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Theoretical study and numerical simulation for a mathematical model of diffusive cancer with effect of stem cell therapy and chemotherapy

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Abstract

Cancer is the most dangerous disease in the world. Therefore, this paper is devoted to studying a mathematical model of diffusive cancer and the effect of its treatments. One of the cancer treatments currently being explored is stem cell transplant, which works to stimulate and strengthen the immune system while the patient receives chemotherapy. This work introduces a mathematical system for the temporal and spatial interactions between the tumor, stem cells and effector cells during chemotherapy and the extent of the spread of these interactions within the tissue. Also, we study the stability of the system through the equilibrium points of the reaction-diffusion model. In addition, the existence, uniqueness, positivity, and boundedness are proven. We found a numerical simulation by the finite difference method and observed a dynamic of the solutions. Also, we described the tumor behaviour before and after the treatments and the effect of its diffusion.

Keywords: Cancer mathematical model, chemotherapy therapy, stem cell transplant, diffusion terms, finite difference method.

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1. Introduction

Cancer is a disease that killed millions of people globally and becomes one of the causes of death in the world. It starts from the abnormal growth of cells in different organs in the body and these cells divide and spread inside the human body without control and are able to penetrate and damage tissues. It is generated by a mutation in a chain of deoxyribonucleic acid-DNA found in cells. This chain in the human body contains a set of instructions prepared for the cells of the body that determine how to grow, develop and divide. While uninfected cells sometimes tend to make changes in their DNA, but they are still able to correct the bulk of these changes. But if they cannot make these corrections, the distorted cells often die. However, some of these deviations are not correctable, which leads to the growth of these cells and their transformation into cancerous cells. These deviations can extend the life of some cells more than their normal life average, this phenomenon causes the accumulation of cancer cells. It is known that many types of treatments are currently available for cancer such as surgery, chemotherapy, radiation therapy, stem cells transplantation, biological (immunotherapy), hormonal therapy, drug therapy, and

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clinical trials. There are many articles that have studied the effect of these treatments on tumor cells by describing the interaction between the tumor and its treatment as a mathematical model [1, 12, 17, 24]. For example, references [15, 18] introduced a mathematical model to describe the interaction between the tumor and the immune therapy. Suddin et al. [22] studied the interactions between the tumor, the immune system, effector cells and the cytokine Interleukine-2 (IL-2) treatment with spread cells by modeling a three-dimensional system of partial differential equations (PDEs) that subjects to initial and boundary conditions. The reference [26] studied the cancer model with immune therapy that containing interleukine-10 (IL-10) and anti-PD-L1 inhibitor. Mathemtically speaking, the cancer model has been examined by fuzzy logic in order to reduce tumor uncertainty and achieve a degree of realism [21]. The interaction between immune system and cancer cells by adding IL-12 cytokine and anti-PD-L1 was studied by considering the system of equations in term of Caputo and Caputo–Fabrizio (CF) derivative [25].

Stem cells have become a great scientific revolution in the treatment of many diseases because they are supporting body cells by differentiation and proliferation in tissue [3, 4, 9, 14, 16, 23]. Researchers believe that it is one of the important solutions in the future to help medical scientists [11]. The mathematical model can describe the dynamics of cancer and help physicians to predict the optimal treatments and control cancer growth by using stem cell and chemotherapy [8]. Practically, we know the ability of the tumor to spread in cells and weaken them, but the stem cells work to develop within tissues during chemotherapy and reduce the destroyed cells [13].

The mathematical model [8] is the first model that combined the cancer mathematical model with stem cell therapy. The model is also represented by fractional order differential equations [19]. However, this model is a system of ordinary differential equations (the functions are only dependent on time). The solutions of this system indicate that the stem cell therapy increase the immune system response and reduce the tumor growth. It is very important to study the effect of spread the tumor or its treatments in the model. The novelty of this work is to study the effect of a diffusion of tumor and treatments. Thus, this article is devoted to extend the mathematical model in reference [8] by accounting the diffusion terms in the mathematical model. In this case, the mathematical model is converted to a system of partial differential equations (PDEs). The article will study the stability, existence and uniqueness of the diffusive mathematical model as well as prove the positivity and boundedness of the solutions. The finite difference method (FDM) will be applied to obtain the numerical simulation. Then, we will explain the dynamic of the solutions and the behavior of tumor cells before and after treatments.

2. The model formulation

We formulated a mathematical model of tumor interactions with chemotherapy and stem cells. The model consists of four populations: $S(t)$ is stem cells, $E(t)$ is effector cells, $T(t)$ is tumor cells, and $M(t)$ is chemotherapy concentration drug of PDEs system, we set the spatial domain $B = (a, b)$, and the space-time domain $\Omega = B \times (0, t^*)$ as below form:

$$\begin{aligned}
\frac{\partial S}{\partial t} &= -\mu_1 S - \alpha_1 M S + d_1 \frac{\partial^2 S}{\partial x^2}, \quad \forall x, t \in \Omega, \\
\frac{\partial E}{\partial t} &= c - \lambda E + \frac{\Gamma E S}{S+1} - p(T+M)E + d_2 \frac{\partial^2 E}{\partial x^2}, \quad \forall x, t \in \Omega, \\
\frac{\partial T}{\partial t} &= \beta(1 - bT)T - (\sigma E + \alpha_2 M)T + d_3 \frac{\partial^2 T}{\partial x^2}, \quad \forall x, t \in \Omega, \\
\frac{\partial M}{\partial t} &= -\mu_2 M + V(t) + d_4 \frac{\partial^2 M}{\partial x^2}, \quad \forall x, t \in \Omega.
\end{aligned} \tag{2.1}$$

The description of the parameters are proposed in Table 1.

