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A FITTED NUMERICAL METHOD FOR A MODEL ARISING IN HIV RELATED CANCER-IMMUNE SYSTEM DYNAMICS

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Abstract. The effect of diseases such as cancer and HIV among our societies is evident. Thus, from the mathematical point of view many models has been developed with the aim to contribute towards understanding the dynamics of diseases. Therefore, in this paper we believe by extending a system of delay differential equations (DDEs) model of HIV related cancer-immune system to a system of delay partial differential equations (DPDEs) model of HIV related cancer-immune dynamics, we can contribute toward understanding the dynamics more clearly. Thus, we analyse the extended models and use the qualitative features of the extended model to derive, analyse and implement a fitted operator finite difference method (FOFDM) and present our results. This FOFDM is analyzed for convergence and it is seen that it has has second-order accuracy. We present some numerical results for some cases of the the model to illustrate the reliability of our numerical method.

Keywords: reaction-diffusion; delay-differential equation; HIV; cancer-immune system; fitted operator; stability analysis.

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1. Introduction

The connection between HIV/AIDS and certain cancers diseases is not completely understood, even though the link is likely to depend on a weakened immune system. However, it is understood that most types of cancer begin when healthy cells change and grow out of control, forming a mass called a tumor. A tumor can be cancerous or benign. A cancerous tumor is malignant, meaning it can grow and spread to other parts of the body. A benign tumor means the tumor can grow but will not spread to other parts of the body. Thus we hope and believe that efforts to cure such diseases are underway all over the world, focusing more on the interface and similarities between HIV cure and cancer research. Thus, as a way forward, toward understanding the connection between HIV/AIDS and certain cancers diseases, Forys̀ and Poleszczuk in [9] derived a system of non-linear delay-differential equations (DDEs) model of HIV related cancer-immune system dynamics as

$$\left.\begin{aligned} T_t &= r_1 T(t) - k_1 T(t)E(t), \\ E_t &= r_2 T(t) + \alpha - \mu_1 E(t) - k_1 T(t)E(t) + (1-\varepsilon)k_1 T(t-\tau)E(t-\tau) \\ &\quad -k_2' E(t)I(t) - k_3 E(t)V(t), \\ I_t &= k_2' E(t)I(t) + k_3 E(t)V(t) - \mu_2 I(t), \\ V_t &= N\delta I(t) - cV(t), \end{aligned}\right\} \tag{1}$$

where, the subscript t denotes the partial derivative with respect to time t, $T(t)$, $E(t)$, $I(t)$, $V(t)$ denote concentration of cancer cells, healthy effector cells (mainly $CD4^+$ T-cells), effector cells infected by the HIV virus, and free HIV viral particles in that order. Since the dynamics of cancer cells are assumed to be governed by cancer cells proliferation, their interactions with the immune system, then the term describing the influence of effector cells on cancer cells is taken proportional to the product of both concentrations [11, 13]. Thus, the parameters r_2, α, μ_1 denote the antigenicity (difference between tumor and normal tissue) of the tumor, normal rate of the flow of mature effector cells into the region of cancer cells localization [12], rate

of elimination of effector cells, in that order. It is understood that the process of effector cells regeneration after the injection of lytic granules into the target cells causes the cytotoxic T-cells to kill target cells mainly using lytic granules containing perforin, granzymes and TNF, by binding to the surface of the target cell. This trigger the extracellular release of perforin molecules from the granules. Thus, polymerize to form trans-membrane channels which may facilitate lysis of the target by permitting entry of granzymes which induce apoptotic cell death through activation of the caspase protease cascade and ultimate fragmentation of nuclear DNA [7]. As a results, effector cells should regenerate lytic granules to this effect. Thus, the term τ denotes the time needed by effector cells to regenerate lytic granules and the time required for some small percentage (ε) to breach into the target T-cells.

The term describing the release of the new free viral particles by the infected cells is multiplied by the additional parameter N to represent the number of those particles released by the single infected cell. Furthermore, Fory$\acute{s}$ and Poleszczuk in [9] assumed that the rate of change of the free HIV viral particles is high relative to the rate of change of the concentration of considered cellular populations. Hence, Fory$\acute{s}$ and Poleszczuk in [9] assumed that the rate of change of the free HIV viral particles is high relative to the rate of change of the concentration of considered cellular populations. Therefore, during the whole process $dV/dt \equiv 0$, that is $V(t) \equiv N\delta/cI(t)$. This implies that the system of non-linear delay differential equations (DDEs) in equation (1) reduces to the following system of three non-linear delay differential equations (DDEs)

$$\left.\begin{aligned} T_t &= r_1 T(t) - k_1 T(t)E(t), \\ E_t &= r_2 T(t) + \alpha - \mu_1 E(t) - k_1 T(t)E(t) + (1-\varepsilon)k_1 T(t-\tau)E(t-\tau) \\ &\quad -k_2' E(t)I(t), \\ I_t &= k_2 E(t)I(t) - \mu_2 I(t), \end{aligned}\right\} \tag{2}$$

where,

$$k_2 = k_2' + k_3 \frac{N\delta}{c}.$$

Since their models take no spacial effects, then in this paper we extend the system of DDEs in equation (2) to a system of delayed partial differential equations (DPDEs) as

$$\left.\begin{aligned}
&T_t - d_1\Delta T = r_1 T(t) - k_1 T(t)E(t),\\
&E_t - d_2\Delta E = r_2 T(t) + \alpha - \mu_1 E(t) - k_1 T(t)E(t) + (1-\varepsilon)k_1 T(t-\tau)E(t-\tau)\\
&-k_2' E(t)I(t),\\
&I_t - d_3\Delta I = k_2 E(t)I(t) - \mu_2 I(t),\\
&\tfrac{\partial T}{\partial \nu}(0,t) = \tfrac{\partial E}{\partial \nu}(0,t) = \tfrac{\partial I}{\partial \nu}(0,t) = 0,\\
&\tfrac{\partial T}{\partial \nu}(x_f,t) = \tfrac{\partial E}{\partial \nu}(x_f,t) = \tfrac{\partial I}{\partial \nu}(x_f,t) = 0, \text{ on } (x,t) \in \Omega \times (0,\infty),\\
&\mathscr{X}_j(x,0) = \eta_j(x), \text{ on } (x,t) \in \bar{\Omega} \times [-\tau,0],\ j = 1,2,3,
\end{aligned}\right\} \tag{3}$$

where d_1, d_2, d_3 denote the cancer cells, healthy effector cells, HIV-infected cells constant diffusion coefficients, Δ denotes the Laplace operator, $\mathscr{X}_j(x,t) = [T,E,I], j = 1,2,3, \Omega \in \mathbb{R}^N$ denotes a bounded domain with smooth boundary $\partial\Omega$ and ν denotes the outward unit normal on $\partial\Omega$. The initial function $\eta_j(x,t)$ is Holder continuous on $[-\tau,0]$ and the no-flux boundary conditions are imposed to ensure the exclusion of external effects. More details on reaction rates can be found in [9].

