_3 = \frac{\mu \sigma_3 \eta_3}{\psi_1}, \quad N_3 = \frac{\Theta_3}{\sigma_3 \eta_3}, \quad V_3 = \frac{\theta \Theta_3 \sigma_3 \mathcal{R}_N}{\psi_1} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N - 1} \right),$$

where $\mathcal{R}_N = 1 + \frac{\eta_1 \Theta_3}{\sigma_1 \eta_1}$ and $\psi_1 = \eta_1 \Theta_3 + \Theta_3 \eta_3$. We note that as $A_3 > 0$, $N_3 > 0$, and $V_3 > 0$ if $\mathcal{R}_N > \mathcal{R}_N$. Thus, the equilibrium point $E_3$ exists if $\mathcal{R}_N > \mathcal{R}_N$. Here, $\frac{\mathcal{R}_N}{\mathcal{R}_N}$ is a threshold number which determines the establishment of SARS-CoV-2 infection in cancer-free patients.

(5) The cancer–CTL equilibrium has the form $E_4 = (A_4, 0, C_4, 0, W_4, 0)$, where

$$A_4 = \frac{\mu \sigma_4 \eta_4 (1 - \rho_1)}{\psi_2}, \quad C_4 = \frac{\Theta_4}{\sigma_4 \eta_4 (1 - \rho_1)}, \quad W_4 = \frac{\theta \Theta_4 \sigma_4 \mathcal{R}_{\text{CW}} (1 - \rho_1)}{\psi_2} \left( \frac{\mathcal{R}_{\text{CW}}}{\mathcal{R}_{\text{CW}} - 1} \right),$$

where $\mathcal{R}_{\text{CW}} = 1 + \frac{\eta_3 \Theta_4}{\sigma_3 \eta_3}$ and $\psi_2 = \eta_3 \Theta_4 + \Theta_4 \eta_4 (1 - \rho_1)$. We see that $A_4 > 0$, $C_4 > 0$, and $W_4 > 0$ if $\mathcal{R}_C > \mathcal{R}_{\text{CW}}$. Hence, $E_4$ exists if $\mathcal{R}_C > \mathcal{R}_{\text{CW}}$. Here, $\frac{\mathcal{R}_C}{\mathcal{R}_{\text{CW}}}$ is a threshold number which determines the activation of CTL immune response against cancer cells when the epithelial cells do not exist.

(6) The virus-free equilibrium is given by $E_5 = (A_5, N_5, C_5, 0, W_5, 0)$, where

$$A_5 = \frac{\Theta_5}{\sigma_5 \eta_5}, \quad N_5 = \frac{\mu \sigma_5 \eta_5 (1 - \rho_1)}{\eta_5 \eta_5 (1 - \rho_1)}, \quad C_5 = \frac{\Theta_5}{\sigma_5 \eta_5 (1 - \rho_1)}, \quad W_5 = \frac{\Theta_5}{\eta_5} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N} - 1 \right).$$

It is clear that $A_5 > 0$, $C_5 > 0$, and $W_5 > 0$ if $\frac{\mathcal{R}_C}{\mathcal{R}_N} > 1$. On the other hand, we have

$$N_5 > 0 \iff \mu \sigma_1 \eta_1 \sigma_4 \eta_4 (1 - \rho_1) > \theta \Theta_1 \sigma_4 \eta_4 (1 - \rho_1) + \Theta_1 \eta_2 \Theta_4$$

$$\iff \frac{\mu \sigma_1 \eta_1 \eta_4 (1 - \rho_1)}{\theta \Theta_1} > 1 + \frac{\eta_2 \Theta_4}{\theta \Theta_4} (1 - \rho_1)$$

$$\iff \mathcal{R}_N > \mathcal{R}_{\text{CW}}.$$ 

Accordingly, $E_5$ exists if $\frac{\mathcal{R}_C}{\mathcal{R}_N} > 1$ and $\mathcal{R}_N > \mathcal{R}_{\text{CW}}$.

(7) The immune-free equilibrium has the form $E_6 = (A_6, N_6, C_6, V_6, 0, 0)$, where

$$A_6 = \frac{\Theta_2}{\sigma_2 \eta_2}, \quad N_6 = \frac{\Theta_3}{\sigma_3 \eta_3}, \quad C_6 = \frac{\Theta_4}{\eta_3} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N} - 1 \right), \quad V_6 = \frac{\Theta_1}{\eta_3} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N} - 1 \right).$$

Thus, the equilibrium point $E_6$ exists if $\frac{\mathcal{R}_N}{\mathcal{R}_N} > 1$ and $\mathcal{R}_C > \mathcal{R}_{\text{CW}}$.

(8) The cancer-free equilibrium is given by $E_7 = (A_7, N_7, 0, V_7, 0, Z_7)$, where

$$A_7 = \frac{\psi_3}{\sigma_1 \eta_1 \rho_1 (1 - \rho_1)}, \quad N_7 = \frac{\theta \Theta_1 \psi_3 \sigma_1 \rho_1 (1 - \rho_1)}{\eta_1 \psi_1} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N} - 1 \right),$$

$$V_7 = \frac{\Theta_3}{\sigma_3 \eta_3 (1 - \rho_1)}, \quad Z_7 = \frac{\theta \Theta_1 \sigma_3 \rho_1 (1 - \rho_1)}{\eta_3 \psi_3} \left( \frac{\mathcal{R}_N}{\mathcal{R}_N} - \frac{\theta \Theta_1 \sigma_3 \rho_1 (1 - \rho_1)}{\sigma_3 \eta_3 (1 - \rho_1)} \right),$$

$\mathcal{R} = 1 + \frac{\eta_3 \Theta_3}{\sigma_3 \eta_3}$ and $\psi_3 = \eta_3 \Theta_3 + \Theta_3 \sigma_3 \rho_1 (1 - \rho_2)$. $\frac{\mathcal{R}_N}{\mathcal{R}_N}$ is a threshold number needed for the activation of antibody immune response against SARS-CoV-2 in cancer-free patients. We note that $A_7 > 0$, $N_7 > 0$ if $\mathcal{R}_N > \mathcal{R}_N$, $V_7 > 0$, and $Z_7 > 0$ if $\mathcal{R}_N > \mathcal{R}_N + \frac{\sigma_1 \rho_1 \sigma_1 \rho_1 (1 - \rho_1)}{\sigma_3 \eta_3 (1 - \rho_1)}$. Thus, $E_7$ exists if $\mathcal{R}_N > \mathcal{R}$ and $\mathcal{R}_N > \mathcal{R}_N + \frac{\sigma_1 \rho_1 \sigma_1 \rho_1 (1 - \rho_1)}{\sigma_3 \eta_3 (1 - \rho_1)}$.

(9) The antibodies-free equilibrium is given by $E_8 = (A_8, N_8, C_8, V_8, W_8, 0)$, where

$$A_8 = \frac{\mu \sigma_1 \eta_1 \sigma_4 \eta_4 (1 - \rho_1)}{\sigma_1 \eta_1 \rho_1 (1 - \rho_1)}, \quad N_8 = \frac{\Theta_5}{\sigma_5 \eta_5}, \quad C_8 = \frac{\Theta_4}{\sigma_4 \eta_4 (1 - \rho_1)}, \quad V_8 = \frac{\theta \Theta_4 \sigma_4 \mathcal{R}_{\text{CW}} (1 - \rho_1)}{\psi_2} \left( \frac{\mathcal{R}_{\text{CW}}}{\mathcal{R}_{\text{CW}} - 1} \right),$$

$$W_8 = \frac{\theta \Theta_4 \sigma_4 \mathcal{R}_{\text{CW}} (1 - \rho_1)}{\psi_2} \left( \frac{\mathcal{R}_{\text{CW}}}{\mathcal{R}_{\text{CW}} - 1} \right).$$
It is clear that $A_8 > 0$, $N_9 > 0$, and $C_8 > 0$. On the other hand, we have

$$V_8 > 0 \iff \mu \sigma_1 \eta_2 \sigma_3 \eta_4 \sigma_4 (1 - \rho_1) > \eta_1 \Theta_1 \sigma_3 \eta_3 \sigma_4 \eta_4 (1 - \rho_1) + \Theta_1 \eta_2 \sigma_3 \eta_3 \Theta_4$$

$$\iff \frac{\mu \sigma_1 \eta_2}{\Theta_1} > 1 + \frac{\eta_3 \Theta_4}{\Theta_4 \eta_4 (1 - \rho_1)} + \frac{\eta_1 \Theta_3}{\eta_3 \Theta_3},$$

$$\iff \mathcal{R}_N > \mathcal{R}_C W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3}.$$  

and

$$W_8 > 0 \iff \mu \sigma_2 \eta_2 \sigma_3 \eta_3 \sigma_4 \eta_4 (1 - \rho_1) > \eta_1 \Theta_2 \sigma_3 \eta_3 \sigma_4 \eta_4 (1 - \rho_1) + \Theta_2 \eta_2 \sigma_3 \eta_3 \Theta_4$$

$$\iff \frac{\mu \sigma_2 \eta_2}{\Theta_2} > 1 + \frac{\eta_3 \Theta_4}{\Theta_4 \eta_4 (1 - \rho_1)} + \frac{\eta_1 \Theta_3}{\eta_3 \Theta_3},$$

$$\iff \mathcal{R}_C > \mathcal{R}_N W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3}.$$  

Accordingly, $E_8$ exists if $\mathcal{R}_N > \mathcal{R}_C W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3}$ and $\mathcal{R}_C > \mathcal{R}_N W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3}$.