Table 1: Descriptions and values of the parameters in system (2.1), see [8].

Initial/Parameters	Description	Estimated values
$S(0)$	The initial concentration of stem cells	1
$E(0)$	The initial concentration of effector cells	1
$T(0)$	The initial density of tumors	1
$M(0)$	The initial concentration of chemotherapy drug	0
μ_1	The decay rate of the stem cells	0.02825
c	The growth rate of the effector cells	0.17
λ	The natural death rate of the effecror cells	0.03
b	Carrying capacity of tumor cells	1×10^{-9}
α_1	Parts stem cells killed by chemotherapy	1
Γ	Maximum proliferation rate of effector cells	0.1245
β	The growth rate of tumor	base in the stability condition
p	Decay rate of the effector cells killed tumor cells and chemotherapy	1
α_2	Parts tumor cells killed by chemotherapy	0.9
σ	Decay rate of the tumor cells killed by the effector cells	0.9
μ_2	Decay rate of chemotherapy drug	6.4
$V(t)$	The time refer to external flow of chemotherapy drug	1
$V(0)$	The initial value of $V(t)$	0

3. Description of the model

The system of PDEs (2.1) explains the relationship between stem cells $S(t)$ proliferation, tumor cells $T(t)$ and the interaction of effector cells $E(t)$, as well as the effect of chemotherapy compounds $M(t)$. In addition, the system includes the effect of diffusion term which is expressed by the second-order partial derivatives with respect to x. The first equation shows the rate change of the stem cells, they can decay naturally at the rate μ_1 and by the chemotherapy at the rate α_1. In the second equation, the rate change of effector cells can be effected positively by the natural growth (c) and the stem cells differentiation (Γ). Also, they can be decayed by the natural death (λ) and by chemotherapy or cancer (p). The third equation is the rate change of tumor cells which grow by natural growth (β). Also, tumor T decays based on its carrying capacity b and by the effect of chemotherapy (σ) and effector cells (α_2). In the last equation, it shows the rate change of chemotherapy which decreases by the rate μ_2 and increase by the effect of the function $V(t)$ which is dependent external influx of chemotherapy. Then, d_1, d_2, d_3, and d_4 are diffusion coefficients of stem cells, effector cells, tumor cells, and chemotherapy, respectively. Also, they show the random motility and supposed to be positive. The diagram in Fig. 1 describes the interactions between the components in aforementioned mathematical model.

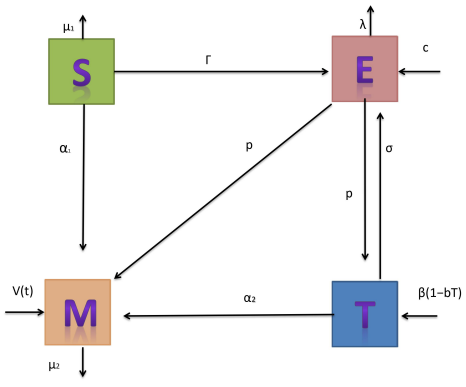

Figure 1: The diagram of the mathematical model (2.1).

4. Equilibrium points and stability

In general, the stability analysis of equilibrium points is important to determine the behavior of the system in the neighborhood of each equilibrium point. The system of equations (2.1) can be rewritten as following:

$$\begin{aligned} &\frac{\partial S}{\partial t} - d_1\frac{\partial^2 S}{\partial x^2} = -\mu_1 S - \alpha_1 MS, && \frac{\partial E}{\partial t} - d_2\frac{\partial^2 E}{\partial x^2} = c - \lambda E + \frac{\Gamma ES}{S+1} - p(T+M)E, \\ &\frac{\partial T}{\partial t} - d_3\frac{\partial^2 T}{\partial x^2} = \beta(1-bT)T - (\sigma E + \alpha_2 M)T, && \frac{\partial M}{\partial t} - d_4\frac{\partial^2 M}{\partial x^2} = -\mu_2 M + V(t). \end{aligned} \tag{4.1}$$

The equilibrium points for two cases as in [8], are as follows:

Free-cancer: In case of free cancer, we have no treatments (i.e., $S = 0,\ M = 0$), and the equilibrium positive point is given by:

$$P_0 = (E, T) = (\frac{c}{\lambda}, 0).$$

This point is defined if $\lambda \neq 0$ and indicates the case of free cancer. The Jacobin matrix for this point is:

$$J_B(P_0) = \begin{pmatrix} -\lambda & -\frac{cp}{\lambda} \\ 0 & \beta - \frac{c\sigma}{\lambda} \end{pmatrix}.$$

The eigenvalues are: $-\lambda$ and $\beta - \frac{c\sigma}{\lambda}$. The eigenvalues have negative real part if $\beta < \frac{c\sigma}{\lambda}$, i.e., $R_0 < 1$, where $R_0 = \frac{\beta\lambda}{c\sigma}$. Therefore, the point is asymptotically stable if $R_0 < 1$.

