

## Post-Treatment Stability Analysis of a Tumor–Immune Model for Non-Small-Cell Lung Cancer under Surgery and Chemotherapy

Fatima S. Sadaga\*, Abdassalam B.H. Aldaikh

*Department of Mathematics, Faculty of Science, University of Omar Al-Mukhtar, El-Beida, Libya*

*\*Corresponding author: fatima.sadaga@omu.edu.ly*

**Abstract.** In this work, we study the post-treatment dynamics of non-small-cell lung cancer through a nonlinear tumor–immune interaction model incorporating the residual effects of surgery and chemotherapy. Tumor cells, cytotoxic CD8<sup>+</sup> T lymphocytes, and dendritic cells are described by a system of ordinary differential equations in which therapeutic interventions are embedded as persistent biological effects acting on both tumor and immune populations. This modeling approach focuses on long-term outcomes following treatment rather than the treatment process itself. The model is shown to be well posed through positivity and boundedness of solutions, ensuring biological feasibility. Three biologically meaningful equilibrium states are identified, corresponding to tumor eradication, immune failure with tumor persistence, and controlled chronic disease. Explicit local stability conditions for these equilibria are derived using linearization and the Routh–Hurwitz criteria, revealing the roles of tumor growth, immune effectiveness, and treatment-induced immune toxicity in shaping post-treatment outcomes. Numerical illustrations support the analytical results and demonstrate robust convergence toward the predicted equilibrium states. A sensitivity analysis highlights the trade-off between chemotherapy-induced tumor killing and immune suppression, emphasizing the importance of immune preservation for favorable long-term tumor control. Overall, the proposed framework provides a mathematically rigorous and biologically interpretable description of post-treatment cancer dynamics and offers qualitative insight into remission, relapse, and disease control following therapy.

### 1. INTRODUCTION

The condition known as cancer is caused by the unchecked growth of altered cells that are subject to natural selection. This includes the genetic and epigenetic alterations that build up within a population of cancer cells and result in the disease's deadly phenotype [1].

Cancer was initially identified as a tumor, which is a growing mass of tissue. They could see how it looked, how quickly it expanded, and how it frequently seemed to "bite" or eats some body parts.

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The tumors themselves were known to be lethal and occasionally appeared to spread to other areas of the body. At this level of comprehension, two things are clear. First of all, it is consistent with a condition characterized by aberrant, unchecked growth that has the potential to spread. Second, the terms tumor and cancer were not distinguished from one another. These names are still frequently used interchangeably nowadays. Rudolf Virchow developed the "cellular theory" of disease in the middle of the 19th century, which holds that all illnesses, including cancer, resulted from alterations in cells. Because of this information, cancer was now recognized as a disease caused by aberrant cell growth [2]. Numerous works from the time period demonstrate how cancer was understood to be caused by cells that proliferate and form a tumor [3]. One characteristic that distinguishes the evolution of cancer is changes in gene frequency within a population. However, somatic evolution or a population of cells displaying genetic heterogeneity are not the only aspects of cancer. Cancer cell populations develop adaptability. Certain phenotypic traits of cancer cells are preferred above others by the tumor microenvironment, and the cancer cells' adaptations feed back into their microenvironment. Increased resource intake, co-optation of normal cells like fibroblasts, immune system evasion or recruitment of protumor components, production of public goods (angiogenesis and extracellular matrix components), and tolerance to acidic environments are all examples of how cancer cells evolve [4] [5] [6]. In order to cause pain, organ failures, and cancer-related disorders like cachexia, cancer cells must proliferate, disseminate, use resources and produce metabolites, damage tissue, and co-opt normal noncancerous cells. This is why cancer is a disease. In addition to destroying a person's body, cancer has a severe detrimental influence on their mental health and the lives of those around them, upsetting friendships and families. Ten million individuals worldwide die from cancer each year, demonstrating how prevalent and deadly the disease is [7].

Lung cancer is a fatal illness that accounts for around 20 percent of all cancer-related fatalities worldwide. Hypoxia, or low oxygen levels in tumor cells, is a major contributing factor to the development of lung cancer and its resistance to treatment [8]. The majority of Lung cancer deaths and illnesses are caused by risk factors such outdoor air pollution, family history of illnesses, and the prevalence of tobacco smoking and another reasons [9]. Lung cancer was one of the most common cancers diagnosed in men in very high HDI and medium HDI nations in 2018 [10]. Over the previous five years, it was discovered that this type of cancer was common in Bangladesh, affecting 13.1 percent of men and 2percent of women [11]. The world health organization reports that there were 108,137 cancer-related deaths and 150,781 cancer patients in Bangladesh overall in 2018. With an 11 percent fatality rate, lung cancer affected 8.2percent of cancer patients. According to the who, there were 10,851 cases of lung cancer in 2012, 12,374 cases in 2018, and 26,738 cases are anticipated in 2040. In 2040, lung cancer will be a more deadly form of the disease than breast cancer [12]. Numerous studies have been conducted to look at the dynamics of cancer. De Pillis et al. Created a mathematical model of the course of cancer [13]. To treat the patients, they combined chemotherapy with injections of activation protein (IL-2) and activated antitumor cell transfer

(TIL). De Pillis et al. [14] also offered a novel mathematical model that illustrates tumor-immune interactions, focusing on the role of CD8<sup>+</sup> T cells and natural killer (NK) cells in tumor surveillance, in order to understand the dynamics of immune-mediated tumor rejection.