(10) The coexistence equilibrium has the form $E_9 = (A_9, N_9, C_9, V_9, W_9, Z_9)$, where

$$A_9 = \frac{\psi_3}{\sigma_1 \eta_1 \sigma_3 \eta_3 (1 - \rho_2)},$$

$$N_9 = \frac{\mu \sigma_2 \eta_2 \sigma_3 \eta_3 \sigma_4 \eta_4 (1 - \rho_1) - \theta_1 \sigma_3 \eta_3 \sigma_4 \eta_4 \eta_5 (1 - \rho_1) (1 - \rho_2) - \eta_1 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1)}{\eta_1 \psi_3 \sigma_4 \eta_4 (1 - \rho_1)},$$

$$C_9 = \frac{\Theta_4}{\sigma_4 \eta_4 (1 - \rho_1)}, \quad V_9 = \frac{\Theta_5}{\sigma_5 \eta_5 (1 - \rho_2)}, \quad W_9 = \frac{\Theta_1 \sigma_2 \eta_2}{\sigma_1 \psi_3 \sigma_4 \eta_4 (1 - \rho_1)},$$

$$Z_9 = \frac{\mu \sigma_1 \eta_1 \sigma_3 \eta_3 \sigma_4 \eta_4 \eta_5 (1 - \rho_1) (1 - \rho_2) - \theta_1 \sigma_3 \eta_3 \sigma_4 \eta_4 \sigma_5 \eta_5 (1 - \rho_1) (1 - \rho_2) - \eta_1 \Theta_1 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1) (1 - \rho_2)}{\eta_1 \psi_3 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1)},$$

$$\frac{\eta_2 \Theta_4}{\eta_2 \Theta_4 (1 - \rho_2)} + \frac{\eta_3 \Theta_4}{\eta_3 \Theta_4 (1 - \rho_2)}.$$  

It is easy to note that $A_9 > 0$, $C_9 > 0$, $V_9 > 0$, and $W_9 > 0$ if $\mathcal{R}_N > \mathcal{R}_C W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3}$. Also, we have

$$N_9 > 0 \iff \mu \sigma_2 \eta_2 \sigma_3 \eta_3 \sigma_4 \eta_4 (1 - \rho_1) (1 - \rho_2) > \theta_1 \sigma_3 \eta_3 \sigma_4 \eta_4 \eta_5 (1 - \rho_1) (1 - \rho_2) + \eta_1 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1)$$

$$\iff \mathcal{R}_N > \mathcal{R}_C W + \frac{\eta_2 \Theta_4}{\Theta_4 \sigma_4 \eta_4 (1 - \rho_1)} + \frac{\eta_3 \Theta_4}{\Theta_4 \sigma_4 \eta_4 (1 - \rho_2)},$$

Similarly,

$$Z_9 > 0 \iff \mathcal{R}_N > \mathcal{R}_C W + \frac{\psi_3 \Theta_5}{\psi_3 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1)} + \frac{\eta_2 \Theta_4}{\Theta_4 \sigma_4 \eta_4 \Theta_5 (1 - \rho_2)} + \frac{\eta_3 \Theta_4}{\Theta_4 \sigma_4 \eta_4 \Theta_5 (1 - \rho_2)},$$

Hence, $E_9$ exists if $\mathcal{R}_N > \mathcal{R}_C W + \frac{\psi_3 \Theta_5}{\psi_3 \sigma_4 \eta_4 \Theta_5 (1 - \rho_1)} + \frac{\eta_2 \Theta_4}{\Theta_4 \sigma_4 \eta_4 \Theta_5 (1 - \rho_2)} + \frac{\eta_3 \Theta_4}{\Theta_4 \sigma_4 \eta_4 \Theta_5 (1 - \rho_2)}$, and $\mathcal{R}_N > \mathcal{R}_C W + \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3} + \frac{\eta_2 \Theta_4}{\Theta_4 \sigma_4 \eta_4 (1 - \rho_1)} + \frac{\eta_3 \Theta_4}{\Theta_4 \sigma_4 \eta_4 (1 - \rho_2)}.$  

\[\square\]

4. Global properties

In this section, we prove the global stability of the equilibrium points of model (1) by constructing Lyapunov functions following the method presented in Korobeinikov [39], Elaiw [40], [41]. From now on, the following simplifications will be considered:

$$A(t) \equiv A, \quad N(t) \equiv N, \quad C(t) \equiv C, \quad V(t) \equiv V, \quad W(t) \equiv W, \quad Z(t) \equiv Z.$$

Theorem 3. The equilibrium $E_0$ is globally asymptotically stable when $\mathcal{R}_N \leq 1$ and $\mathcal{R}_C \leq 1$. It becomes unstable when $\mathcal{R}_N > 1$ or $\mathcal{R}_C > 1$.

Proof. Define a Lyapunov function $P_0(A, N, C, V, W, Z)$ as

$$P_0 = A_0 \left( \frac{A}{A_0} - 1 - \ln \frac{A}{A_0} \right) + \frac{1}{\sigma_1} N + \frac{1}{\sigma_2} C + \frac{1}{\sigma_3} V + \frac{1}{\sigma_4} W + \frac{1}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)}.$$
Then, we obtain
\[ \frac{dp_0}{dt} = \left(1 - \frac{A_0}{A} \right) \left[ \frac{\mu - \theta A - \eta_1 AN - \eta_2 AC}{\sigma_1} \right] + \frac{1}{\sigma_1} \left[ \sigma_1 \eta_1 AN - \eta_3 NV - \Theta_1 N \right] \\
+ \frac{1}{\sigma_2} \left[ \sigma_2 \eta_2 AC - \eta_4 CW - \Theta_2 C \right] + \frac{1}{\sigma_3} \left[ \sigma_3 \eta_3 NV - \eta_5 VZ - \Theta_3 V \right] \\
+ \frac{1}{\sigma_4} \left[ \sigma_4 \eta_4 (1 - \rho_1) CW - \Theta_4 W \right] + \frac{1}{\sigma_5} \left[ \sigma_5 \eta_5 (1 - \rho_2) VZ - \Theta_5 Z \right] \\
= -\frac{\theta (A - A_0)^2}{A} + \frac{\Theta_1}{\sigma_1} \left( \frac{\mu \sigma_1 \eta_1}{\theta \Theta_1} - 1 \right) N + \frac{\Theta_2}{\sigma_2} \left( \frac{\mu \sigma_2 \eta_2}{\theta \Theta_2} - 1 \right) C - \frac{\Theta_3}{\sigma_3} V \\
- \frac{\Theta_4}{\sigma_4} \left( \frac{\sigma_4 \eta_4 (1 - \rho_1)}{A} \right) W - \frac{\Theta_5}{\sigma_5 \sigma_5 (1 - \rho_2)} Z. \]

We note that \( \frac{dp_0}{dt} \leq 0 \) for all \( A, N, C, V, W, Z > 0 \) if \( R_N \leq 1 \) and \( R_C \leq 1 \). Also, \( \frac{dp_0}{dt} = 0 \) when \( (R_N - 1)N = 0, (R_C - 1)C = 0, A = A_0 \) and \( V = W = Z = 0 \). Then, we discuss four cases:

(i) If \( R_N = 1 \) and \( R_C = 1 \), then \( \frac{dp_0}{dt} = 0 \) when \( A = A_0 \) and \( V = W = Z = 0 \). We need to show that \( N = C = 0 \). As \( A = A_0 \), we get from the first equation of system (1) that
\[ 0 = \frac{dA}{dt} = \mu - \theta A - \eta_1 A N - \eta_2 A C. \]  
(3)

We obtain from Eq. (3) that \( A_0 (\eta_1 N + \eta_2 C) = 0 \). As \( A_0 \neq 0 \) and \( N, C \geq 0 \), we have \( N = C = 0 \).

(ii) If \( R_N = 1 \) and \( R_C < 1 \), then \( \frac{dp_0}{dt} = 0 \) when \( A = A_0 \) and \( C = V = W = Z = 0 \). From the first equation of system (1) we get
\[ 0 = \frac{dA}{dt} = \eta_1 A N, \]
which implies that \( N = 0 \).

(iii) If \( R_N < 1 \) and \( R_C = 1 \), then \( \frac{dp_0}{dt} = 0 \) when \( A = A_0 \) and \( N = V = W = Z = 0 \). From model (1) we get \( 0 = \frac{dA}{dt} = \eta_2 A C \), which implies that \( C = 0 \).

(iv) If \( R_N < 1 \) and \( R_C < 1 \), then \( \frac{dp_0}{dt} = 0 \) when \( A = A_0 \) and \( N = C = V = W = Z = 0 \).

For these four cases the singleton \([E_0]\) is the largest invariant subset of \( \{ (A, N, C, V, W, Z) \mid \frac{dp_0}{dt} = 0 \} \). According to LaSalle’s invariance principle [42], \( E_0 \) is globally asymptotically stable if \( R_N \leq 1 \) and \( R_C \leq 1 \).

To check the local instability of \( E_0 \) when \( R_N > 1 \) or \( R_C > 1 \), we compute the characteristic equation. The Jacobian matrix evaluated at \( E_0 \) is given by
\[ J(E_0) = \begin{bmatrix} -\theta & -\eta_1 A_0 & -\eta_2 A_0 & 0 & 0 & 0 \\ 0 & \sigma_1 \eta_1 A_0 - \Theta_1 & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma_2 \eta_2 A_0 - \Theta_2 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\Theta_3 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\Theta_4 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\Theta_5 \end{bmatrix}. \]

The associated characteristic equation is
\[ (\lambda + \theta)(\lambda + \Theta_1)(\lambda + \Theta_2)(\lambda + \Theta_3)(\lambda - \sigma_1 \eta_1 A_0 + \Theta_1)(\lambda - \sigma_2 \eta_2 A_0 + \Theta_2) = 0. \]  
(4)

We note that two of the eigenvalues of Eq. (4) are given by
\[ \lambda_1 = \sigma_1 \eta_1 A_0 - \Theta_1 = \Theta_1 (R_N - 1) > 0 \quad \text{if} \quad R_N > 1, \]
\[ \lambda_2 = \sigma_2 \eta_2 A_0 - \Theta_2 = \Theta_2 (R_C - 1) > 0 \quad \text{if} \quad R_C > 1. \]

This implies that \( E_0 \) is unstable when \( R_N > 1 \) or \( R_C > 1 \). \( \square \)

**Theorem 4.** Suppose that \( R_N > 1 \) and \( R_C \leq R_N \leq R_{NW} \). Then, the healthy-cell equilibrium \( E_1 \) is globally asymptotically stable.