Many mathematical models such as those in [1, 2, 6, 13, 14, 16, 17, 21] has been derived in order to shed more light as to how the dynamics of such virus takes place. While the authors made the utmost efforts to include whatever we could, we would like to apologize if there are any omissions which are totally unintentional.

In this paper, our focus is on the model in which the issue of immune reaction against tumor and HIV to dissemination arising from the work of Foryś and Pleszczuk in [9], in vivo. We also would like to acknowledge the work done by Nunnari et al. [18], Resclgnow and Delisi [23] and by Rong et al. [24], where a significant increase in the incidence of neoplasms accompany the acquired immunodeficiency syndrome (AIDS), a delay in the formation of killer lymphocytes was introduced to allow tumor development from a single cell, steps between viral infection of $CD^{+}4T$ cells and the production of $HIV-1$ visions have been incorporated by an eclipse phase, an $HIV-1$ dynamical model was developed which incorporate AIDS-related cancer cells in which cancer cells, healthy $CD4+$ T lymphocytes and infected $CD4+$ T lymphocytes can have six steady states, in that order.

Assuming that the cancer-immune system interactions dynamics is governed by cancer cells proliferation and their interaction with the immune system, thus our first aim in this paper is to present the fact that in the absence of the cancer and HIV infections, the governing dynamics of the extended model tends to the expected physiological level and derive the corresponding stability conditions of the extended model. Our second aim is to develop a fitted operator numerical method, analyse, implement and present our numerical results with regard to the governing dynamics.

The rest of paper is organized in the following way. In Section 2, we analyse the extended model, whereas in Section 3 we derive, analyse our numerical method. We present our numerical results in Section 4 and conclude the paper with Section 5.

2. Mathematical analysis of the model

First and foremost, we verify that the extended model in equation (3) reflects the normal physiological level (α/μ_1) of the healthy effector cells E, as it is determined by Foryś and Poleszczuk in [9]. To do that, we solve equation (3) in the absence of the cancer cells $(T \equiv 0)$ and HIV-infected effector cells $(I \equiv 0)$. Thus, in such absence the system of DPDEs in equation (3) reduces to,

$$\frac{dE}{dt} - d_2 \Delta E + \mu_1 E = \alpha. \tag{4}$$

Following the techniques in [4], we have

$$E(x,t) = u(x) + w(x,t) \tag{5}$$

where $u := f(x)$ is independent of the time t and satisfies the boundary value problem (BVP)

$$-d_2 u_{xx} + \mu_1 u = \alpha, \text{ with } u'(0) = u'(x_f) = 0, \tag{6}$$

and $w := f(x,t)$, which satisfies the BVP

$$w_t = d_2 w_{xx} - \mu_1 w, \text{ with } w'(0) = w'(x_f) = 0 \text{ and } w(x,0) = -u(x). \tag{7}$$

Since the solution for the homogeneous ordinary differential equation (ODE) in equation (6) is

$$u_c(x) = c_1 \exp\left(-\sqrt{\frac{\mu_1}{d_2}}x\right) + c_2 \exp\left(\sqrt{\frac{\mu_1}{d_2}}x\right), \tag{8}$$

then we let the corresponding particular solution to the ODE in equation (6) to be

$$u_p(x) = c_3 x + c_4, \tag{9}$$

where, c_1, c_2, c_3, c_4, are constants to be determined. Thus,

$$\mu_1(c_3 x + c_4) = \alpha, \Rightarrow \mu_1 c_3 x + \mu_1 c_4 = \alpha. \tag{10}$$

Equating terms of same coefficients in equation (10), we find $c_3 = 0$ and $c_4 = \frac{\alpha}{\mu_1}$, which implies that the solution to the BVP in equation (6) becomes

$$u(x) = c_1 \exp\left(-\sqrt{\frac{\mu_1}{d_2}}x\right) + c_2 \exp\left(\sqrt{\frac{\mu_1}{d_2}}x\right) + \frac{\alpha}{\mu_1}. \tag{11}$$

Using the boundary conditions in equation (6) we find

$$u'(x) = -c_1\sqrt{\frac{\mu_1}{d_2}} \exp\left(-\sqrt{\frac{\mu_1}{d_2}}x\right) + c_2\sqrt{\frac{\mu_1}{d_2}} \exp\left(\sqrt{\frac{\mu_1}{d_2}}x\right), \tag{12}$$

so that at $x = 0$, we have

$$u'(0) = -c_1\sqrt{\frac{\mu_1}{d_2}} + c_2\sqrt{\frac{\mu_1}{d_2}} = 0, \tag{13}$$

which implies that

$$c_1 = c_2. \tag{14}$$

Similarly, At $x = x_f$, we find

$$u'(x_f) = -c_1\sqrt{\frac{\mu_1}{d_2}}\exp\left(-\sqrt{\frac{\mu_1}{d_2}}x_f\right) + c_2\sqrt{\frac{\mu_1}{d_2}}\exp\left(\sqrt{\frac{\mu_1}{d_2}}x_f\right) = 0, \tag{15}$$

which is equivalent to

$$c_2\sqrt{\frac{\mu_1}{d_2}}\exp\left(2\sqrt{\frac{\mu_1}{d_2}}x_f\right) = c_1\sqrt{\frac{\mu_1}{d_2}}. \tag{16}$$

In view of equation (14), equation (16) becomes

$$c_2\exp\left(2\sqrt{\frac{\mu_1}{d_2}}x_f\right) = c_2, \Rightarrow c_2 = 0. \tag{17}$$

Hence, the solution in equation (11) becomes,

$$u(x) = \frac{\alpha}{\mu_1}. \tag{18}$$

Let $w(x,t) = X(x)T(t)$, then applying the method of separation of variables [4] to the BVP in (7), we have

$$X(x)T'(t) = T(t)\left(d_2X''(x) - \mu_1X(x)\right), \Rightarrow \frac{T'(t)}{T(t)} = \frac{d_2X''(x) - \mu_1X(x)}{X(x)} = -\rho^2, \tag{19}$$

where ρ is an arbitrary separation constant. Solving for $T(t)$ we have

$$\frac{d}{dt}\left(T(t)\exp(\rho^2t)\right) = 0, \tag{20}$$

which is equivalent to

$$T(t)\exp(\rho^2t) = c_5, \tag{21}$$

where c_5 is a constant of integration. Hence,

$$T(t) = c_5\exp(-\rho^2t). \tag{22}$$

Solving for $X(x)$ in equation (19), we have

$$\begin{aligned} X''(x) + \frac{(\rho^2 - \mu_1)}{d_2}X(x) &= 0, \\ \Rightarrow X(x) &= c_6\cos\left(\sqrt{\frac{(\rho^2 - \mu_1)}{d_2}}x\right) + c_7\sin\left(\sqrt{\frac{(\rho^2 - \mu_1)}{d_2}}x\right). \end{aligned} \tag{23}$$