## 2. MATHEMATICAL MODEL AND BIOLOGICAL ASSUMPTIONS

When Fibonacci developed the famous Fibonacci series in the 13th century to explain population growth, mathematics was first used in biology. Later, Daniel Bernoulli used mathematical concepts to explain how the morphologies of microscopic creatures were affected, and Johannes Reinke first used the phrase "bio math" in 1901. In essence, biomathematics is the theoretical study of mathematical models to examine the fundamental ideas guiding the composition and dynamics of biological systems.

Mathematics has played a pivotal role in advancing the natural sciences and can similarly revolutionize biological research [15]. Mathematics provides us with models to help us understand the intriguing complexities posed by biology, and biology, in turn, assesses these mathematical models. Complex mathematical problems are now easier to handle thanks to recent advances in computer algebra systems. Consequently, this frees up researchers to concentrate on understanding mathematical biology instead of figuring out how to solve problems [16]. Understanding diseases with high worldwide mortality rates, such as cancer and infectious diseases, is highly prioritized. Mathematical modeling is a useful technique for assessing diseases that affect people globally in order to reach this understanding [17]. Notwithstanding advances in science and medicine, cancer continues to be a major health concern that claims lives [18]. Cancer that begins in the lungs is known as lung cancer. A person with lung cancer has aberrant cells that group together to create a tumor. Cancer cells, in contrast to healthy cells, proliferate uncontrollably and kill the surrounding healthy lung tissue. We refer to these kinds of tumors as malignant tumors. While dendritic cells are being triggered to mature in response to the presence of tumor cells, tumor cells proliferate logistically and interact to harm CD8<sup>+</sup> T lymphocytes. So, a mathematical model is developed based on the Lotka-Volterra and the logistic model. Motivated by these considerations, the present work investigates the local stability properties of a tumor-immune interaction model for NSCLC after surgical and chemotherapeutic intervention, where the model consists of three variables such as tumor cells, CD8<sup>+</sup> T cells it's play a distinct role in adaptive immune responses [19], and dendritic cells, where dendritic cells (DCs) are sentinel leukocytes that play a key role in the initiation and regulation of adaptive immune responses, as well as in innate immunity [20], which are denoted by  $T(t)$ ,  $C(t)$ , and  $D(t)$ , respectively. Certain tumor cells are eliminated by CD8<sup>+</sup> T lymphocytes when they contact with tumor cells. Once more, certain tumor cells are destroyed by dendritic cells when they come into touch with tumor cells.

**2.1. State Variables.** Let  $T(t)$ ,  $C(t)$ , and  $D(t)$  denote the densities of tumor cells, CD8<sup>+</sup> T lymphocytes, and dendritic cells at time  $t \geq 0$ , respectively. All state variables are assumed to be nonnegative and continuously differentiable. Tumor cells represent the malignant population,

$CD8^+$  T cells mediate cytotoxic immune responses, and dendritic cells facilitate antigen presentation and immune activation.

## 2.2. Model Equations without Treatment.

$$\frac{dT}{dt} = \alpha T(1 - \beta T) - \gamma T - \phi CT \quad (2.1)$$

where the logistic growth of the tumor is represented by the term  $\alpha T(1 - \beta T)$ , the rate at which  $CD8 + T$  lymphocytes kill tumor cells is  $\phi$ , and  $\gamma$  is the constant rate at which tumor cells are destroyed by dendritic cells. Some  $CD8 + T$  cells are killed by tumor cells, which is one way that tumor cells interact with  $CD8 + T$  cells. Additionally, certain  $CD8 + T$  lymphocytes are stimulated as a result of interaction between dendritic cells and tumor cells. The following is a mathematical representation of this:

$$\frac{dC}{dt} = vT - \eta CT - kC. \quad (2.2)$$

Here, constant rate  $v$  represents the activation rate of  $CD8 + T$  cells due to contact between dendritic cells and tumor cells,  $\eta$  represents the inactivation rate of  $CD8 + T$  cells by tumor cells, and  $k$  represents the  $CD8 + T$  cell natural death rate. Hematopoietic bone marrow progenitor cells give rise to dendritic cells, which are initially immature. Under normal conditions, they can be found all over the body. They become activated mature cells as a result of coming into contact with tumor cells. Some dendritic cells then go dormant as a result of  $CD8 + T$  cells being activated.

$$\frac{dD}{dt} = \mu + \sigma DT - \rho CD - \omega D. \quad (2.3)$$

$\mu$  represents the sources of dendritic cell generation,  $\sigma$  represents the rate at which tumor cells attract dendritic cells,  $\rho$  represents the rate at which  $CD8 + T$  lymphocytes inactivate dendritic cells, and  $\omega$  represents the rate at which dendritic cells naturally die.