**Proof.** Define a Lyapunov function \( P_1(A, N, C, V, W, Z) \) as
\[ P_1 = A_1 \left[ \frac{A}{1 - \ln \frac{A}{A_1}} \right] + \frac{1}{\sigma_1} N_1 \left[ \frac{N}{\rho_1} - 1 - \ln \frac{N}{\rho_1} \right] + \frac{1}{\sigma_2} C + \frac{1}{\sigma_3} V + \frac{1}{\sigma_4 (1 - \rho_1)} W + \frac{1}{\sigma_5 (1 - \rho_2)} Z. \]
Then, we get

\[
\frac{d\rho_1}{dt} = \left(1 - \frac{A_1}{A}\right) \left[\mu - \theta A - \eta_1 AN - \eta_2 AC\right] + \frac{1}{\sigma_1} \left(1 - \frac{N_1}{N}\right) \left[\sigma_1 \eta_1 AN - \eta_3 NV - \Theta_1 N\right]
\]

\[
+ \frac{1}{\sigma_2} \left[\sigma_2 \eta_2 AC - \eta_4 CW - \Theta_2 C\right] + \frac{1}{\sigma_1 \sigma_3} \left[\sigma_3 \eta_3 NV - \eta_5 VZ - \Theta_3 V\right]
\]

\[
+ \frac{1}{\sigma_2 \sigma_4 (1 - \rho_1)} \left[\sigma_4 \eta_4 (1 - \rho_1) CW - \Theta_4 W\right] + \frac{1}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} \left[\sigma_5 \eta_5 (1 - \rho_2) VZ - \Theta_5 Z\right].
\]

By using the equilibrium conditions at $E_1$

\[
\begin{align*}
\mu &= \theta A_1 + \eta_1 A_1 N_1, \\
\eta_1 A_1 N_1 &= \frac{\Theta_1}{\sigma_1} N_1,
\end{align*}
\]

the time derivative of $\rho_1$ in (5) is reduced to

\[
\frac{d\rho_1}{dt} = \left(1 - \frac{A_1}{A}\right) \left(\theta A_1 - \theta A\right) + \eta_1 A_1 N_1 \left(2 - \frac{A_1}{A}\right) + \frac{\sigma_3}{\sigma_2} \left(\frac{\sigma_2 \eta_1 \Theta_1}{\sigma_1 \eta_1 \Theta_1} - 1\right) C + \frac{\eta_1}{\sigma_1} \left(\frac{\rho_1}{\sigma_2} N_1 - \frac{\eta_1}{\sigma_1} \frac{\Theta_1}{\sigma_1} \right) V
\]

\[
- \frac{\sigma_2 \rho_1}{\sigma_1 \sigma_2 (1 - \rho_1)} W - \frac{\eta_1}{\sigma_1 \sigma_3 (1 - \rho_2)} Z.
\]

Thus, \(\frac{d\rho_1}{dt} \leq 0\) if \(\frac{R_N}{R_C} \leq 1\) and \(R_N \leq R_N\). In addition, \(\frac{d\rho_1}{dt} = 0\) when \(A = A_1\) and \(C = V = W = Z = 0\). Let $\Gamma_1'$ be the largest invariant subset of \(\Gamma_1 = \left\{(A, N, C, V, W, Z) \mid \frac{d\rho_1}{dt} = 0\right\}\). Hence, the solutions of system (1) converge to $\Gamma_1'$ which includes elements with \(A = A_1\) and \(C = V = W = Z = 0\). From system (1) we have \(0 = \frac{dA}{dt} = \mu - \theta A_1 - \eta_1 A_1 N_1\) which gives \(N = N_1\). It follows that $\Gamma_1' = \left\{E_1\right\}$. Based on LaSalle's invariance principle [42], the equilibrium $E_1$ is globally asymptotically stable if \(R_C \leq R_N \leq R_N\). \(\Box\)

From the proof of Theorem 3, we see that $E_0$ is the only stable equilibrium when \(R_N \leq 1\) and \(R_C \leq 1\). When \(R_N > 1\) and \(R_C \leq R_N \leq R_N\), $E_0$ loses its stability and $E_1$ becomes globally asymptotically stable according to Theorems 3 and 4. This means that a transcritical bifurcation occurs at $R_N = 1$.

**Theorem 5.** Suppose that \(R_C > 1\) and \(R_N \leq R_C \leq R_C\). Then, the cancer-cell equilibrium $E_2$ is globally asymptotically stable.

**Proof.** Define a Lyapunov function

\[
P_2(A, N, C, V, W, Z) = A_2 \left(1 - \frac{N_2}{A_2}\right) + \frac{1}{\sigma_1} N + \frac{1}{\sigma_2} C_2 \left(1 - \ln \frac{C_2}{C_2}\right) + \frac{1}{\sigma_1 \sigma_5} V
\]

\[
+ \frac{1}{\sigma_2 \sigma_4 (1 - \rho_1)} W + \frac{1}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} Z.
\]

By using the equilibrium conditions at $E_2$

\[
\begin{align*}
\mu &= \theta A_2 + \eta_2 A_2 C_2, \\
\eta_2 A_2 C_2 &= \frac{\Theta_2}{\sigma_2} C_2,
\end{align*}
\]

we obtain

\[
\frac{dP_2}{dt} = \left(1 - \frac{A_2}{A}\right) \left(\theta A_2 - \theta A\right) + \eta_2 A_2 C_2 \left(2 - \frac{A_2}{A}\right) + \frac{\Theta_1}{\sigma_1} \left(\frac{\sigma_1 \eta_1 \Theta_2}{\sigma_2 \eta_2 \Theta_1} - 1\right) N + \frac{\eta_4}{\sigma_2} (C_2 - C_4) W - \frac{\Theta_3}{\sigma_1 \sigma_3} V
\]

\[
- \frac{\sigma_2 \rho_1}{\sigma_1 \sigma_2 (1 - \rho_1)} W - \frac{\eta_1}{\sigma_1 \sigma_3 (1 - \rho_2)} Z.
\]

It is clear that \(\frac{d\rho_2}{dt} \leq 0\) if \(\frac{R_N}{R_C} \leq 1\) and \(R_C \leq R_C\). Also, one can show that \(\frac{d\rho_2}{dt} = 0\) if \(A = A_2\), \(C = C_2\), and \(N = W = V = Z = 0\). Thus, the singleton \(\{E_2\}\) is the largest invariant subset of \(\left\{(A, N, C, V, W, Z) \mid \frac{d\rho_2}{dt} = 0\right\}\). Accordingly, the global asymptotic stability of $E_2$ is guaranteed by LaSalle's invariance principle [42] when $R_N \leq R_C \leq R_C$. \(\Box\)

According to Theorem 3, $E_0$ is the only stable equilibrium when $R_N \leq 1$ and $R_C \leq 1$. When $R_C > 1$ and $R_N \leq R_C \leq R_C$, $E_0$ becomes unstable and $E_2$ appears and it is globally asymptotically stable as stated in Theorems 3 and 5. Hence, we have a transcritical bifurcation at $R_C = 1$. 

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Theorem 6. Suppose that $\mathcal{R}_N < \mathcal{R}_V < \mathcal{R}_N + \frac{\psi_4 \psi_5}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)}$ and $\mathcal{R}_C \leq \mathcal{R}_N$. Then, the infection equilibrium $E_3$ is globally asymptotically stable.

Proof. Define a Lyapunov function $\mathcal{P}_3(A, N, C, V, W, Z)$ as

\[
\mathcal{P}_3 = A_3 \left( \frac{A}{A_3} - 1 - \ln \frac{A}{A_3} \right) + \frac{1}{\sigma_1} N_3 \left( \frac{C}{C_3} - 1 - \ln \frac{C}{C_3} \right) + \frac{1}{\sigma_2} C + \frac{1}{\sigma_3} V_3 \left( \frac{V}{V_3} - 1 - \ln \frac{V}{V_3} \right)
\]

From Eq. (2), $E_3$ at the equilibrium state satisfies the conditions

\[
\left\{ \begin{array}{l}
\mu = \theta A_3 + \eta_1 A_3 N_3, \\
\eta_1 A_3 N_3 = \frac{n_1}{\sigma_1} N_3 V_3 + \frac{\rho_1}{\sigma_1} N_3, \\
\frac{3}{\sigma_1} N_3 V_3 = \frac{n_3}{\sigma_3} V_3.
\end{array} \right.
\]

By using the above conditions, the time derivative of $\mathcal{P}_3$ can be written as:

\[
\frac{d\mathcal{P}_3}{dt} = - (\theta + \eta_1 N_3) \frac{(A - A_3)^2}{A} + \eta_2 (A_3 - A_6) C - \frac{\Theta_4}{\sigma_2 \sigma_4 (1 - \rho_1)} W + \frac{\eta_5}{\sigma_1} (V_3 - V_7) Z.
\]

By using the value of $A_3$ of the equilibrium $E_3$ and the value of $A_6$ of the equilibrium $E_6$ computed in the proof of Theorem 2, we get

\[
A_3 - A_6 = \frac{\theta \Theta_2 \sigma_3 \eta_3}{\psi_1 / \psi_2 \eta_2} \left( \mu \sigma_2 \eta_2 / \theta \Theta_2 - 1 - \frac{\eta_1 \Theta_3}{\Theta_3 \eta_3} \right)
\]

Also, from the equilibrium points $E_3$ and $E_7$ computed in the proof of Theorem 2 we obtain

\[
V_3 - V_7 = \frac{\theta \Theta_3 \sigma_3}{\psi_1} \left[ \frac{\mathcal{R}_C - \mathcal{R}_N}{\mathcal{R}_N} - \frac{\Theta_3}{\sigma_3 \eta_3 (1 - \rho_2)} \right],
\]