Thus,

$$w(x,t) = c_5 \exp(-\rho^2 t)\left(c_6 \cos\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x\right) + c_7 \sin\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x\right)\right). \tag{24}$$

Applying the boundary conditions in equation (7) to the equation in (24), we have

$$\begin{aligned} w'(x,t) &= -c_5 c_6 \sqrt{\frac{(\rho^2-\mu_1)}{d_2}} \exp(-\rho^2 t) \sin\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x\right) \\ &\quad + c_7 c_5 \sqrt{\frac{(\rho^2-\mu_1)}{d_2}} \exp(-\rho^2 t) \cos\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x\right). \end{aligned} \tag{25}$$

Assuming that $c_5 \neq 0$, then at $x = 0$, equation (25) becomes

$$0 = c_7 c_5 \sqrt{\frac{(\rho^2-\mu_1)}{d_2}} \exp(-\rho^2 t), \Rightarrow c_7 = 0. \tag{26}$$

Thus, at $x = x_f$, we see that $c_6 \neq 0$, so that

$$\begin{aligned} 0 &= -c_5 c_6 \sqrt{\frac{(\rho^2-\mu_1)}{d_2}} \exp(-\rho^2 t) \sin\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x\right) \\ &\iff \sin\left(\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x_f\right) = 0. \end{aligned} \tag{27}$$

Hence, for $j = 1,2,3,\ldots$, we have from equation (27) that

$$\sqrt{\frac{(\rho^2-\mu_1)}{d_2}}x_f = \pm j\pi. \tag{28}$$

This implies that

$$w(x,t) = c_j \exp(-\rho^2 t) \sin(j\pi x), \quad \text{for } j = 1,2,3,\ldots. \tag{29}$$

Thus, in view of the solutions in (18) and (29) the equation in (5) clearly present the fact that in the absence of the tumor and HIV-infected effector cells, the solution $E(t)$ in equation (5) of the extended model in equation (3) converges to the normal physiological level α/μ_1 as $t \to \infty$. This implies that our extended model in equation (3) reflects the normal physiological level (α/μ_1) of the healthy effector cells E, as it is determined by Fory$\acute{s}$ and Poleszczuk in [9] for the model in equation (1).

Stability analysis of the equilibria when $\tau = 0$

When the regeneration of lytic granules by the effector cells and breaching of some effector cells into T-cells happens instantaneously, Foryś and Poleszczuk in [9] established that when there is no HIV-infected cells, the set $\mathscr{D} = \mathbb{R}^2_+$ is invariant for system (3) at the unique strictly positive steady state $(\bar{T}, \bar{E}) = (\frac{\mu_1 r_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1})$, which implies that the immune system is capable to successfully prevent further cancer development. Therefore, for every solution in $\mathscr{D}$ there is $E(t) \leq \max\{E(0), \frac{r_2}{\varepsilon k_1}, \frac{r_1}{k_1}\}$, such that, if $r_1 > \frac{\alpha k_1}{\mu_1}$,

- for $\varepsilon < \frac{r_2}{r_1}$, then the unique positive steady state $(\bar{T}, \bar{E})$ is globally stable in $\mathscr{D}$,
- for $\varepsilon > \frac{r_2}{r_1}$ there is no positive steady state as $T(t) \to \infty$, $\forall t \to \infty$.

Thus, the rate of tumor growth reflected by the parameter r_1 and rate of cancer elimination by the immune system, reflected by the parameter value k_1, plays an integral part in the investigation of the governing dynamics of our model. When the concentration of HIV-infected effector cells is present, Foryś and Poleszczuk in [9] showed that the set $\mathscr{D} = \mathbb{R}^3_+$ is invariant for system (3) at the unique strictly positive steady state $(\bar{T}, \bar{E}, \bar{I}) = (\frac{\mu_1 r_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1}, 0)$. That is, if $r_1 > \frac{\alpha k_1}{\mu_1}$, then $(0, \frac{\alpha k_1}{\mu_1}, 0)$ is unstable. In addition if $r_1 < \frac{\mu_2 k_1}{k_2}$,

- if $\varepsilon < \frac{r_2}{r_1}$ then $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1}, 0)$ is locally asymptotic stable,
- if $\alpha > \frac{\mu_1 \mu_2}{k_2}$, then $(0, \frac{\mu_2}{k_2}, \frac{\alpha k_2 - \mu_1 \mu_2}{\mu_2 k_2})$ is locally asymptotic stable.

Thus, the above facts present that there is no steady state describing the coexistence of the concentration of cancer and HIV-infected effector cells in vivo, even at the instantaneously pace.

Stability analysis of the equilibria when $\tau > 0$

In this section we examine the case for the regeneration of lytic granules by the effector cells and breaching of some effector cells into T-cells require sometimes to take place, with respect to the governing dynamics in the previous section. In view of the governing dynamics in the previous section, we see that the steady states for the system in (3) is same as the steady states of the corresponding reduced system in equation (3). Therefore, it suffices to consider the stability for the positive steady states of the equation in (3). Thus, for the extended model in equation

(3), the jacobian matrix is

$$\Delta(\lambda,\tau) = \begin{pmatrix} d_1 & 0 & 0 \\ 0 & d_2 & 0 \\ 0 & 0 & d_3 \end{pmatrix}$$

$$+ \begin{pmatrix} 0 & -k_1\bar{T} & 0 \\ r_2 - r_1 + (1-\varepsilon)r_1\exp(-\lambda\tau) & -\mu_1 - k_1\bar{T} + (1-\varepsilon)k_1\bar{T}\exp(-\lambda\tau) & -k_2\bar{E} \\ 0 & 0 & k_2\bar{E} - \mu_2 \end{pmatrix}$$

$$= \begin{pmatrix} d_1 & -k_1\bar{T} & 0 \\ r_2 - r_1 + (1-\varepsilon)r_1\exp(-\lambda\tau) & d_2 - (\mu_1 + k_1\bar{T} - (1-\varepsilon)k_1\bar{T}\exp(-\lambda\tau)) & -k_2\bar{E} \\ 0 & 0 & d_3 - (\mu_2 - k_2\bar{E}) \end{pmatrix}.$$