Endemic point before treatment: The endemic point before treatment is: $P_1 = (E, T) = (\frac{c}{\lambda + pT^*}, T^*)$, where

$$T^* = \frac{(\beta p - b\beta\lambda) + \sqrt{(\beta p - b\beta\lambda)^2 - 4(\beta bp)(c\sigma - \beta\lambda)}}{2b\beta p}.$$

The point is positive if $R_0 = \frac{\beta\lambda}{c\sigma} > 1$. The Jacobin matrix at P_1 is:

$$J_B(P_1) = \begin{pmatrix} -(\lambda + pT^*) & -\frac{cp}{\lambda + pT^*} \\ -\sigma T^* & \beta(1 - 2bT^*) - \frac{c\sigma}{\lambda + pT^*} \end{pmatrix}.$$

The eigenvalues of $J_B(P_1)$ is in the form

$$\frac{-A_1 \pm \sqrt{A_1^2 - 4A_2}}{2\sigma},$$

where $A_2 = \lambda\left(\beta(2bT^* - 1) + \frac{c\sigma}{\lambda + pT^*}\right) + \beta pT^*(2bT^* - 1)$ and $A_1 = \beta(2bT^* - 1) + \frac{c\sigma}{\lambda + pT^*} + \lambda + pT^*$. Thus, if $A_2 = 0$, we have

$$\frac{-A_1 \pm \sqrt{A_1^2}}{2\sigma},$$

there is one eigenvalue. If $A_2 > 0$, we have two eigenvalues with negative real parts, if $A_2 < 0$, we have at least one positive eigenvalue. Therefore, P_1 is asymptotically stable if $A_2 > 0$. Therefore, the point is stable if $T^* > \frac{1}{2b}$ and $R_0 > 1$.

Endemic point after treatment: The third positive equilibrium point for system is:

$$P_2 = (S, E, T, M) = (0, \frac{c}{\lambda + M_2 p + pT_2}, T_2, M_2),$$

where

$$T_2 = \frac{-B_1 + \sqrt{B_1^2 - 4\beta b\left(c\mu_2^2 p\sigma + p\left(\alpha_2 - \beta\mu_2\right)\left(\lambda\mu_2 + p\right)\right)}}{2b\beta\mu_2 p},$$

$M_2 = \frac{1}{\mu_2}$, $B_1 = \left(b\beta\lambda\mu_2 + b\beta p + \alpha_2 p - \beta\mu_2 p\right)$. The point P_2 exists if

$$\beta > \frac{c\mu_2^2\sigma + \alpha_2\left(\lambda\mu_2 + p\right)}{\mu_2\left(\lambda\mu_2 + p\right)}.$$

The Jacobin matrix at the point P_2 ($J_A(P_2)$) is as follows:

$$\begin{pmatrix} -\alpha_1 M_2 - \mu_1 & 0 & 0 & 0 \\ \frac{c\Gamma}{\lambda + M_2 p + p T_2} & -\lambda - p(M_2 + T_2) & -\frac{cp}{\lambda + M_2 p + p T_2} & -\frac{cp}{\lambda + M_2 p + p T_2} \\ 0 & -\sigma T_2 & -2b\beta T_2 + \beta - \frac{c\sigma}{\lambda + M_2 p + p T_2} - \alpha_2 M_2 & -\alpha_2 T_2 \\ 0 & 0 & 0 & -\mu_2 \end{pmatrix}.$$

The characteristic polynomial of $J_A(P_2)$ satisfies:

$$(-\mu_2 - L)(-\alpha_1 M_2 - \mu_1 - L)(L^2 + D_1 L + D_2),$$

where L denotes the eigenvalues, $D_1 = \beta\left(2bT_2 - 1\right) + \frac{c\sigma}{\lambda + M_2 p + p T_2} + \lambda + M_2\left(\alpha_2 + p\right) + pT_2$ and $D_2 = \left(2bT_2 - 1\right) + M_2\left(\beta\left(2bT_2 - 1\right)p + \frac{cp\sigma}{\lambda + M_2 p + p T_2} + \alpha_2\left(\lambda + pT_2\right)\right) + \frac{c\lambda\sigma}{\lambda + M_2 p + p T_2} + \alpha_2 M_2^2 p + \beta\left(\lambda + pT_2\right)$. The point is asymptotically stable if : $T_2 > \frac{1}{2b}$, and $\beta > \frac{c\mu_2^2\sigma + \alpha_2(\lambda\mu_2 + p)}{\mu_2(\lambda\mu_2 + p)}$.