Hence, Eq. (6) can be rewritten as

\[
\frac{d\mathcal{P}_3}{dt} = - (\theta + \eta_1 N_3) \frac{(A - A_3)^2}{A} + \eta_2 (A_3 - A_6) C - \frac{\Theta_4}{\sigma_2 \sigma_4 (1 - \rho_1)} W + \frac{\eta_5}{\sigma_1} (V_3 - V_7) Z
\]

We see that $\frac{d\mathcal{P}_3}{dt} \leq 0$ if $\mathcal{R}_C \leq \mathcal{R}_N$ and $\mathcal{R}_N \leq \mathcal{R}_C + \frac{\psi_4 \psi_5}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)}$. One can show that $\frac{d\mathcal{P}_3}{dt} = 0$ if $A = A_3$, $N = N_3$, $V = V_3$, and $C = W = Z = 0$. Thus, the singleton $E_3$ is the largest invariant subset of $\left\{ (A, N, C, V, W, Z) \mid \frac{d\mathcal{P}_3}{dt} = 0 \right\}$. Accordingly, LaSalle’s invariance principle guarantees the global stability of $E_3$ when $\mathcal{R}_C \leq \mathcal{R}_N$ and $\mathcal{R}_N \leq \mathcal{R}_C + \frac{\psi_4 \psi_5}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)}$. □

Theorem 7. Suppose that $\mathcal{R}_N \leq \mathcal{R}_C$. Then, the cancer-CTL equilibrium $E_4$ is globally asymptotically stable.

Proof. Consider the following Lyapunov function

\[
\mathcal{P}_4(A, N, C, V, W, Z) = A_4 \left( \frac{A}{A_4} - 1 - \ln \frac{A}{A_4} \right) + \frac{n_4}{\sigma_1} V_4 \left( \frac{V}{V_4} - 1 - \ln \frac{V}{V_4} \right) + \frac{1}{\sigma_1} W_4 \left( \frac{W}{W_4} - 1 - \ln \frac{W}{W_4} \right)
\]

By using the equilibrium conditions at $E_4$,

\[
\left\{ \begin{array}{l}
\mu = \theta A_4 + \eta_2 A_4 C_4, \\
\eta_2 A_4 C_4 = \frac{n_4}{\sigma_2} W_4 + \frac{\rho_2}{\sigma_2} C_4, \\
\frac{n_4}{\sigma_2} C_4 W_4 = \frac{\psi_2}{\sigma_4 (1 - \rho_1)} W_4,
\end{array} \right.
\]

we get

\[
\frac{d\mathcal{P}_4}{dt} = \left( 1 - \frac{A_4}{A} \right) (\theta A_4 - \theta A) + \eta_2 A_4 C_4 \left( 2 - \frac{A_4}{A_4} - \frac{A}{A_4} \right) + \eta_1 (A_4 - A_5) N - \frac{\Theta_3}{\sigma_1 \sigma_3} V - \frac{\Theta_5}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} W
\]

Using the same arguments as in Theorems 3–6, we conclude that $E_4$ is globally asymptotically stable if $\mathcal{R}_N \leq \mathcal{R}_C$. □
Theorem 8. Assume that \( \frac{RC}{N_0} > 1 \) and \( R_{CW} < R_N \leq R_{CW} + \frac{\eta_1 \Theta_3}{\sigma_3 \sigma_3} \). Then, the virus-free equilibrium \( E_5 \) is globally asymptotically stable.

Proof. Take a Lyapunov function

\[ P_5(A, N, C, V, W, Z) = A_5 \left( A - 1 - \ln \frac{A}{A_5} \right) + \frac{1}{\sigma_1} N_5 \left( \frac{N}{N_5} - 1 - \ln \frac{N}{N_5} \right) + \frac{1}{\sigma_2} C_5 \left( \frac{C}{C_5} - 1 - \ln \frac{C}{C_5} \right) + \frac{1}{\sigma_1 \sigma_3} V + \frac{1}{\sigma_2 \sigma_3 (1 - \rho_1)} W_5 \left( W - 1 - \ln \frac{W}{W_5} \right) + \frac{1}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} Z. \]

At the equilibrium state, \( E_5 \) satisfies the following system of equations

\[
\begin{align*}
\mu &= \theta A_5 + \eta_1 A_5 N_5 + \eta_2 A_5 C_5, \\
\eta_1 A_5 N_5 &= \frac{\sigma_1}{\sigma_3} N_5, \\
\eta_2 A_5 C_5 &= \frac{\sigma_2}{\sigma_3} C_5 W_5 + \frac{\sigma_3}{\sigma_3} C_5, \\
\frac{\sigma_3}{\sigma_3} C_5 W_5 &= \frac{\sigma_3}{\sigma_3} (1 - \rho_1) W_5.
\end{align*}
\]

By using the above conditions, we have

\[
\frac{dP_5}{dt} = \left( 1 - \frac{A_5}{A} \right) (\theta A_5 - \theta A) + \eta_1 A_5 N_5 \left( 2 - \frac{A_5}{A} - \frac{A}{A_5} \right) + \eta_2 A_5 C_5 \left( 2 - \frac{A_5}{A} - \frac{A}{A_5} \right) + \frac{\eta_3}{\sigma_1} (N_5 - N_8) V
\]

\[
- \frac{\Theta_3}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} Z.
\]

Thus, \( \frac{dP_5}{dt} \leq 0 \) if \( R_N \leq \frac{\eta_1 \Theta_3}{\sigma_3 \sigma_3} \). Also, \( \frac{dP_5}{dt} = 0 \) when \( A = A_5 \), \( V = 0 \), and \( Z = 0 \). Let \( \Gamma_5' \) be the largest invariant subset of

\[ \Gamma_5 = \{ (A, N, C, V, W, Z) \mid \frac{dP_5}{dt} = 0 \}. \]

Hence, the solutions of system (1) converge to \( \Gamma_5' \) which includes elements with \( A = A_5 \), \( V = 0 \), and \( Z = 0 \). From the first equation of system (1), we find

\[
0 = \frac{dA}{dt} = \mu - \theta A_5 - \eta_1 A_5 N - \eta_2 A_5 C.
\]

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

\[
\frac{dN}{dt} = \frac{\sigma_1}{\sigma_3} \eta_1 A_5 N - \Theta_1 N = (\sigma_1 \eta_1 A_5 - \Theta_1) N = 0.
\]

Hence, \( N = \text{constant} = \bar{N} \). Substituting this value of \( N \) in Eq. (7), we get

\[
0 = \mu - \theta A_5 - \eta_1 A_5 \bar{N} - \eta_2 A_5 C.
\]

By solving Eq. (8) for \( C \), we find that \( C = \text{constant} = \bar{C} \). Consequently, we have \( \frac{dC}{dt} = 0 \). From the third equation of system (1), we obtain

\[
0 = \sigma_2 \eta_2 A_5 \bar{C} - \eta_4 \bar{C} W - \Theta_2 \bar{C}.
\]

By solving Eq. (9) for \( W \), we find that \( W = W_5 \) and so \( \frac{dW}{dt} = 0 \). Then, from the fifth equation of system (1) we get \( \bar{C} = C_5 \). Accordingly, from Eq. (7) we get \( \bar{N} = N_5 \). It follows that \( \Gamma_5' = \{ E_5 \} \). Based on LaSalle’s invariance principle [42], the equilibrium \( E_5 \) is globally asymptotically stable if \( R_N \leq \frac{\eta_1 \Theta_3}{\sigma_3 \sigma_3} \). \( \square \)

Theorem 9. Assume that \( 1 < \frac{R_C}{C_0} \leq \bar{R} \) and \( R_{CN} < \bar{R} \leq \frac{\eta_2 \Theta_4}{\sigma_4 \sigma_4 (1 - \rho_1)} \). Then, the immune-free equilibrium \( E_6 \) is globally asymptotically stable.

Proof. Take a Lyapunov function

\[ P_6(A, N, C, V, W, Z) = A_6 \left( A - 1 - \ln \frac{A}{A_6} \right) + \frac{1}{\sigma_1} N_6 \left( \frac{N}{N_6} - 1 - \ln \frac{N}{N_6} \right) + \frac{1}{\sigma_2} C_6 \left( \frac{C}{C_6} - 1 - \ln \frac{C}{C_6} \right) + \frac{1}{\sigma_1 \sigma_3} V + \frac{1}{\sigma_2 \sigma_3 (1 - \rho_1)} W + \frac{1}{\sigma_1 \sigma_3 \sigma_5 (1 - \rho_2)} Z. \]

The equilibrium conditions at \( E_6 \) are given by

\[
\begin{align*}
\mu &= \theta A_6 + \eta_1 A_6 N_6 + \eta_2 A_6 C_6, \\
\eta_1 A_6 N_6 &= \frac{\sigma_1}{\sigma_3} N_6 V_6 + \frac{\sigma_2}{\sigma_3} C_6, \\
\eta_2 A_6 C_6 &= \frac{\sigma_2}{\sigma_3} C_6, \\
\frac{\sigma_3}{\sigma_3} N_6 V_6 &= \frac{\sigma_3}{\sigma_3} V_6.
\end{align*}
\]
After using the equilibrium conditions, we obtain
\[
\frac{d\eta_6}{dt} = \left(1 - \frac{\eta_6}{A}\right)(\theta A - \theta A) + \eta_1 A_6 N_6 \left(2 - \frac{\eta_6}{A} - \frac{\eta_4}{A}\right) + \eta_2 A_6 C_6 \left(2 - \frac{\eta_6}{A} - \frac{\eta_4}{A}\right) + \frac{\eta_6}{\sigma_1} (C_6 - C_8) W + \frac{\eta_6}{\sigma_{1}\sigma_7} (V_6 - V_9) Z
\]
\[= - (\theta + \eta_1 N_6 + \eta_2 C_6) \frac{(A - A_7)^2}{A} + \frac{\eta_6}{\sigma_1} \left[R_C - R_{NC} - \frac{\eta_6}{\sigma_{1}\sigma_7(1 - \rho_1)} W + \frac{\Theta_4}{\sigma_2\sigma_4(1 - \rho_1)} \left(\frac{\eta_6}{\sigma_{1}} - \tilde{R}\right) Z\right].\]