Hence, the characteristic matrix for the steady state for cancer-immune system interactions with the concentration of HIV-infected effector cells is

$$\begin{aligned} \det(\Delta(\lambda,\tau)) &= (d_1-\lambda)[(d_2 - (\mu_1 + k_1\bar{T} - (1-\varepsilon)k_1\bar{T}\exp(-\lambda\tau)) - \lambda](d_3 - (\mu_2 - k_2\bar{E})) - \lambda) \\ &\quad + k_1\bar{T}[(r_2 - r_1 + (1-\varepsilon)r_1\exp(-\lambda\tau)](d_3 - (\mu_2 - k_2\bar{E})) - \lambda), \end{aligned}$$

in which we let

$$\begin{aligned} W(\lambda,\tau) &= \det(\Delta(\lambda,\tau)) = (d_3 - (\mu_2 - k_2\bar{E})) - \lambda)W_2(\lambda,\tau), \\ W_2(\lambda,\tau) &= P(\lambda) + Q(\lambda)\exp(-\lambda\tau), \end{aligned} \tag{30}$$

where W_2 denotes the characteristic quasi-polynomial for the reduced two-variable system in (3) with $I \equiv 0$,

$$\begin{aligned} P(\lambda) &= (d_1-\lambda)(d_2 - (\mu_1 + k_1\bar{T}) - \lambda) + (r_2 - r_1)k_1\bar{T}, \\ &= \lambda^2 + (\mu_1 + k_1\bar{T} - (d_1 + d_2))\lambda + (r_2 - r_1)k_1\bar{T} + d_1d_2. \end{aligned}$$

and

$$\begin{aligned} Q(\lambda) &= k_1\bar{T}(1-\varepsilon)(-\lambda + r_1), \\ &= -k_1\bar{T}\lambda + \varepsilon k_1\bar{T}\lambda + r_1k_1\bar{T} - \varepsilon r_1k_1\bar{T}. \end{aligned}$$

Since $\exp(-\lambda\tau) > 0$ for all values of λ and τ, then we have

$$P(\lambda) + Q(\lambda) = \lambda^2 + (\mu_1 + \varepsilon k_1 \bar{T} - (d_1 + d_2))\lambda + r_2 k_1 \bar{T} - \varepsilon r_1 k_1 \bar{T} + d_1 d_2.$$

However, the Routh-Hurwitz criteria requires that, all the roots of (30) have negative real parts. This implies that

$$(d_3 - (\mu_2 - k_2\bar{E})) > 0,\ (\mu_1 + \varepsilon k_1 \bar{T} - (d_1 + d_2)) > 0 \text{ and } r_2 k_1 \bar{T} - \varepsilon r_1 k_1 \bar{T} + d_1 d_2 > 0,$$

which is equivalent to

$$\mu_2 < k_2\bar{E} - d_3,\ (\mu_1 + \varepsilon k_1 \bar{T}) > d_1 + d_2,\ r_2 k_1 \bar{T} + d_1 d_2 > \varepsilon r_1 k_1 \bar{T}.$$

This enable us to obtain the following results.

Corollary 2.1. *If $r_2 k_1 \bar{T} + d_1 d_2 > \varepsilon r_1 k_1 \bar{T}$ and*

- *$\mu_2 < k_2\bar{E} - d_3$, then if $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1})$ is stable as a steady state in the two-variable system, then $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1}, 0)$ is stable as a steady state for system in equation (3),*
- *$\mu_2 > k_2\bar{E} - d_3$, then $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1}, 0)$ is unstable.*

Since there is no steady state describing the coexistence of the tumor cells with the HIV infection in vivo and in view of the results in Corollary (), we see that the steady states for the system in (3) under the governing dynamics are the same as for the governing dynamics without the infection, then in the next section it suffices to examine the existence of Hopf bifurcation for the reduced (two-variable) system in equation (3).

Existence of Hopf bifurcation

If $r_2 k_1 \bar{T}_3 + d_1 d_2 > \varepsilon r_1 k_1 \bar{T}_3$, then $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1})$ is stable for $\tau = 0$. Therefore, for stability switches we follow the ideas from Cooke and Driessche in [5], that the necessary condition for stability switches is the existence of purely imaginary eigenvalue

$$\lambda = i\omega,\ \omega > 0 \text{ for some threshold value } \tau_{th}.$$

If $i\omega$ is an eigenvalue for τ_{th}, then

$$W_2(i\omega, \tau_{th}) = 0 \Rightarrow P(i\omega) = -Q(i\omega)\exp(i\omega\tau_{th})$$

which implies

$$\|P(i\omega)\| = \|Q(i\omega)\|.$$

Defining

$$F(\omega) = \|P(i\omega)\|^2 - \|Q(i\omega)\|^2,$$

where

$$F(y) = y^2 + Ay + B,\ y = \omega^2,$$

$$\begin{aligned} A &= \varepsilon(2-\varepsilon)k_1^2\bar{T}^2 + 2(\mu_1 - r_2 + r_1)k_1\bar{T} + \mu_1^2 - 2(\mu_1 + k_1\bar{T})d_1d_2 + d_1^2d_2^2 > 0, \\ B &= (r_2 - r_1(2-\varepsilon))(r_2 - r_1\varepsilon)k_1^2\bar{T}^2 > 0, \end{aligned}$$

if $r_2 - r_1\varepsilon > 0$, $\varepsilon < 1$, and if

- $r_2 - r_1(2-\varepsilon) > 0$, then there is no positive roots of F.
- $r_2 - r_1(2-\varepsilon) < 0$, then F has exactly one positive root $\bar{y}$.

These above two facts enable us to state the following results.

Theorem 2.1. *Assume that the steady state* $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1})$ *exists. Then if*

- $r_2 - r_1(2-\varepsilon) > 0$*, then* $(\bar{T}, \bar{E})$ *is stable for any positive delay* $\tau > 0$.
- $r_2 - r_1(2-\varepsilon) < 0$*, then there exists the threshold dealy* $\tau_{th} > 0$ *such that* $(\bar{T}, \bar{E})$ *is stable for* $\tau < \tau_{th}$*, loses stability at* $\tau = \tau_{th}$ *in which Hopf bifurcation occurs.*

Remark 2.1. *From the analysis presented above it is obvious that the state* $(\frac{\mu_1 - \alpha k_1}{k_1(r_2 - \varepsilon r_1)}, \frac{r_1}{k_1}, 0)$ *cannot recover stability for larger values of* τ.

3. Derivation and analysis of the numerical method

In this section, we describe the derivation of the fitted numerical method for solving the system in equation (3). We determine an approximation to the derivatives of the functions $T(t,x), E(t,x)$ and $I(t,x)$ with respect to the spatial variable x.