Cure of cancer: The fourth positive equilibrium point for system (4.1) is:

$$P_3 = (S, E, T, M) = (0, \frac{c\mu_2}{\lambda\mu_2 + p}, 0, \frac{1}{\mu_2}).$$

This point indicates cure of cancer. The point is defined if $\mu_2 \neq 0$, and $p \neq 0$. The Jacobin matrix for this point is:

$$J_A(P_3) = \begin{pmatrix} -\frac{\alpha_1}{\mu_2} - \mu_1 & 0 & 0 & 0 \\ \frac{c\Gamma\mu_2}{\lambda\mu_2 + p} & -\lambda - \frac{p}{\mu_2} & -\frac{c\mu_2 p}{\lambda\mu_2 + p} & -\frac{c\mu_2 p}{\lambda\mu_2 + p} \\ 0 & 0 & -\frac{\alpha_2}{\mu_2} + \beta - \frac{c\mu_2\sigma}{\lambda\mu_2 + p} & 0 \\ 0 & 0 & 0 & -\mu_2 \end{pmatrix}.$$

The characteristic polynomial of L satisfies:

$$\det(J_A(P_3) - LI) = (-\mu_2 - L)(-\frac{\alpha_1}{\mu_2} - \mu_1 - L)(L^2 + C_1 L + C_2),$$

where $C_1 = -\beta + \frac{c\mu_2\sigma}{\lambda\mu_2 + p} + \lambda + \frac{\alpha_2 + p}{\mu_2}$, and $C_2 = -\beta\lambda + c\sigma + \frac{\alpha_2(\lambda\mu_2 + p)}{\mu_2^2} - \frac{\beta p}{\mu_2}$. The point is asymptotically stable if: $\lambda > \beta$, and $1 > R_0 + \frac{\beta p}{c\mu_2\sigma}$ (i.e., $R_0 < \frac{\lambda\mu_2}{p+1}$).

5. Numerical simulation

In literature there are many numerical methods to solve system of PDEs [5–7, 10, 20]. In this section, we will use the Finite Difference Method (FDM) with exponential technique. Assume the real numbers a, b, t^* such that $a > b$ and $t^* > 0$. We fix the spatial domain $B = (a, b)$ and the space-time domain $\Omega = B \times (0, t^*)$, where ∂B is the boundary of B. The PDEs in the system (2.1) are two-dimensional equations subjected to the initial-boundary conditions. In this section, we proposed numerical simulations

by applying the finite-difference method [2]. Beforehand, notice that the discrete model is an explicit scheme and the initial and boundary conditions are as follows:

$$\begin{aligned} S(x,0) &= G_S(x), \quad \forall x \in B, & E(x,0) &= G_E(x), \quad \forall x \in B, \\ T(x,0) &= G_T(x), \quad \forall x \in B, & M(x,0) &= G_M(x), \quad \forall x \in B, \end{aligned}$$

and the boundary conditions are:

$$\begin{aligned} S(x,t) &= \omega_S, \quad \forall x,t \in \partial B \times [0,t^*], & E(x,t) &= \omega_E, \quad \forall x,t \in \partial B \times [0,t^*], \\ T(x,t) &= \omega_T, \quad \forall x,t \in \partial B \times [0,t^*], & M(x,t) &= \omega_M, \quad \forall x,t \in \partial B \times [0,t^*]. \end{aligned}$$

We consider that S, E, T, and M are positive vectors of solution of system (2.1), and let $\xi \in \mathbb{R}^+$ be a constant. Dividing both sides of each equation in the system by $S(x,t)+\xi$, $E(x,t)+\xi$, $T(x,t)+\xi$, and $M(x,t)+\xi$, respectively, and using the chain rule at the left-hand side of each equation we obtain the following form:

$$\begin{aligned} \frac{\partial}{\partial t}\ln(S+\xi) &= \frac{1}{(S+\xi)}\left[-\mu_1 S - \alpha_1 MS + d_1\frac{\partial^2 S}{\partial x^2}\right], \\ \frac{\partial}{\partial t}\ln(E+\xi) &= \frac{1}{(E+\xi)}\left[c - \lambda E + \frac{\Gamma ES}{S+1} - p(T+M)E + d_2\frac{\partial^2 E}{\partial x^2}\right], \\ \frac{\partial}{\partial t}\ln(T+\xi) &= \frac{1}{(T+\xi)}\left[\beta(1-bT)T - (\sigma E + \alpha_2 M)T + d_3\frac{\partial^2 T}{\partial x^2}\right], \\ \frac{\partial}{\partial t}\ln(M+\xi) &= \frac{1}{(M+\xi)}\left[-\mu_2 M + V(t) + d_4\frac{\partial^2 M}{\partial x^2}\right]. \end{aligned} \tag{5.1}$$

For fixed $N, K \in \mathbb{N}$, define the sets $I_p = 1,2,\ldots,p$ for each $p \in \{N,K\}$, and $\bar{I}_p = \{0\} \cup I_p$, where $\bar{I}_p$ is the closure of I_p. Also, we define $\partial J = \bar{I}_N \cap \partial B$. Assume the discrete partition for the t and x on the domain $[a,b]$, and $[0,t^*]$ as following:

$$\begin{aligned} a = x_0 < x_1,\ldots,x_n < x_{n+1} < \cdots < x_N = b, \quad \forall n \in I_N, \\ 0 = t_0 < t_1,\ldots,t_k < t_{k+1} < \cdots < t_K = t^*, \quad \forall k \in I_K. \end{aligned}$$