Thus, \(\frac{d\eta_6}{dt} \leq 0\) if \(R_C \leq R_{NC} + \frac{\eta_6}{\sigma_{1}\sigma_7(1 - \rho_1)} \) and \(\frac{\eta_6}{\sigma_{1}} \leq \tilde{R}\). Also, \(\frac{d\eta_8}{dt} = 0\) when \(A = A_6\), \(W = 0\), and \(Z = 0\). Let \(\Gamma'_6\) be the largest invariant subset of \(\Gamma_6 = \{(A, N, C, V, W, Z) \mid \frac{d\eta_6}{dt} = 0\}\). From the first equation of system (1), we find
\[
0 = \frac{d A}{dt} = \mu - \theta A_6 - \eta_1 A_6 N_6 - \eta_2 A_6 C_6. \tag{10}
\]
From the third equation of system (1), we get
\[
\frac{d C}{dt} = \sigma_2 \eta_2 A_6 C - \Theta_2 C = (\sigma_2 \eta_2 A_6 - \Theta_2) C = 0.
\]
This implies that \(C = \text{constant} = \tilde{C}\). Substituting this value of \(C\) in Eq. (10) gives
\[
0 = \mu - \theta A_6 - \eta_1 A_6 N_6 - \eta_2 A_6 \tilde{C}. \tag{11}
\]
By solving Eq. (11) for \(N\), we get \(N = \text{constant} = \tilde{N}\). This gives \(\frac{d N}{dt} = 0\), and from the second equation of system (1), we have
\[
0 = \sigma_1 \eta_1 A_6 \tilde{N} - \eta_3 \tilde{N} V - \Theta_1 \tilde{N}. \tag{12}
\]
Solving Eq. (12) for \(V\) gives \(V = V_6\) and as a result we have \(\frac{d V}{dt} = 0\). Then, from the fourth equation of (1) we obtain \(\tilde{N} = N_6\). By substituting \(N_6\) into Eq. (11), we get \(\tilde{C} = C_6\). It follows that \(\Gamma'_6 = \{E_6\}\). Based on LaSalle’s invariance principle [42], the equilibrium \(E_6\) is globally asymptotically stable if \(R_C \leq R_{NC} + \frac{\eta_6}{\sigma_{1}\sigma_7} (1 - \rho_1) \) and \(\frac{\eta_6}{\sigma_{1}} \leq \tilde{R}\). □

**Theorem 10.** Suppose that \(R_N > \tilde{R}\) and \(R_N > R_{NC} + \frac{\eta_6}{\sigma_{1}\sigma_7\sigma_9} (1 - \rho_1) \). Then, the cancer-free equilibrium \(E_7\) is globally asymptotically stable if \(R \leq \frac{\eta_6}{\sigma_{1}^2}\).

**Proof.** Consider a Lyapunov function
\[
\mathcal{P}_7(A, N, C, V, W, Z) = A_7 \left(\frac{A}{A_7} - 1 - \ln \frac{A}{A_7}\right) + \frac{1}{\sigma_1} N_7 \left(\frac{N}{N_7} - 1 - \ln \frac{N}{N_7}\right) + \frac{1}{\sigma_2} C + \frac{1}{\sigma_3} V_7 \left(\frac{V}{V_7} - 1 - \ln \frac{V}{V_7}\right) + \frac{1}{\sigma_{1}\sigma_3(1 - \rho_1)} Z_7 \left(\frac{Z}{Z_7} - 1 - \ln \frac{Z}{Z_7}\right).
\]

By using the following equilibrium conditions at \(E_7\)
\[
\begin{align*}
\mu &= \theta A_7 + \eta_1 A_7 N_7, \\
\eta_1 A_7 N_7 &= \frac{\eta_6}{\sigma_1} N_7 V_7 + \frac{\eta_4}{\sigma_1} N_7, \\
\frac{\eta_6}{\sigma_1} N_7 V_7 &= \frac{\eta_5}{\sigma_1} \sigma_2 V_7 Z_7 + \frac{\Theta_4}{\sigma_1} V_7, \\
\frac{\eta_5}{\sigma_1} \sigma_2 V_7 Z_7 &= \frac{\Theta_4}{\sigma_{1}\sigma_7(1 - \rho_1)} Z_7,
\end{align*}
\]

we get
\[
\frac{d\mathcal{P}_7}{dt} = \left(1 - \frac{A}{A_7}\right)(\theta A - \theta A) + \eta_1 A_7 N_7 \left(2 - \frac{A}{A_7} - \frac{A}{A_7}\right) + \eta_2 A_7 C_7 \left(2 - \frac{A}{A_7} - \frac{A}{A_7}\right) + \frac{\Theta_4}{\sigma_2\sigma_4(1 - \rho_1)} W
\]
\[= - (\theta + \eta_1 N_7) \frac{(A - A_7)^2}{A} + \frac{\Theta_4}{\sigma_1\sigma_7} \left(\tilde{R} - \frac{R_N}{R_C}\right) C - \frac{\Theta_4}{\sigma_2\sigma_4(1 - \rho_1)} W.
\]

Thus, \(\frac{d\mathcal{P}_7}{dt} \leq 0\) if \(\tilde{R} \leq \frac{\eta_6}{\sigma_{1}^2}\). Also, \(\frac{d\mathcal{P}_7}{dt} = 0\) when \(A = A_7\), \(C = 0\), \(W = 0\). Let \(\Gamma'_7\) be the largest invariant subset of \(\Gamma_7 = \{(A, N, C, V, W, Z) \mid \frac{d\mathcal{P}_7}{dt} = 0\}\). From the first equation of system (1), we have
\[
0 = \mu - \theta A_7 - \eta_1 A_7 N_7
\]
which gives \(N = N_7\). From the second equation of system (1), we get
\[
0 = \frac{d N}{dt} = \sigma_1 \eta_1 A_7 N_7 - \eta_3 N_7 V - \Theta_1 N_7
\]
which gives \(V = V_7\). Then, the fourth equation of system (1) gives
\[
0 = \frac{d V}{dt} = \sigma_3 \eta_3 N_7 V - \eta_5 V_7 Z - \Theta_3 V_7.
\]
which yields \( Z = Z_7 \). It follows that \( \Gamma' = \{ E_7 \} \). Based on LaSalle’s invariance principle [42], the equilibrium \( E_7 \) is globally asymptotically stable if \( \bar{R} \leq \frac{R_N}{R_C} \). □

**Theorem 11.** Suppose that \( R_N > R_{CW} + \frac{\nu_1 \psi_5}{\sigma_4 \theta_4} \) and \( R_C > R_{NV} + \frac{\nu_2 \psi_5}{\theta_5} \), Then, the antibodies-free equilibrium \( E_8 \) is stable if \( R_N \leq R_{NV} + \frac{\nu_1 \psi_5}{\sigma_4 \theta_4} + \frac{\nu_2 \psi_5}{\theta_5} \). 

**Proof.** Define a Lyapunov function \( \mathcal{P}_8(A, N, C, V, W, Z) \) as follows

\[
\mathcal{P}_8(A, N, C, V, W, Z) = A_9 \left( \frac{A}{A_9} - 1 - \ln \frac{A}{A_9} \right) + \frac{1}{\sigma_4} N_9 \left( \frac{N}{N_9} - 1 - \ln \frac{N}{N_9} \right) + \frac{1}{\sigma_4} C_8 \left( \frac{C}{C_8} - 1 - \ln \frac{C}{C_8} \right) + \frac{1}{\sigma_4} V_9 \left( \frac{V}{V_9} - 1 - \ln \frac{V}{V_9} \right) + \frac{1}{\sigma_4} W_8 \left( \frac{W}{W_8} - 1 - \ln \frac{W}{W_8} \right) + \frac{1}{\sigma_4} Z_8 \left( \frac{Z}{Z_8} - 1 - \ln \frac{Z}{Z_8} \right).
\]

The equilibrium conditions at \( E_8 \) are provided by the following equations

\[
\begin{align*}
\mu &= \theta A_8 + \eta_1 A_8 N_8 + \eta_2 A_8 C_8, \\
\eta_1 A_8 N_8 &= \frac{\nu_1}{\sigma_4} N_9 V_9 + \frac{\nu_2}{\sigma_4} N_8, \\
\eta_2 A_8 C_8 &= \frac{\nu_1}{\sigma_4} C_8 W_8 + \frac{\nu_2}{\sigma_4} C_8, \\
\frac{\mu}{\eta_1} N_9 V_9 &= \frac{\nu_1}{\sigma_4} V_9, \\
\frac{\mu}{\eta_2} C_8 W_8 &= \frac{\nu_1}{\sigma_4} W_8.
\end{align*}
\]

After rearranging and using the above conditions, we obtain

\[
\frac{d\mathcal{P}_8}{dt} = \left( 1 - \frac{A}{A_9} \right) (\theta A_8 - \theta A) + \eta_1 A_8 N_8 \left( \frac{2 - A_8}{A_8} - \frac{A}{A_9} \right) + \eta_2 A_8 C_8 \left( \frac{2 - A_8}{A_8} - \frac{A}{A_9} \right) + \frac{\psi_1 \psi_5}{\sigma_4} \left( \frac{R_N - R_{NV}}{\theta_1 \theta_4 \psi_4 \theta_5} \right) Z_8.
\]

Thus, \( \frac{d\mathcal{P}_8}{dt} \leq 0 \) if \( R_N \leq R_{NV} + \frac{\psi_1 \psi_5}{\theta_1 \theta_4 \psi_4 \theta_5} \). This implies that \( E_8 \) is stable if \( R_N \leq R_{NV} + \frac{\psi_1 \psi_5}{\theta_1 \theta_4 \psi_4 \theta_5} \). □

**Theorem 12.** Suppose that \( \bar{R} > \frac{R_N}{R_C} \), \( R_N > \bar{R} + \frac{\nu_2 \psi_5}{\theta_5} \) and \( R_N > R_{NV} + \frac{\nu_2 \psi_5}{\theta_5} \). Then, the coexistence equilibrium \( E_9 \) is stable.