Let N_x be a positive integer. Discretize the interval $[0,x_f]$ through the points

$$x_0 = 0 < x_1 < x_2 < \cdots < x_{N_x} = x_f,$$

where the step-size $\Delta x = x_{j+1} - x_j = x_f/N_x,\ j = 0,1,\ldots,N_x$. Let $\mathscr{T}_j(t), \mathscr{E}_j(t), \mathscr{I}_j(t)$ denote the numerical approximations of $T(t,j), E(t,j), I(t,j)$, then we approximate the second order spatial derivative terms by

$$\Delta T(t,x_j) \approx \frac{\mathscr{T}_{j+1} - 2\mathscr{T}_j + \mathscr{T}_{j-1}}{\phi_T^2},\ \Delta E(t,x_j) \approx \frac{\mathscr{E}_{j+1} - 2\mathscr{E}_j + \mathscr{E}_{j-1}}{\phi_E^2},\ \Delta I(t,x_j) \approx \frac{\mathscr{I}_{j+1} - 2\mathscr{I}_j + \mathscr{I}_{j-1}}{\phi_j^2}, \tag{31}$$

where

$$\phi_T^2 \quad = \quad \frac{(\exp(\sigma_T \Delta x) - 1)}{\sigma_T},\ (\phi_E)_j = \frac{4}{\sigma_E^2} \sinh^2\left(\frac{\sigma_E \Delta x}{2}\right),\ \phi_I = \frac{4}{\sigma_I^2} \sinh^2\left(\frac{\sigma_I \Delta x}{2}\right),$$

and

$$\sigma_T = \sqrt{\frac{r_1}{d_1}},\ \sigma_E = \sqrt{\frac{\mu_1}{d_2}},\ \sigma_I = \sqrt{\frac{\mu_2}{d_3}}.$$

It is not that difficult to see that $\phi_T \to \Delta x$, $\phi_E \to \Delta x$ and $\phi_I \to \Delta x$, as $\Delta x \to 0$.

Let N_t be a positive integer and $\Delta t = H/Nt$ where $0 < t < H$. Discretizing the time interval $[0,H]$ through the points

$$0 = t_0 < t_1 < \cdots < t_{N_t} = H,$$

where

$$t_{n+1} - t_n = \Delta t,\ n = 0,1,\ldots,(N_t - 1).$$

We approximate the time derivative at t_n by

$$\frac{d\mathscr{T}_j(t_n)}{dt} \approx \frac{\mathscr{T}_j^{n+1} - \mathscr{T}_j^n}{\psi_T},\ \frac{d\mathscr{E}_j(t_n)}{dt} \approx \frac{\mathscr{E}_j^{n+1} - \mathscr{E}_j^n}{\psi_E},\ \frac{d\mathscr{I}_j(t_n)}{dt} \approx \frac{\mathscr{I}_j^{n+1} - \mathscr{I}_j^n}{\psi_I}, \tag{32}$$

where

$$\psi_T = (1 - \exp(-r_1\Delta t) - 1)/r_1,\ \psi_E = (\exp(\mu_1 \Delta t) - 1)/\mu_1,\ \psi_I = (\exp(\mu_2 \Delta t) - 1)/\mu_2,$$

where we see that $\psi_T \to \Delta t$, $\psi_E \to \Delta t$ and $\psi_I \to \Delta t$ as $\Delta t \to 0$.

The denominator functions in (31) and (32) are used explicitly to remove the inherent stiffness in the central finite derivatives parts and are derived by using the theory of nonstandard finite difference methods, see, e.g., [15, 19, 20] and references therein.

Combining the equation (31) for the spatial derivatives with equation (32) for time derivatives, we obtain

$$\left.\begin{aligned}
&\tfrac{\mathscr{T}_j^{n+1}-\mathscr{T}_j^n}{\psi_T} = d_1 \tfrac{\mathscr{T}_{j+1}^{n+1}-2\mathscr{T}_j^{n+1}+\mathscr{T}_{j-1}^{n+1}}{\phi_T^2} + r_1\mathscr{T}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n,\\
&\tfrac{\mathscr{E}_j^{n+1}-\mathscr{E}_j^n}{\psi_E} = d_2 \tfrac{\mathscr{E}_{j+1}^{n+1}-2\mathscr{E}_j^{n+1}+\mathscr{E}_{j-1}^{n+1}}{\phi_E^2} + r_2\mathscr{T}_j^n - \mu_1\mathscr{E}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n + (1-\varepsilon)k_1(\mathscr{H}_T)_j^n(\mathscr{H}_E)_j^n\\
&\qquad\qquad -k_2'\mathscr{E}_j^n\mathscr{I}_j^n + \alpha,\\
&\tfrac{\mathscr{I}_j^{n+1}-\mathscr{I}_j^n}{\psi_I} = d_3 \tfrac{\mathscr{I}_{j+1}^{n+1}-2\mathscr{I}_j^{n+1}+\mathscr{I}_{j-1}^{n+1}}{\phi_I^2} + k_2\mathscr{E}_j^n\mathscr{I}_j^n - \mu_2\mathscr{I}_j^n,\\
&\mathscr{T}_1^n = \mathscr{T}_{-1}^n,\ \mathscr{T}_1^n = \mathscr{T}_{-1}^n,\ \mathscr{T}_1^n = \mathscr{T}_{-1}^n, \text{ and } \mathscr{T}_{N_x}^n = \mathscr{T}_{N_x-1}^n,\ \mathscr{T}_{N_x}^n = \mathscr{T}_{N_x-1}^n,\ \mathscr{T}_{N_x}^n = \mathscr{T}_{N_x-1}^n,\\
&\mathscr{E}_j^0 = 780,\ \mathscr{T}_j^0 = 10,\ \mathscr{I}_j^0 = 10.
\end{aligned}\right\} \tag{33}$$

where

$$(\mathscr{H}_T)_j^n \approx T(t_n-\tau,x_j) \text{ and } (\mathscr{H}_E)_j^n \approx E(t_n-\tau,x_j), \tag{34}$$

are the history functions corresponding to the equations in T and E for $j = 1,2,\ldots,N_x-1$, $n = 0,1,\ldots,N_t-1$.