The discrete operators for each $n \in I_{N-1}, k \in I_{K-1}$ are

$$\delta_t W_n^k = \frac{W_n^{k+1} - W_n^k}{\tau}, \quad \delta_x^2 W_n^k = \frac{W_{n+1}^k - 2W_n^k + W_{n-1}^k}{h^2},$$

where $W = \{S,E,T,M\}$. Substituting these discrete operators at the time t_k into model (5.1) gives:

$$\begin{aligned} \delta_t \ln(S_n^k+\xi) &= \frac{1}{(S_n^k+\xi)}[-\mu_1 S_n^k - \alpha_1 M_n^k S_n^k + d_1\delta_x^2 S_n^k], \\ \delta_t \ln(E_n^k+\xi) &= \frac{1}{(E_n^k+\xi)}[c - \lambda E_n^k + \frac{\Gamma E_n^k S_n^k}{S_n^k+1} - p(T_n^k+M_n^k)E_n^k + d_2\delta_x^2 E_n^k], \\ \delta_t \ln(T_n^k+\xi) &= \frac{1}{(T_n^k+\xi)}[\beta(1-bT_n^k)T_n^k - (\sigma E_n^k + \alpha_2 M_n^k)T_n^k + d_3\delta_x^2 T_n^k], \\ \delta_t \ln(M_n^k+\xi) &= \frac{1}{(M_n^k+\xi)}[-\mu_2 M_n^k + V(t) + d_4\delta_x^2 M_n^k]. \end{aligned}$$

We have obtained an exponential mathematical system that can be rewritten as follows:

$$\begin{aligned} S_n^{k+1} = F_S = (S_n^k+\xi)\exp(\phi_S) - \xi, \quad E_n^{k+1} = F_E = (E_n^k+\xi)\exp(\phi_E) - \xi, \\ T_n^{k+1} = F_T = (T_n^k+\xi)\exp(\phi_T) - \xi, \quad M_n^{k+1} = F_M = (M_n^k+\xi)\exp(\phi_M) - \xi, \end{aligned} \tag{5.2}$$

where

$$\phi_S = \frac{\tau((-\mu_1 S_n^k - \alpha_1 M_n^k S_n^k + d_1 \delta_x^2 S_n^k)}{S_n^k + \xi},$$
$$\phi_E = \frac{\tau(c - \lambda E_n^k + \frac{\Gamma E_n^k S_n^k}{S_n^k + 1} - p(T_n^k + M_n^k) E_n^k + d_2 \delta_x^2 E_n^k)}{E_n^k + \xi},$$
$$\phi_T = \frac{\tau((\beta(1 - bT_n^k) T_n^k - (\sigma E_n^k + \alpha_2 M_n^k) T_n^k + d_3 \delta_x^2 T_n^k)}{T_n^k + \xi},$$
$$\phi_M = \frac{\tau(-\mu_2 M_n^k + V + d_4 \delta_x^2 M_n^k)}{M_n^k + \xi},$$

subjected to:

$$S_n^0 = G_S(x_n)\,, E_n^0 = G_E(x_n)\,, T_n^0 = G_T(x_n)\,, M_n^0 = G_M(x_n), \quad \forall n \in \bar{I}_N\,,$$

also,

$$S_n^k = w_S(x_n, t_k), \quad \forall (n,k) \in \partial J \times \bar{I}_K, \qquad E_n^k = w_E(x_n, t_k), \quad \forall (n,k) \in \partial J \times \bar{I}_K,$$
$$T_n^k = w_T(x_n, t_k), \quad \forall (n,k) \in \partial J \times \bar{I}_K, \qquad M_n^k = w_M(x_n, t_k), \quad \forall (n,k) \in \partial J \times \bar{I}_K,$$

and define the $(N+1)$-dimensional real vectors as

$$W^k = (W_0^k, W_1^k, W_2^k, \ldots, W_n^k, \ldots, W_{N-1}^k, W_N^k).$$

Theorem 5.1 (Existence and uniqueness). *Let $W_n^k > 0$ and $\xi > 0$. Then, the discrete model (5.2) has a unique solution W_n^{K+1}.*

Proof. Since $W_n^k > 0$, $\xi > 0$, and W_n^{k+1} is defined uniquely in the system (5.2), the solution exists and is unique. □

Theorem 5.2 (Constant solutions). *Let W_n^k be the zero vectors for fixed $k \in \bar{I}_k$. Then, the sequence $(W_n^k)_{k=0}^K$ is a solution for the system (5.2) if $G_W \equiv 0$, $\omega_W \equiv 0$, and $c = 0$.*

Proof. Assume the vectors $W_n^0 = 0$ satisfy the system (5.2) and the initial and boundary conditions. For some $k \in \bar{I}_{K-1}$, if $W_n^k = 0$, then $G_W = 0$ and $\omega_W = 0$, by the system (5.2) becomes: $W_n^{k+1} = F_W(0) = 0$, for each $n \in I_{N-1}$. Therefore, the zero vector is the constant solution. □

Lemma 5.3. *Define the function $F_W(w) = g_W \exp(\phi_W) - \xi$, where $g_W(w) = w + \xi$ as in (5.2). Assume F_W, ϕ and g are mapping from $[0,1]$ to $\mathbb{R}$, ϕ and g_W are differential for each $w \in [0,1]$ and for some $\xi \in \mathbb{R}$, then $F_W(w)$ is increasing in $[0,1]$ if $F'_W(w) = g_W(w)\phi'(w) + g'_W(w) > 0$.*