**Proof.** Define a Lyapunov function \( \mathcal{P}_9(A, N, C, V, W, Z) \) as follows

\[
\mathcal{P}_9(A, N, C, V, W, Z) = A_9 \left( \frac{A}{A_9} - 1 - \ln \frac{A}{A_9} \right) + \frac{1}{\sigma_4} N_9 \left( \frac{N}{N_9} - 1 - \ln \frac{N}{N_9} \right) + \frac{1}{\sigma_4} C_8 \left( \frac{C}{C_8} - 1 - \ln \frac{C}{C_8} \right) + \frac{1}{\sigma_4} V_9 \left( \frac{V}{V_9} - 1 - \ln \frac{V}{V_9} \right) + \frac{1}{\sigma_4} W_8 \left( \frac{W}{W_8} - 1 - \ln \frac{W}{W_8} \right) + \frac{1}{\sigma_4} Z_8 \left( \frac{Z}{Z_8} - 1 - \ln \frac{Z}{Z_8} \right)
\]

After rearranging and using equilibrium conditions, the time derivative of \( \mathcal{P}_9 \) is given by

\[
\frac{d\mathcal{P}_9}{dt} = - (\theta + \eta_1 N_9 + \eta_2 C_8) \left( \frac{A}{A_9} - 1 \right)^2.
\]

We see that \( \frac{d\mathcal{P}_8}{dt} \leq 0 \) which implies the stability of \( E_9 \). As it is not easy to show that \( \frac{d\mathcal{P}_9}{dt} = 0 \) at \( E_9 \), we will show the local asymptotic stability of \( E_9 \) numerically in the next section. □

5. Numerical simulations

In this section, we carry out some numerical simulations to advocate the results obtained in the previous section. Also, we discuss the effect of lymphopenia on the growth of tumor and SARS-CoV-2 virus. For this purpose, we choose the following initial conditions of system (1):

\[
A(0) = 0.5, \quad N(0) = 0.1, \quad C(0) = 0.05, \quad V(0) = 0.02, \quad W(0) = 0.004, \quad Z(0) = 0.002.
\]

According to Theorems 3–12, the stability is ensured for any other initial conditions. We divide the numerical simulations into ten cases corresponding to the stability of each equilibrium point computed in Theorem 2. We get these cases by varying the values of \( \eta_1, \eta_2, \eta_4, \eta_5, \theta_1, \theta_2, \theta_3, \theta_4, \) and \( \theta_5 \). The values of all other parameters are fixed and given in Table 2. The values of \( \rho_1 \) and \( \rho_2 \) are fixed to \( \rho_1 = \rho_2 = 0 \) in all cases. Accordingly, we get the following cases:
Fig. 1. The numerical simulations of system (1) for cases 1–5. The figures show the global stability of (a) the trivial equilibrium $E_0$, (b) the healthy-cell equilibrium $E_1$, (c) the cancer-cell equilibrium $E_2$, (d) the infection equilibrium $E_3$, and (e) the cancer-CTL equilibrium $E_4$. 
Case 1: We choose the values $ \eta_1 = 0.03, \eta_2 = 0.03, \eta_4 = 0.03, \eta_5 = 0.3, \theta_1 = 0.1, \theta_2 = 0.08, \theta_3 = 0.5, \theta_5 = 0.9$, and $\theta_5 = 0.07$. This gives $R_N = 0.2 < 1$ and $R_C = 0.24 < 1$. According to Theorem 3, the equilibrium $E_0 = (1.0, 0.0, 0.0, 0.0)$ is globally asymptotically stable as shown in Fig. 1a. At this point, there is no competition between healthy epithelial cells and cancer cells. As a result, the concentrations of SARS-CoV-2 particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies vanish.

Case 2: We take the values of parameters as $\eta_1 = 0.1, \eta_2 = 0.03, \eta_4 = 0.03, \eta_5 = 0.3, \theta_1 = 0.02, \theta_2 = 0.08, \theta_3 = 0.5, \theta_4 = 0.9$, and $\theta_5 = 0.07$. These values give $R_N = 2 > 1$, $R_C = 0.12 < 1$, and $R_N < 20.697 = R_N$. These thresholds lead to the global asymptotic stability of $E_1 = (0.5, 0.2, 0.0, 0.0, 0.0)$, which agrees with Theorem 4 (see Fig. 1b). This point represents the ideal situation in which the patient is cancer-free and coronavirus-free at the same time. This situation can be reached under functional treatments or effective immune responses. Of note, treating cancer and COVID-19 simultaneously is one of the most active research areas [18].

Case 3: We take the values $\eta_1 = 0.03, \eta_2 = 0.1, \eta_4 = 0.03, \eta_5 = 0.3, \theta_1 = 0.1, \theta_2 = 0.01, \theta_3 = 0.5, \theta_4 = 0.9$, and $\theta_5 = 0.07$. Then, we have $R_C = 2.6667 > 1$, $R_N = 0.075 < 1$, and $R_C < 1.5343 \times 10^3 = R_CW$. Under these conditions and in agreement with Theorem 5, the equilibrium $E_2 = (0.3750, 0.0333, 0.0, 0.0)$ is globally asymptotically stable as shown in Fig. 1c. At this point, the epithelial cells become extinct under the competition with cancer cells and so there is no infection with COVID-19 in this situation.

Case 4: We consider the values of parameters as $\eta_1 = 0.3, \eta_2 = 0.03, \eta_4 = 0.03, \eta_5 = 0.3, \theta_1 = 0.02, \theta_2 = 0.08, \theta_3 = 0.01, \theta_4 = 0.9$, and $\theta_5 = 0.07$. The corresponding thresholds are $R_N = 6 > 4.4091 = R_N$, $R_C = 0.24 < R_N$, and $R_N < 95.3466 = R_N + \psi_1$ and $\eta_4 = \eta_5$. This causes the solutions of system (1) to asymptotically converge the equilibrium $E_3 = (0.2268, 0.2273, 0.0, 0.0262, 0.0)$ as exhibited in Fig. 1d and supported by Theorem 6. At this point, the number of healthy epithelial cells decreases due to SARS-CoV-2 infection with no immune response. Also, the cancer cells are eliminated, which is not likely to happen in COVID-19 patients with progressive cancer.

Case 5: We select the values $\eta_1 = 0.03, \eta_2 = 0.1, \eta_4 = 0.9, \eta_5 = 0.3, \theta_1 = 0.1, \theta_2 = 0.0005, \theta_3 = 0.5, \theta_4 = 0.0005$, and $\theta_5 = 0.07$. For this set of parameters, we get $R_C = 3.9024 > 2.1389 = R_CW$ and $R_N = 0.2 < R_CW$. This causes the equilibrium $E_4 = (0.4675, 0.02278, 0.0088, 0)$ to be globally asymptotically stable as shown in Fig. 1e, which supports Theorem 7. In this case, the cancer-specific CTL immune response is activated to eliminate cancer cells, while the healthy epithelial cells are not present.

Case 6: We choose the values $\eta_1 = 0.1, \eta_2 = 0.1, \eta_4 = 0.9, \eta_5 = 0.3, \theta_1 = 0.01, \theta_2 = 0.0005, \theta_3 = 0.5, \theta_4 = 0.0005$, and $\theta_5 = 0.07$. This gives $R_N = 1.4634 > 1$, $R_N = 2.6667 > 2.1389 = R_N$, and $R_N < 21.8359 = R_N + \psi_1 \eta_4$. In agreement with Theorem 8, the equilibrium $E_5 = (0.375, 0.1056, 0.2278, 0.0106, 0)$ is globally asymptotically stable as can be seen in Fig. 2a. This point represents the situation in which the cancer patient infected with COVID-19 becomes COVID-19 free. Therefore, it is one of the goals that medical experiments try to reach.

Case 7: We consider the values $\eta_1 = 0.3, \eta_2 = 0.2, \eta_4 = 0.03, \eta_5 = 0.3, \theta_1 = 0.02, \theta_2 = 0.02, \theta_3 = 0.0005, \theta_4 = 0.9$, and $\theta_5 = 0.07$. This selection of parameter values gives $R_N = 1.5 > 1$, $R_C = 4.3325 = R_N$, $R_C = 3.07 \times 10^3 = R_N$ and $\eta_4 \psi_1 \eta_4$. This leads to the global asymptotic stability of $E_7 = (0.084, 0.2423, 0.00718, 0.0014)$, which agrees with the result of Theorem 9. In this case, the patient has only SARS-CoV-2 mono-infection with active SARS-CoV-2-specific antibody immune response.

Case 8: We select the values $\eta_1 = 0.9, \eta_2 = 0.03, \eta_4 = 1.4, \theta_1 = 0.001, \theta_2 = 0.08, \theta_3 = 0.01, \theta_4 = 0.9$, and $\theta_5 = 0.0001$. This gives $R_N = 34.2857 > 2.8801 = R_N$, $R_N > 32.3357 = R_N + \theta_1 \eta_4 \psi_1 \eta_4$, and $R_N < 124.8257 = \frac{R_N}{\psi_1 \eta_4}$. This leads to the global asymptotic stability of $E_8 = (0.25, 0.1553, 0.067, 0.0364, 0)$ is globally asymptotically stable as shown in Fig. 2b and supported by Theorem 10. Here, both types of immune responses in a COVID-19 cancer patient are not active. This may cause the patient to suffer from severe COVID-19 infection.