The system in equation (33) can be further be simplified as

$$\left.\begin{aligned}
&-\tfrac{d_1}{\phi_T^2}\mathscr{T}_{j-1}^{n+1} + \left(\tfrac{1}{\psi_T}+\tfrac{2d_1}{\phi_T^2}\right)\mathscr{T}_j^{n+1} - \tfrac{d_1}{\phi_T^2}\mathscr{T}_{j+1}^{n+1} = \left(\tfrac{1}{\psi_T}+r_1\right)\mathscr{T}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n,\\
&-\tfrac{d_2}{\phi_E^2}\mathscr{E}_{j-1}^{n+1} + \left(\tfrac{1}{\psi_E}+\tfrac{2d_2}{\phi_E^2}\right)\mathscr{E}_j^{n+1} - \tfrac{d_2}{\phi_E^2}\mathscr{E}_{j+1}^{n+1} = r_2\mathscr{T}_j^n\\
&+\left(\tfrac{1}{\psi_E}-\mu_1\right)\mathscr{E}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n + (1-\varepsilon)k_1(\mathscr{H}_T)_j^n(\mathscr{H}_E)_j^n - k_2'\mathscr{E}_j^n\mathscr{I}_j^n + \alpha,\\
&-\tfrac{d_3}{\phi_I^2}\mathscr{I}_{j-1}^{n+1} + \left(\tfrac{1}{\psi_I}+\tfrac{2d_3}{\phi_I^2}\right)\mathscr{I}_j^n - \tfrac{d_3}{\phi_I^2}\mathscr{I}_{j+1}^{n+1} = k_2\mathscr{E}_j^n\mathscr{I}_j^n + \left(\tfrac{1}{\psi_I}-\mu_2\right)\mathscr{I}_j^n.
\end{aligned}\right\} \tag{35}$$

Consequently, the system in equation (35) can be written as a tridiagonal system given by

$$\left.\begin{aligned} A_T\mathscr{T}_j^{n+1} &= \left(\tfrac{1}{\psi_T}+r_1\right)\mathscr{T}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n, \\ A_E\mathscr{E}_j^{n+1} &= r_2\mathscr{T}_j^n + \left(\tfrac{1}{\psi_E}-\mu_1\right)\mathscr{E}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n + (1-\varepsilon)k_1(\mathscr{H}_T)_j^n(\mathscr{H}_E)_j^n \\ &\qquad -k_2'\mathscr{E}_j^n\mathscr{I}_j^n + \alpha, \\ A_I\mathscr{I}_j^{n+1} &= k_2\mathscr{E}_j^n\mathscr{I}_j^n + \left(\tfrac{1}{\psi_I}-\mu_2\right)\mathscr{I}_j^n, \end{aligned}\right\} \tag{36}$$

where $j = 1,\ldots,N_x-1$, $n = 0,\ldots,N_t-1$ and

$$\left.\begin{aligned} A_T &= \mathrm{Tri}\left(-\tfrac{d_1}{\phi_T)^2},\tfrac{1}{\psi_T}+\tfrac{2d_1}{\phi_T^2},-\tfrac{d_1}{\phi_T^2}\right),\ A_E = \mathrm{Tri}\left(\tfrac{d_2}{\phi_E^2},\tfrac{1}{\psi_E}+\tfrac{2d_2}{\phi_E^2},\tfrac{d_2}{\phi_E^2}\right), \\ A_I &= \mathrm{Tri}\left(-\tfrac{d_3}{\phi_I^2},\tfrac{1}{\psi_I}+\tfrac{2d_3}{\phi_I^2},-\tfrac{d_3}{\phi_I^2}\right). \end{aligned}\right\}$$

On the interval $[0,\tau]$ the delayed arguments $t_n-\tau$ belong to $[-\tau,0]$, and therefore the delayed variables in equation (36) are evaluated directly from the history functions $T^0(t,x), E^0(t,x)$ as

$$(\mathscr{H}_T)_j^n \approx T^0(t_n-\tau,x_j) \text{ and } (\mathscr{H}_E)_j^n \approx E^0(t_n-\tau,x_j), \tag{37}$$

and equation (36) becomes

$$\left.\begin{aligned} A_T\mathscr{T}_j^{n+1} &= \left(\tfrac{1}{\psi_T}+r_1\right)\mathscr{T}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n, \\ A_E\mathscr{E}_j^{n+1} &= r_2\mathscr{T}_j^n + \left(\tfrac{1}{\psi_E}-\mu_1\right)\mathscr{E}_j^n - k_1\mathscr{T}_j^n\mathscr{E}_j^n \\ &\qquad +(1-\varepsilon)k_1T^0(t_n-\tau,x_j)E^0(t_n-\tau,x_j) - k_2'\mathscr{E}_j^n\mathscr{I}_j^n + \alpha, \\ A_I\mathscr{I}_j^{n+1} &= k_2\mathscr{E}_j^n\mathscr{I}_j^n + \left(\tfrac{1}{\psi_I}-\mu_2\right)\mathscr{I}_j^n. \end{aligned}\right\} \tag{38}$$

Let s be the largest integer such that $\tau_s \le \tau$. By using the system equation (38) we can compute $\mathscr{T}_j^n, \mathscr{E}_j^n, \mathscr{I}_j^n$ for $1 \le n \le s$. Up to this stage, we interpolate the data

$$(t_0,\mathscr{T}_j^0), (t_1,\mathscr{T}_j^1),\ldots,(t_s,\mathscr{T}_j^s) \text{ and } (t_0,\mathscr{E}_j^0), (t_1,\mathscr{E}_j^1),\ldots,(t_s,\mathscr{E}_j^s),$$

using an interpolating cubic Hermite spline $\varphi_j(t)$. Then

$$\mathscr{T}_j^n = \varphi_T(t_n,x_j) \text{ and } \mathscr{E}_j^n = \varphi_E(t_n,x_j),$$

for all $n = 0, 1, \ldots, s$ and $j = 1, 2, \ldots, N_x - 1$.

For $n = s+1, s+2, \ldots, N_t - 1$, when we move from level n to level $n+1$ we extend the definitions of the cubic Hermite spline $\varphi_j(t)$ to the point $(t_n + \Delta t, \mathscr{T}_j^n, \mathscr{E}_j^n)$. Then the history terms $(\mathscr{H}_T)_j^n$ and $(\mathscr{H}_E)_j^n$ can be approximated by the functions $\varphi_j(t_n - \tau)$ for $n \geq s$. This implies that,

$$(\mathscr{H}_T)_j^n \approx (\varphi_T)_j(t_n - \tau) \text{ and } (\mathscr{H}_E)_j^n \approx (\varphi_E)_j(t_n - \tau), \tag{39}$$

and equation (33) becomes

$$\left.\begin{aligned} A_T \mathscr{T}_j^{n+1} &= \left(\tfrac{1}{\psi_T} + r_1\right)\mathscr{T}_j^n - k_1 \mathscr{T}_j^n \mathscr{E}_j^n, \\ A_E \mathscr{E}_j^{n+1} &= r_2 \mathscr{T}_j^n + \left(\tfrac{1}{\psi_E} - \mu_1\right)\mathscr{E}_j^n - k_1 \mathscr{T}_j^n \mathscr{E}_j^n + (1-\varepsilon) k_1 \varphi_T(t_n - \tau)\varphi_E(t_n - \tau) \\ &\quad - k_2' \mathscr{E}_j^n \mathscr{I}_j^n + \alpha, \\ A_I \mathscr{I}_j^{n+1} &= k_2 \mathscr{E}_j^n \mathscr{I}_j^n + \left(\tfrac{1}{\psi_I} - \mu_2\right)\mathscr{I}_j^n, \end{aligned}\right\} \tag{40}$$

where

$$\varphi_T(t_n - \tau) = [(\mathscr{H}_T)_1^n, (\mathscr{H}_T)_2^n \ldots, (\mathscr{H}_T)_{N_x-1}^n]', \ \varphi_E(t_n - \tau) = [(\mathscr{H}_E)_1^n, (\mathscr{H}_E)_2^n \ldots, (\mathscr{H}_E)_{N_x-1}^n]'.$$