Theorem 5.4 (Increasing functions). *Assume the function $F_W(w)$ is as defined in Lemma 5.3. Then, $F_S(w)$, $F_E(w)$, $F_T(w)$, and $F_M(w)$ are increasing functions if they satisfy the following conditions respectively:*

$$\tau B_S < \xi, \qquad \tau B_E < \xi\left(\frac{\Gamma S \tau}{S+1} + 1\right), \qquad \tau B_T < \xi(\beta + 1), \qquad \tau B_M < \xi,$$

where

$$B_S = d_1\left(a_{S,n}^k + e_{S,n}^k + \frac{2\xi}{h^2}\right) + \xi\left(\mu_1 + \alpha_1 M_n^k\right),$$
$$B_E = c + d_2\left(a_{E,n}^k + e_{E,n}^k\right) + \xi\left(\frac{2d_2}{h^2} + \lambda + pM_n^k + pT_n^k\right),$$
$$B_T = d_3\left(a_{T,n}^k + e_{T,n}^k\right) + \xi\left(b\beta T_n^k + \frac{2d_3}{h^2} + \alpha_2 M_n^k + \sigma E_n^k\right),$$
$$B_M = d_4\left(a_{M,n}^k + e_{M,n}^k\right) + \xi\left(\frac{2d_4}{h^2} + \mu_2\right) + V(t).$$

Proof. Let $H_W(w) = g_W(w)\phi'(w) + g'_W(w)$, where $g_W(w) = w + \xi$ and $g'_W(w) = 1$, and for each $W \in \{S, E, T, M\}$, $H_W(w)$ can be found as

$$H_S(w) = \frac{R_S(w)}{w+\xi}, \quad H_E(w) = \frac{R_E(w)}{w+\xi}, \quad H_T(w) = \frac{R_T(w)}{w+\xi}, \quad H_M(w) = \frac{R_M(w)}{w+\xi}, \quad \forall w \in [0,1],$$

where

$$R_S(w) = w + \xi - \tau B_S, \quad \forall w \in [0,1], \qquad R_E(w) = w + \xi - \tau B_E + \frac{\xi\Gamma S\tau}{S+1},$$
$$R_T(w) = w + \xi - \tau B_T + \xi\beta, \qquad R_M(w) = w + \xi - \tau B_M,$$

where

$$B_S = d_1\left(a^k_{S,n} + e^k_{S,n} + \frac{2\xi}{h^2}\right) + \xi\left(\mu_1 + \alpha_1 M^k_n\right),$$
$$B_E = c + d_2\left(a^k_{E,n} + e^k_{E,n}\right) + \xi\left(\frac{2d_2}{h^2} + \lambda + pM^k_n + pT^k_n\right),$$
$$B_T = d_3\left(a^k_{T,n} + e^k_{T,n}\right) + \xi\left(b\beta T^k_n + \frac{2d_3}{h^2} + \alpha_2 M^k_n + \sigma E^k_n\right),$$
$$B_M = d_4\left(a^k_{M,n} + e^k_{M,n}\right) + \xi\left(\frac{2d_4}{h^2} + \mu_2\right) + V(t).$$

It is obvious that $H_S(w) > 0$, $H_E(w) > 0$, $H_T(w) > 0$, and $H_M(w) > 0$, if they satisfy the following conditions, respectively,

$$\tau B_S < \xi, \quad \tau B_E < \xi\left(\frac{\Gamma S\tau}{S+1} + 1\right), \quad \tau B_T < \xi(\beta+1), \quad \tau B_M < \xi.$$

By Lemma 5.3 the functions $F^k_{W_n}(w)$ are increasing functions for $\forall\, w \in [0,1]$, $\forall\, n \in I_{N-1}$ and $k \in \bar{I}_{K-1}$. Using the hypotheses, the vectors a^k_W and e^k_W are defined as follows: $|\, a^k_{W_n} \,| \leqslant \frac{1}{h^2}$ and $|\, e^k_{W_n} \,| \leqslant \frac{1}{h^2}$ for each $k \in \bar{I}_K$ and $W \in \{S, E, T, M\}$. □

Theorem 5.5 (Boundedness)**.** *Let $w \in [0,1]$, $\xi > 0$. If $c + \Gamma/2 < \lambda + 2p$, $\beta < b\beta + \sigma + \alpha_2$, and $V(t) < \mu_2$ hold, then there are unique sequences of vectors $(W^k)_{k=0}^K$ that satisfies $0 < W^k < 1$, for each $W \in \{S, E, T, M\}$.*

Proof. Let F_W is a mapping function in the domain $[0,1]$. Then, we have the initial value at $w = 0$ as

$$F_S(0) = \xi\exp(0) - \xi, \quad F_E(0) = \xi\exp\left(\frac{\tau}{\xi}c\right) - \xi, \quad F_T(0) = \xi\exp(0) - \xi, \quad F_M(0) = \xi\exp\left(\frac{\tau}{\xi}V(t)\right) - \xi.$$

Thus $F_W(0) = 0$ if $c = 0$ and $V(t) = 0$. On other hand, we get

$$\phi_S(1) < \frac{\tau}{1+\xi}(-\mu_1 - \alpha_1), \qquad \phi_E(1) < \frac{\tau}{1+\xi}(c - \lambda + \Gamma/2 - 2p),$$
$$\phi_T(1) < \frac{\tau}{1+\xi}(\beta(1-b) - \sigma - \alpha_2), \qquad \phi_M(1) < \frac{\tau}{1+\xi}(-\mu_2 + V(t)).$$