Case 9: We consider the values $\eta_1 = 0.2, \eta_2 = 0.3, \eta_4 = 1.2, \eta_5 = 0.3, \theta_1 = 0.01, \theta_2 = 0.008, \theta_3 = 0.0005, \theta_4 = 0.0001$, and $\theta_5 = 0.07$. The corresponding thresholds are $R_N = 5.3333 > 5.0655 = R_CW + \psi_1 \eta_4 \eta_4$, $R_N = 8.5714 > 5.0655 = R_CW$ and $\eta_4 \psi_1 \eta_4 \eta_4$. In agreement with Theorem 11, the equilibrium $E_9 = (0.1974, 0.1553, 0.1675, 0.0029, 0.0161, 0)$ is stable as shown in Fig. 2c. In this case, the SARS-CoV-2-specific antibody immune response in a COVID-19 cancer patient has not been activated yet. This may allow a rapid replication of SARS-CoV-2 particles and cause disease progression.

Case 10: We select the values $\eta_1 = 0.9, \eta_2 = 0.5, \eta_4 = 1.7, \eta_5 = 1.7, \theta_1 = 0.0001, \theta_2 = 0.0003, \theta_3 = 0.0003, \theta_4 = 0.0001$, and $\theta_5 = 0.0001$. This gives $R_N = 2.6176 > 1.8179 = \frac{R_N}{\psi_1 \eta_4}$, $R_N = 35.8209 > 10.3551 = R_N + \eta_4 \psi_1 \eta_4 \eta_4$. Accordingly, the equilibrium $E_0 = (0.0731, 0.2162, 0.1182, 0.0591, 0.0053, 0.0048)$ is stable as shown in Fig. 2e, which agrees with Theorem 12. Here, both immune responses are active. The cancer-specific CTL immune response works on killing cancer cells, while the SARS-CoV-2-specific antibody immune response works on clearing the virus. However, the effectiveness of these roles depends on the functionality of immune responses.
Fig. 2. The numerical simulations of system (1) for cases 6–10. The figures show the stability of (a) the virus-free equilibrium $E_5$, (b) the immune-free equilibrium $E_6$, (c) the cancer-free equilibrium $E_7$, (d) the antibodies-free equilibrium $E_8$, and (e) the coexistence equilibrium $E_9$. 

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To further confirm the asymptotic stability of $E_0$ and $E_9$ in Cases 9 and 10, we compute the Jacobian matrix of system (1) as follows

$$J(E) = \begin{bmatrix}
-\theta - \eta_1 N - \eta_2 C & -\eta_1 A - \eta_1 V - \Theta_1 & -\eta_2 A & 0 & 0 & 0 \\
\sigma_1 \eta_1 N & \sigma_1 \eta_1 A - \eta_1 V - \Theta_1 & 0 & 0 & 0 & 0 \\
\sigma_2 \eta_2 C & 0 & \sigma_2 \eta_2 A - \eta_2 W - \Theta_2 & 0 & 0 & 0 \\
0 & 0 & \sigma_3 \eta_3 A - \eta_3 W - \Theta_2 & 0 & 0 & 0 \\
0 & 0 & \sigma_4 \eta_4 (1 - \rho_1) W & 0 & 0 & 0 \\
0 & 0 & \sigma_5 \eta_5 (1 - \rho_2) V - \Theta_3 & 0 & 0 & 0
\end{bmatrix}$$

After that, we compute the eigenvalues $\lambda_i$ ($i = 1, 2, \ldots, 6$) of the Jacobian matrix $J$ at all possible equilibrium points. For the stability of $E_0$ and $E_9$, we need to show that

$$\text{Re}(\lambda_i) < 0 \quad \forall \ i = 1, 2, \ldots, 6,$$

while all other equilibria have eigenvalues with positive real parts. The results are given in Table 1.

### 5.1. The effect of lymphopenia on SARS-CoV-2/cancer patients

A functional exhaustion of immune responses due to lymphopenia can be seen by increasing the values of $\rho_1$ and $\rho_2$ in Case 10 while keeping all other parameters fixed. Increasing the values of $\rho_1$ and $\rho_2$ means decreasing the efficacies of cancer-specific CTL immune response and SARS-CoV-2-specific antibody immune response, respectively. Fig. 3 shows the effect of increasing values from $\rho_1 = \rho_2 = 0$ to $\rho_1 = \rho_2 = 0.1$ and $\rho_1 = \rho_2 = 0.2$. As we can see, the concentration of cancer cells increases with the increase in $\rho_1$. Similarly, the concentration of SARS-CoV-2 particles increases with the increase in $\rho_2$. This can worsen the state of tumor and cause severe COVID-19 outcomes. The patients with this condition might be at a high risk of death.

### 6. Discussion

COVID-19 is a new respiratory disease caused by SARS-CoV-2 virus. The virus has reached most countries of the world, and the total number of deaths is increasing everyday [2]. Mathematical modeling is a promising tool that can support laboratory experiments and clinical trials. We studied a within-host model of six ordinary differential equations. The model studies the interactions between nutrient, healthy epithelial cells, cancer cells, SARS-CoV-2 virus particles, cancer-specific CTLs, and SARS-CoV-2-specific antibodies. It has ten possible equilibrium points corresponding to the following ten cases:

(a) The trivial equilibrium $E_0$ always exists, and it is globally asymptotically stable if $R_N \leq 1$ and $R_C \leq 1$.
(b) The healthy-cell equilibrium $E_1$ exists if $R_N > 1$, and it is globally asymptotically stable if $R_C \leq R_N \leq R_{NV}$. The healthy epithelial cells population dominates at this point, while all other populations of cells and virus particles disappear.
(c) The cancer-cell equilibrium $E_2$ is defined if $R_C > 1$, and it is globally asymptotically stable if $R_N \leq R_C \leq R_{CW}$. At this point, the cancer cells population dominates and the other populations vanish.
(d) The infection equilibrium $E_4$ exists if $R_N > R_{NW}$, while it is globally asymptotically stable if $R_C \leq R_{NW}$ and $R_N \leq R_{NW} + \frac{\psi_1 \theta_5}{\sigma_{\theta_1} \sigma_{\theta_5} (1 - \rho_2)}$. Here, COVID-19 infection of epithelial cells is established, while cancer cells disappear due to the competition with healthy cells.

(e) The cancer-CTL equilibrium $E_6$ is defined if $R_C > R_{CW}$, and it globally attracts all solutions if $R_N \leq R_{CW}$. Here, the SARS-CoV-2 particles and epithelial target cells are eliminated. The complete elimination of target cells and its validity were discussed in Wang et al. [37].

(f) The virus-free equilibrium $E_9$ exists if $\frac{R_N}{R_C} > 1$ and $R_N > R_{CW}$, while it is globally asymptotically stable if $R_N \leq R_{CW} + \frac{\eta_2 \theta_4}{\sigma_{\theta_4} (1 - \rho_4)}$. In this situation, the cancer patient becomes COVID-19 free. Hence, the parameters used in this case could help in drug discovery experiments.

(g) The immune-free equilibrium $E_6$ is defined if $\frac{R_N}{R_C} > 1$ and $R_C > R_{NV}$, while it is globally asymptotically stable if $R_C \leq R_{NV} + \frac{\eta_2 \theta_4}{\sigma_{\theta_4} (1 - \rho_4)}$ and $\frac{R_N}{R_C} < \hat{R}$. At this point, the immune responses in COVID-19 cancer patient are not active. This may lead to the growth of cancer and cause severe COVID-19 infection.

(h) The cancer-free equilibrium $E_7$ is defined if $R_N > \hat{R}$ and $R_N > R_{NV} + \frac{\psi_1 \theta_5}{\sigma_{\theta_1} \sigma_{\theta_5} (1 - \rho_2)}$, and it is globally asymptotically stable if $\hat{R} \leq \frac{R_N}{R_C}$. Here, the cancer cells are eliminated, and the SARS-CoV-2-specific antibody immune response is activated to fight the viral infection.

(i) The antibodies-free equilibrium $E_8$ exists if $R_N > R_{CW} + \frac{\eta_2 \theta_4}{\sigma_{\theta_4} (1 - \rho_4)}$ and $R_C \geq R_{NV} + \frac{\eta_2 \theta_4}{\sigma_{\theta_4} (1 - \rho_4)}$. It is stable if $R_N \leq R_{NV} + \frac{\psi_1 \theta_5}{\sigma_{\theta_1} \sigma_{\theta_5} (1 - \rho_2)} + \frac{\eta_2 \theta_4}{\sigma_{\theta_4} (1 - \rho_4)} + \frac{\psi_4 \theta_5}{\sigma_{\theta_4} \sigma_{\theta_5} (1 - \rho_4)}$. The SARS-CoV-2-specific antibody immune response is not active at this point.

(j) The coexistence equilibrium $E_9$ is defined and stable if $\hat{R} > \frac{R_N}{R_C}$, $R_N > \hat{R}$, and $R_N > R_{NV} + \frac{\sigma_{\theta_4} \theta_5}{\sigma_{\theta_4} (1 - \rho_4)} + \frac{\sigma_{\theta_4} \theta_5}{\sigma_{\theta_4} (1 - \rho_4)}$ and $R_N > R_{NV} + \frac{\psi_1 \theta_5}{\sigma_{\theta_1} \sigma_{\theta_5} (1 - \rho_2)} + \frac{\sigma_{\theta_4} \theta_5}{\sigma_{\theta_4} (1 - \rho_4)} + \frac{\psi_4 \theta_5}{\sigma_{\theta_4} \sigma_{\theta_5} (1 - \rho_4)}$. The cancer-specific CTL immunity is activated to eradicate cancer cells, while the SARS-CoV-2-specific antibody immunity is activated to clear the virus. Notably, the immune responses are not able to completely eliminate cancer cells or virus particles.