Our FOFDM is then consists of equations (33)-(41). Re-writing the scheme in (41) in a form of a system of equations

$$\left.\begin{aligned} A_T \mathscr{T} &= F_T, \\ A_E \mathscr{E} &= F_E, \\ A_I \mathscr{I} &= F_I, \end{aligned}\right\} \tag{41}$$

we see that the local truncation errors $(\varsigma_T)_j^n, (\varsigma_E)_j^n, (\varsigma_I)_j^n$ are given by

$$\left.\begin{aligned} (\varsigma_T)_j^n &= (A_T T)_j^n - (F_T)_j^n = (A_T(T-\mathscr{T}))_j^n, \\ (\varsigma_E)_j^n &= (A_E)_j^n - (F_E)_j^n = (A_E(E-\mathscr{E}))_j^n, \\ (\varsigma_I)_j^n &= (A_I I)_j^n - (F_I)_j^n = (A_I(I-\mathscr{I}))_j^n, \end{aligned}\right\} \tag{42}$$

Thus,

$$\left.\begin{aligned} \max_{n,j}|T_j^n - \mathscr{T}_j^n| &\le ||A_T^{-1}||\max_{n,j}|\varsigma_T|, \\ \max_{n,j}|E_j^n - \mathscr{E}_j^n| &\le ||A_E^{-1}||\max_{n,j}|\varsigma_E|, \\ \max_{n,j}|I_j^n - \mathscr{I}_j^n| &\le ||A_I^{-1}||\max_{n,j}|\varsigma_I|, \end{aligned}\right\} \tag{43}$$

where

$$\left.\begin{aligned} \max_{n,j}|\varsigma_T| &\le \tfrac{\Delta t}{2}\left|T_{tt}(\xi,x_j)\right| + \tfrac{(\Delta x)^2}{12}\left|T_{xxxx}(t_n,\zeta)\right|, \\ \max_{n,j}|\varsigma_E| &\le \tfrac{\Delta t}{2}\left|E_{tt}(\xi,x_j)\right| + \tfrac{(\Delta x)^2}{12}\left|E_{xxxx}(t_n,\zeta)\right|, \\ \max_{n,j}|\varsigma_I| &\le \tfrac{\Delta t}{2}\left|I_{tt}(\xi,x_j)\right| + \tfrac{(\Delta x)^2}{12}\left|I_{xxxx}(t_n,\zeta)\right|, \end{aligned}\right\} \tag{44}$$

$t_{n-1} \le \xi \le t_{n+1}, x_{j-1} \le \zeta \le x_{j+1}$ and by the result in [25], we obtain

$$\left.\begin{aligned} ||A_T^{-1}|| &\le \Xi_T, \\ ||A_E^{-1}|| &\le \Xi_E, \\ ||A_I^{-1}|| &\le \Xi_I. \end{aligned}\right\} \tag{45}$$

Using (46) and (45) into (43), we obtain the following results.

Theorem 3.1. *Let $F_T(x,t), F_E(x,t), F_I(x,t)$ be sufficiently smooth functions so that $T(x,t), E(x,t), I(x,t) \in C^{1,2}([1,N_x]\times[1,N_t])$. Let $(\mathscr{T}_j^n, \mathscr{E}_j^n, \mathscr{I}_j^n)$, $j = 1,2,\ldots S_x, n = 1,2,\ldots N_t$ be*

the approximate solutions to (3), obtained using the FOFDM with $\mathscr{T}_j^0 = T_j^0, \mathscr{E}_j^0 = E_j^0, \mathscr{I}_j^0 = I_j^0$,. *Then there exists* Ξ_T, Ξ_E, Ξ_I *independent of the step sizes* Δt *and* Δx *such that*

$$\left.\begin{aligned} &\max_{n,j} |T_j^n - \mathscr{T}_j^n| \leq \Xi_T [\tfrac{\Delta t}{2} \left|T_{tt}(\xi, x_j)\right| + \tfrac{(\Delta x)^2}{12} |T_{xxxx}(t_n, \zeta)|], \\ &\max_{n,j} |E_j^n - \mathscr{E}_j^n| \leq \Xi_E [\tfrac{\Delta t}{2} \left|E_{tt}(\xi, x_j)\right| + \tfrac{(\Delta x)^2}{12} |E_{xxxx}(t_n, \zeta)|], \\ &\max_{n,j} |I_j^n - \mathscr{I}_j^n| \leq \Xi_I [\tfrac{\Delta t}{2} \left|I_{tt}(\xi, x_j)\right| + \tfrac{(\Delta x)^2}{12} |I_{xxxx}(t_n, \zeta)|]. \end{aligned}\right\} \tag{46}$$

Hence, we conclude our analysis with the following result.

Theorem 3.2. (Fatunla [8], Trefethen [26]) *A difference scheme is said to be convergent if and only if it is consistent and stable.*

4. Numerical results and discussions

Taking the diffusion constants d_1, d_2, d_3 in $[10^{-1}, 10^{-20}]$, using the parameter values in Table 1, and using the fact that the regeneration of lytic granules by the effector cells and the breaching of some effector cells into T-cells requires time τ to happened, then we present our numerical solutions for the case when $\tau \neq 0$ and $\tau = 0$ as follows. In (a) and (b), we have the situation when a host is infected by the concentration of cancer cells only, (c) and (d), the situation when a host is infected by the concentrations of cancer cells, then becomes infected with HIV at a later stage, whereas in (e) and (f) we have the case when a host is infected with HIV then at a later stage becomes infected with cancer too.

In (a) we see the immune cells raising to their steady states, whereas the cancer cells drastically being reduced to nothing. We also see similar interactions in (b) even though the immune healthy effector healthy cells start with a slow decrease due to the infection inflicted by the cancer cells, before it converges to its steady state.

In (c) and (d) the situation which is depicted in (a) and (b) changes, due to the introduction of the HIV-infected effector cells. In (c), we see healthy effector cells raises before the introduction of the HIV-infected effector cells. We also see that HIV-infected cells raised to some magnitude which causes the healthy cells to drastically drop to a low steady state. As soon as the healthy

effector cells drops low so does the HIV-infected cells. This we see that it paves the way for cancer cells to raise. In (d) we see similar behaviors to the behaviors in (c) at a magnified pace.