Thus, $\phi_W(1) < 0$ if $c + \Gamma/2 < \lambda + 2p$, $\beta < b\beta + \sigma + \alpha_2$, $V(t) < \mu_2$. If $\phi_W(1) < 0$, then $F_W(1) < 1$. Since the functions are increasing in $[0,1]$, and $0 < F_W(0) < F_W(1) < 1$, then $F_W(w)$ is bounded in $[0,1]$. Let the sequence W^k_n such as $0 < W^k_n < 1$, we have $W^{k+1}_n = F_W(W^k_n)$, therefore $0 < W^{k+1}_n < 1$. □

6. Dynamics of the system

6.1. Before treatment

First, we study the system (2.1) before starting the treatments (i.e., $M = S = 0$). Assume the initial conditions of system (5.2) as follows:

$$T(x,0) = T_0 e^x, \quad E(x,0) = E_0 e^{1-x}.$$

The value of β has been chosen based on stability condition and the other value of parameters are in Table 1. Figure 2 Shows decrease in the concentration of effector cell E_0 to fight cancer, and tumor cell T_0 grows fast. The parameters used are $\beta = 5.2,\ c = 0.17,\ \xi = 0.1,\ \tau = 0.0001$, and $N = 1000$, with diffusion coefficients: $d_2 = 0.1,$ and $d_3 = 0.98111$. Figure 2 indicates that the tumor cells are expected to grow and the effector cells decay.

6.2. After treatment

Next, we study the diffusive system which includes stem cells transplant and chemotherapy. In this case, we consider $S > 0$ and $M > 0$. We assume the initial conditions of the system (5.2) as follows:

$$S(x,0) = S_0 e^{-x}, \quad T(x,0) = T_0 e^x, \quad E(x,0) = E_0 e^{1-x}, \quad M(x,0) = M_0 e^x.$$

The stem cells decay because of their ability to differentiate, the chemotherapy drug and effector cells increase in space while the tumor cells decay as we can see in Figure 3. Also, the numerical solutions at the time $t = 1, 3, 5$ are plotted in Figure 3. However, Figures 2 and 3 present the biological meaning. Before the treatment, tumor infection starts in Figure 2, the concentration of effector cells tends to decrease because interaction with tumor cells into the tissue, while tumor cells increasing. While after treatment, the stem cells decrease because they differentiate into other type of cells or another stem cells. Also, the tumor cells decrease as a results of the treatments effects, which means an infected cell could die or return to being an uninfected cell. As a result, the infected cells, and the concentration of chemotherapy decreases as we see in Figure 4.

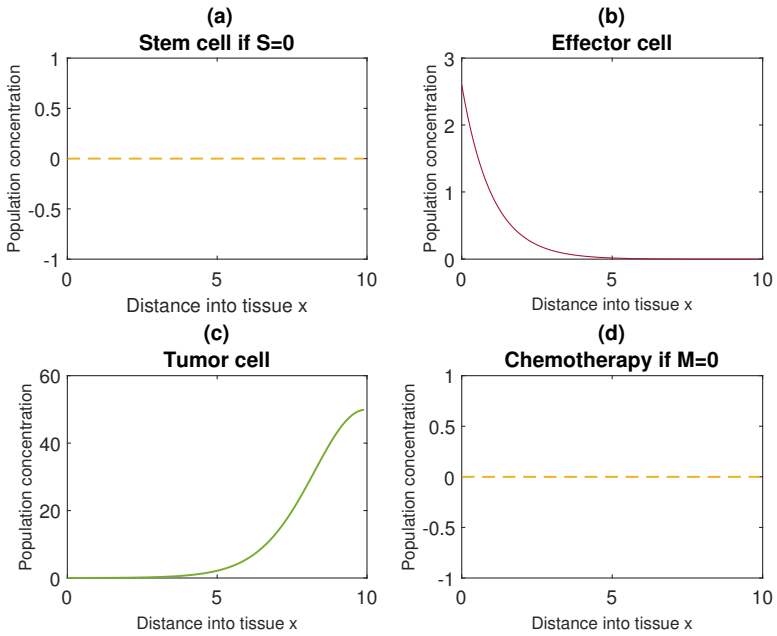

Figure 2: The plots present the beginning of infection where no therapy started ($S = 0,\ M = 0$).