We found that the numerical results are fully aligned with the theoretical results. Lymphopenia in COVID-19 cancer patients increases the concentrations of cancer cells and SARS-CoV-2 particles, which may cause severe complications and lead to death. Moreover, we noted that the immune responses in Case 10 (see numerical simulation section) are not able to remove cancer cells or virus particles even if there is no lymphopenia ($\rho_1 = \rho_2 = 0$). Thus, the values of these two parameters should be carefully controlled. Recent studies have shown that cancer and COVID-19 may be comitantly aggravated by lymphopenia [1,7,10,43]. It has been found that SARS-CoV-2/cancer patients with lymphopenia are at four times higher risk for hospitalization and ten times higher risk for death compared with COVID-19 patients without cancer [7]. In fact, the possibility of developing effective immune responses during SARS-CoV-2 infection in cancer patients is an active area of research. Comparing with the existing mathematical models of COVID-19, the model developed in this paper is the first within-host model that studies COVID-19 infection in cancer patients with a full analysis. Treating COVID-19 cancer patients is one of the most difficult challenges for the health sector [5,18]. Therefore, our results can be tested clinically to measure its accuracy. The results can be used to understand the interactions between healthy cells and cancer cells in COVID-19 cancer patients. Also, the results can be used to explore the importance of effective immune responses in this group of patients. Understanding complicated issues that may occur during COVID-19 infection in cancer patients can help in (i) developing more effective ways to deal with this group; (ii) finding effective treatments that may target both cancer and COVID-19 infection [43]. The model studied in this paper can be developed in many ways. First, by adding a coinfection term to model (1) as the following
Third, by considering time delays that will convert model (1) into delay differential equations model. Finally, by considering space variations and consequently studying partial differential equations model.

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**Declaration of Competing Interest**

The authors declare that they have no conflict of interest.

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**References**

[1] F. Slimano, A. Baudouin, J. Zerbit, A. Toulemonde-Delcliqué, et al., Cancer, immune suppression and coronavirus disease-19 (COVID-19): need to manage drug safety (French society for oncology pharmacy [SFPO] guidelines), Cancer Treat. Rev. 88 (2020) 102063.

[2] Coronavirus disease (COVID-19). Weekly Epidemiological Update (23 August 2020), World Health Organization (WHO), 2020.

[3] World health organization (WHO) coronavirus disease (COVID-19) advice for the public, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public.

[4] Q. Zhao, M. Meng, R. Kumar, Y. Wu, et al., Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a systemic review and meta-analysis, Int. J. Infect. Dis. 96 (2020) 131–135.

[5] S.M. Akula, S.L. Abrams, L.S. Steelman, S. Candido, et al., Cancer therapy and treatments during COVID-19 era, Adv. Biol. Regul. 77 (2020) 100739.

[6] J. Wang, Mathematical models for COVID-19: applications, limitations, and potentials, J. Public Health Emerg. 4 (3) (2020) 1–4.

[7] B. Dariya, G.P. Nagaraju, Understanding novel COVID-19: its impact on organ failure and risk assessment for diabetic and cancer patients, Cytokine Growth Factor Rev. 53 (2020) 43–52.

[8] S.Q. Du, W. Yuan, Mathematical modeling of interaction between innate and adaptive immune responses in COVID-19 and implications for viral pathogenesis, J. Med. Virol. 92 (9) (2020) 1615–1628.

[9] C. Addeo, A. Friedlaender, Cancer and COVID-19: unmasking their ties, Cancer Treat. Rev. 88 (2020) 102041.

[10] A. Indini, E. Rijavec, M. Ghidini, C. Bareggi, et al., Coronavirus infection and immune system: an insight of COVID-19 in cancer patients, Crit. Rev. Oncol. Hematol. 153 (2020) 103059.

[11] W. Guan, Z. Ni, Y. Hu, W. Liang, et al., Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (18) (2020) 1708–1720.

[12] F. Gennaro, O. Pizzolo, C. Marotta, M. Antunes, et al., Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review, Int. J. Environ. Res. Public Health 17 (8) (2020) 2690.

[13] W. Liu, Z. Tao, L. Wang, M. Yuan, et al., Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease, Chin. Med. J. 133 (9) (2020) 1032–1038.

[14] O. Cohen, M. Eisenberg, B. Caveney, P. Kirchgraber, et al., Dynamics of SARS-CoV-2 and the adaptive immune response, LabCorp (2020) 1–12.

[15] S. Assaad, V. Avrillon, M. Fournier, B. Mastroianni, et al., High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-CoV-2 on RT-PCR, Eur. J. Cancer 135 (2020) 251–259.

[16] N.M. Kuderer, T.K. Choueiri, D.P. Shah, Y. Shyr, et al., Clinical impact of COVID-19 on patients with cancer (CICC19): a cohort study, Lancet Oncol 20 (2020) 1907–1918.

[17] A. Landman, L. Feetham, D. Stuckey, Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China, Lancet Oncol. 21 (3) (2020) 335–337.

[18] N. Jyotsana, M. King, The impact of COVID-19 on cancer risk and treatment, Cell. Mol. Bioeng. (2020), doi:10.1155/2016/5230219.

[19] C. Gunase, J. Fowler, K. Kotsiadas, T. Monis, How simulation modelling can help reduce the impact of COVID-19, J. Simul. 14 (2) (2020) 83–97.

[20] M.V. Krishna, J. Prakash, Mathematical modelling on phase based transmissibility of coronavirus, Infect. Dis. Model. 5 (2020) 375–385.

[21] K. Rajagopal, N. Hasanczadeh, F. Parastesh, I. Hamarash, et al., A fractional-order model for the novel coronavirus (COVID-19) outbreak, Nonlinear Dyn. 101 (2020) 711–718.

[22] T. Chen, J. Rui, Q. Wang, Z. Zhao, et al., A mathematical model for simulating the phase-based transmissibility of a novel coronavirus, Infect. Dis. Poverty 9 (2020) 1–8.

[23] C. Yang, J. Wang, A mathematical model for the novel coronavirus epidemic in Wuhan, China, Math. Biosci. Eng. 17 (3) (2020) 2708–2724.

[24] Z. Liu, P. Magal, O. Seydi, G. Webb, Understanding unreported cases in the COVID-19 epidemic outbreak in Wuhan, China, and the importance of major public health interventions, Biology 9 (3) (2020) 1–12.

[25] M.A. Nowak, C.R.M. Bangham, Population dynamics of immune responses to persistent viruses, Science 272 (1996) 74–79.

[26] A.D. AlAgha, A.M. Elaiw, Stability of a general reaction-diffusion HIV-1 dynamics model with humoral immunity, Eur. Phys. J. Plus 134 (8) (2019) 1–18.

[27] A.M. Elaiw, N.A. Almuallem, Global properties of delayed-HIV dynamics models with differential drug efficacy in cocirculating target cells, Appl. Math. Comput. 265 (2015) 1067–1089.

[28] A. Perelson, D. Krischner, R. De Boer, Dynamics of HIV infection of CD4+ T cells, Math. Biosci. 114 (1) (1993) 81–125.

[29] A.M. Elaiw, A.D. Al Agha, Global dynamics of a general diffusive HIV infection model with capsids and adaptive immune response, Adv. Differ. Equ. 2019 (510) (2019) 1–31.

[30] K. Wang, W. Propagation of HBV with spatial delay, Math. Biosci. 210 (2007) 78–95.

[31] K. Hattaf, N. Yousfi, A generalized HBV model with diffusion and two delays, Comput. Math. Appl. 69 (2015) 31–40.

[32] A.M. Elaiw, S.E. Almalki, A.D. Hobiny, Global properties of saturated chikungunya virus dynamics models with cellular infection and delays, Adv. Differ. Equ. 2019 (476) (2019) 1–33.

[33] C. Li, J. Xu, J. Liu, Y. Zhou, The within-host viral kinetics of SARS-CoV-2, Math. Biosci. Eng. 17 (4) (2020) 2853–2861.

[34] I. Ghosh, Within host dynamics of SARS-CoV-2 in humans: modeling immune responses and antiviral treatments (2020) arXiv:2006.02936.

[35] K. Hattaf, N. Yousfi, Dynamics of SARS-CoV-2 infection model with two modes of transmission and immune response, Math. Biosci. Eng. 17 (5) (2020) 5326–5340.

[36] A. Pinkny, H.M. Dobrovolsky, SARS-CoV-2 coinfections: could influenza and the common cold be beneficial? J. Med. Virol. (2020) 1–8, doi:10.1002/jmv. 26098.

[37] Z. Wang, Z. Guo, H. Peng, A mathematical model verifying potent oncolytic efficacy of m1 virus, Math. Biosci. 276 (2016) 19–27.
[38] A.M. Elaiw, A.D. Hobiny, A.D. Al Agha, Global dynamics of reaction-diffusion oncolytic m1 virotherapy with immune response, Appl. Math. Comput. 367 (2020) 1–21.
[39] A. Korobeinikov, Global properties of basic virus dynamics models, Bull. Math. Biol. 66 (4) (2004) 879–883.
[40] A.M. Elaiw, Global properties of a class of HIV models, Nonlinear Anal. 11 (4) (2010) 2253–2263.
[41] A.M. Elaiw, Global properties of a class of virus infection models with multitarget cells, Nonlinear Dyn. 69 (1–2) (2012) 423–435.
[42] H.K. Khalil, Nonlinear Systems, Prentice-Hall, New Jersey, 1996.
[43] L. Derosa, C. Melenotte, F. Griscelli, B. Gachot, et al., The immuno-oncological challenge of COVID-19, Nat. Cancer 1 (10) (2020) 946–964.
[44] Z. Bakouny, J.E. Hawley, T.K. Choueiri, S. Peters, et al., COVID-19 and cancer: current challenges and perspectives, Cancer Cell 38 (2020) 629–646.