In (e) we see HIV-infected cells raising causing the healthy immune cells to flactuate towards their steady states. Such flactuations can be seen in the behaviour of the HIV-infected cells due to the strength of the immune healthy cells. However, the introduction of cancer cells weaken the immune healthy cells which in turn subject the HIV-infected cells to raise high. The dynamics in (f) are straight forward a except that the HIV-infected cells eventual converge to their low staedy state. This is due to the impaired healthy immune healthy cells by both infections.

5. Conclusion

In this paper, we investigated the extended model arising in HIV related cancer-immune system dynamics and we were able to show that the physiological level of our extended model coincides with the original model in equation (1). Our numerical results present a clear fact played by the inclusion of a delay term (τ) in the dynamics of our extended model. We also see the crucial agreement of our results that the healthy immune system is able to successfully prevent the development of the cancer infection in a host and unable to do so when a host is infected by an additional infection, such as HIV. However, when a host is infected with HIV our results clearly shows that the healthy immune system is unable to prevent further development of the HIV-infected cells. Consequently, our results also present the fact that the weakened immune system cannot prevent the growth of the cancerous cells. Thus, the work in this paper, should be seen as the first attempt to provide an in depth information about the growth rate of tumor cells is relatively larger than the rate of elimination of cancerous cells by the healthy immune system..

Conflict of Interests

The authors declare that there is no conflict of interests.

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TABLE 1. The ranges of parameters values and corresponding references

r_1[13]	k_1[13]	r_2	α/μ_1[10]	k_2'[13]	k_3[6]
$0.05 \sim 0.5$	$10^{-5} \sim 10^{-3}$	$0 \sim 0.05$	$800 \sim 1200$	$10^{-5} \sim 5 \times 10^{-4}$	2.4×10^{-5}
μ_2[13]	δ[21]	c[21]	μ_1	ε[2]	N[6]
0.3	$0.3 \sim 0.7$	$2.1 \sim 3.8$	0.03	0.1	$100 \sim 2000$
r_1	k_1	r_2[11]	α/μ_1	k_2'	k_3
0.1	10^{-4}	0.03	800	5×10^{-5}	2.4×10^{-5}
μ_2	δ	c	μ_1[11]	ε	N
0.3	0.3	3.8	0.03	0.1	275

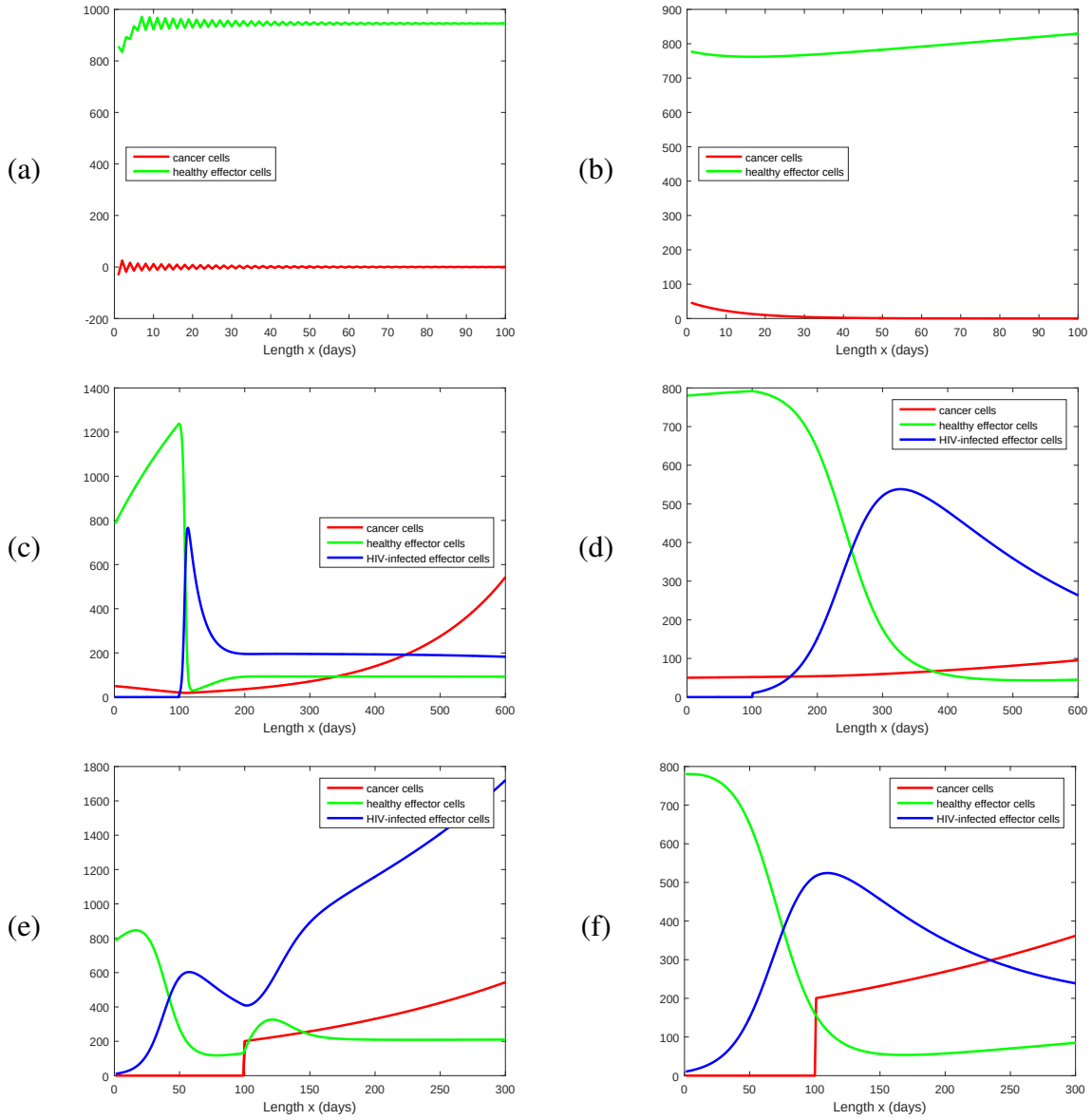

FIGURE 1. Numerical solution of the concentrations of cancer, HIV-infected and healthy effector cells interaction model. Plots (a-f) correspond to the concentrations of cancer and healthy effector cells with delay $= 5$, without delay, with introduction of HIV-infected effector cells with delay $= 5$, with introduction of HIV-infected effector cells without delay, with the introduction of the concentration of cancer cells with delay $= 5$, and the introduction of the concentration of cancer cells without delay. Parameters are given in Table 1