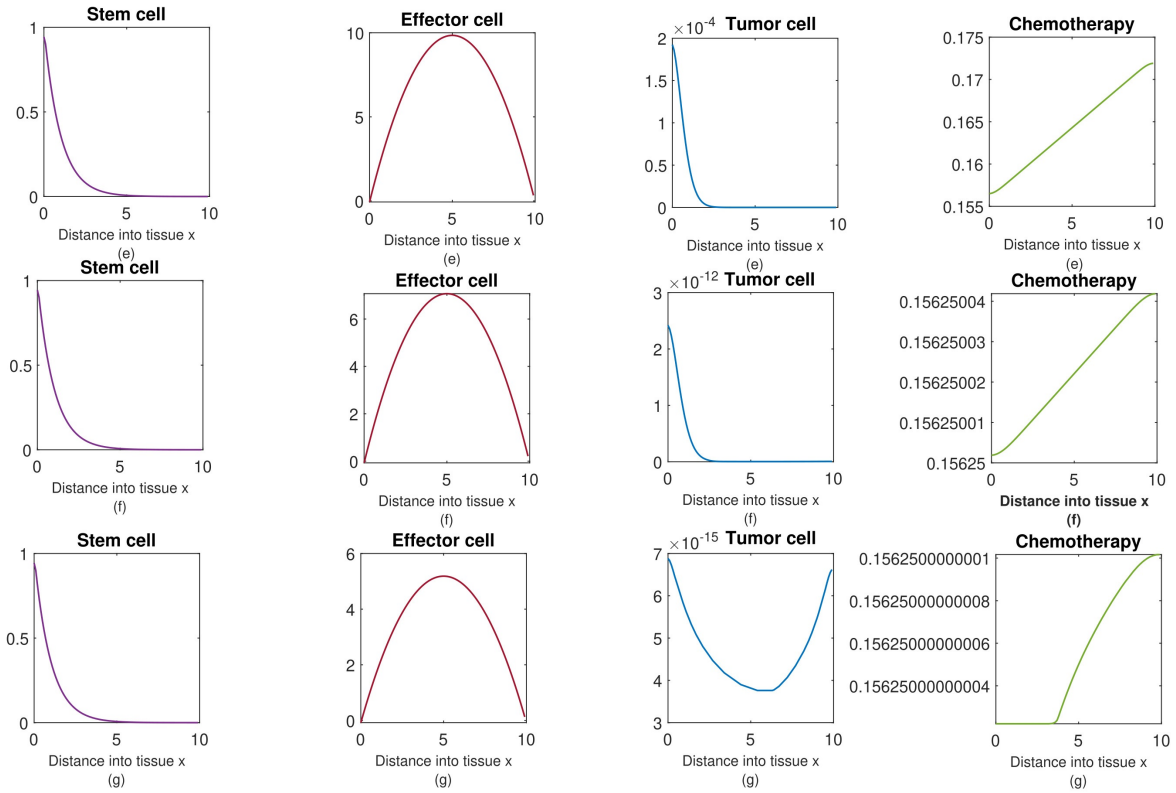

Figure 3: The plot of S, E, T, M at $t = 1$ graph (e), $t = 3$ graph (f), $t = 5$ graph (g); with diffusion coefficients: $d_1 = 0.1, d_2 = 0.1, d_3 = 0.5,$ and $d_4 = 0.1$.

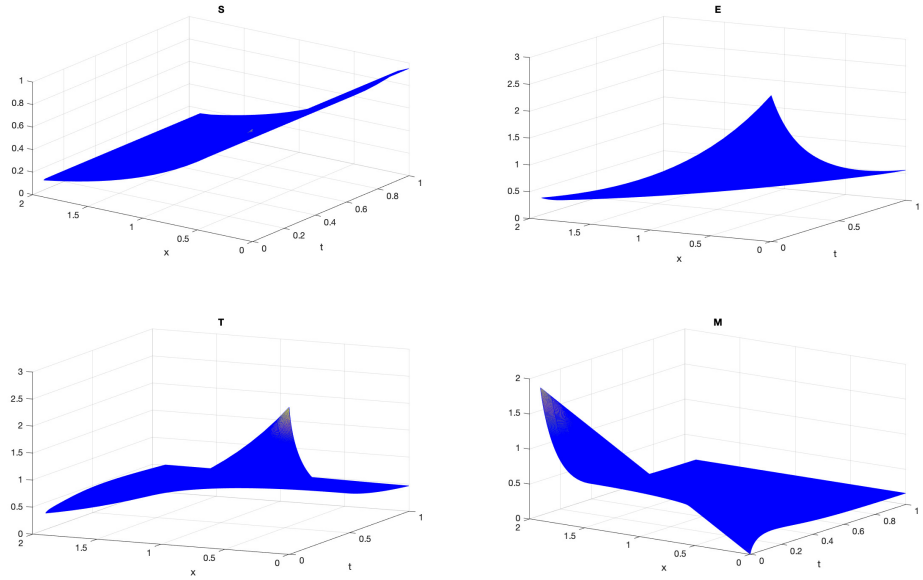

Figure 4: The 3D-plot of S, E, T, M, $d_1 = 0.1, d_2 = 0.1, d_3 = 0.5,$ and $d_4 = 0.1$.

7. Conclusion

In this paper, we reviewed a new mathematical model and studied the interaction between cancer cells, chemotherapy and stem cells, and the effect of effector cells by their diffusion terms. As well, we deduced the numerical simulation by (FDM) with helping an exponential type technique. Also, We observed the dynamics of the mathematical system of two cases with proposed conditions. So that, the first case is that the cancer is present and free of treatment as a result the previously used parameters and coefficients indicate that the cancer continues its attack inside the tissue cells and spreads despite the resistance of the effector cells. Finally, in the second case, the treatment is present (under the initial conditions) so that the stem cells with effector cells are supportive of the chemotherapy, which strengthens the resistant immune system and can eliminate cancer and reduce its spread. As a results of this work, we are able to notice the behavior of the components of the system with respect to the space (x) as following: (i) the stem cell decay in the body as a result of its ability to differentiate to different type of cell; (ii) the concentration of chemotherapy increase in cells; (iii) the tumor decays; and (iv) the concentration of effector cell decreases in space x because the effect of chemotherapy.

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