## 3. POST-TREATMENT MODEL INCORPORATING SURGERY AND CHEMOTHERAPY

Following the formulation of the baseline tumor-immune dynamics and the establishment of fundamental mathematical properties, we now specify the post-treatment model that incorporates the residual effects of surgery and chemotherapy. The purpose of this section is to define the treated system whose long-term behavior will be analyzed in subsequent sections.

In clinical practice, surgical resection and chemotherapy are administered to reduce tumor burden and suppress malignant progression. However, even after treatment, residual tumor cells may persist, and immune populations may remain suppressed or partially depleted. The present model focuses on this post-treatment phase, where therapeutic interventions have already occurred and their biological consequences continue to influence the system.

**3.1. Incorporation of Surgical Effects.** Surgical resection is primarily intended to eliminate a significant portion of tumor cells. In the post-treatment setting, the effect of surgery is represented by an effective tumor cell loss term. Let  $\xi_{100} > 0$  denote the tumor cell death rate caused by surgery. This parameter summarizes the net impact of surgical intervention on tumor viability in the post-treatment phase, without explicitly modeling the surgical event itself.

**3.2. Incorporation of Chemotherapy Effects.** Chemotherapy aims to destroy remaining tumor cells following surgery but often produces collateral damage to immune cells. In the post-treatment model, chemotherapy effects are incorporated through effective loss parameters acting continuously on the system.

The parameter  $\psi_{128} > 0$  represents chemotherapy-induced tumor cell death throw 128 days, while  $\tau_{128} > 0$  and  $\zeta_{128} > 0$  describe the corresponding suppression of  $CD8^+$  T lymphocytes and dendritic cells, respectively throw 128 days. These parameters quantify the persistent biological influence of chemotherapy on tumor-immune dynamics after treatment completion.

#### 4. FORMULATION OF THE MATHEMATICAL MODEL WITH SURGERY AND CHEMOTHERAPY

Assume that following surgery, some cancer cells might still be present. Consequently, the cancer can return. For individuals with early-stage non-small cell lung cancer (NSCLC), postoperative chemotherapy can help lower the risk of recurrence. Assuming surgery is done 100 days following tumor growth, we expect stay that 5 percent of tumor cells survive surgery and 1 percent stay after chemotherapy. It was suggested that chemotherapy be started. On day 128 and usually starts eight weeks after surgery. Additionally, It was expected chemotherapy will kill 2 percent of  $CD8 + T$  cells and dendritic cells. Consequently, the following is a mathematical model [21] for NSCLC treatment:

$$\begin{aligned}\frac{dT}{dt} &= \alpha T(1 - \beta T) - \gamma T - \phi CT - \xi_{100}T - \psi_{128}T \\ \frac{dC}{dt} &= vT - \eta CT - kC - \tau_{128}C \\ \frac{dD}{dt} &= \mu + \sigma DT - \rho CD - \omega D - \zeta_{128}D.\end{aligned}\tag{4.1}$$

Where  $\xi_{100}$  and  $\psi_{128}$  represent the tumor cell death rates caused by surgery on day 100 and chemotherapy on day 128 respectively. The chemotherapy-induced death rates of  $CD8 + T$  cells and dendritic cells on day 128 are denoted by  $\tau_{128}$  and  $\zeta_{128}$  correspondingly.

TABLE 1. Parameter values and their descriptions

| Descriptions of the parameter                                                             | Notations |
|-------------------------------------------------------------------------------------------|-----------|
| Tumor growth rate                                                                         | $\alpha$  |
| $1/\beta$ is carrying capacity                                                            | $\beta$   |
| Tumor cells killing by dendritic cells                                                    | $\gamma$  |
| Tumor cells killing rate by $CD8^+$ T cells                                               | $\phi$    |
| Activation rate of $CD8^+$ T cells for the interaction of dendritic cells and tumor cells | $v$       |
| Inactivation rate of $CD8^+$ T cells by tumor cells                                       | $\eta$    |
| Death rate of $CD8^+$ T cells                                                             | $k$       |
| Constant source of dendritic cells                                                        | $\mu$     |
| Proliferation rate of dendritic cells due to tumor cells                                  | $\sigma$  |
| Inactivation rate of dendritic cells by $CD8^+$ T cells                                   | $\rho$    |
| Death rate of dendritic cells                                                             | $\omega$  |

## 5. BASIC PROPERTIES OF THE POST-TREATMENT MODEL

### 5.1. Positivity of Solutions.

**Theorem 5.1.** *Let  $(T(0), C(0), D(0)) \in \mathbb{R}_{\geq 0}^3$  be any nonnegative initial condition. Then the solutions  $(T(t), C(t), D(t))$  of system 4.1 remain nonnegative for all  $t \geq 0$ .*

*Proof.* The right-hand sides of equations in system 4.1 are locally Lipschitz continuous in  $\mathbb{R}_{\geq 0}^3$ , guaranteeing local existence and uniqueness of solutions.

We evaluate each equation on the boundary of the nonnegative orthant. If  $T = 0$ , then

$$\left. \frac{dT}{dt} \right|_{T=0} = 0,$$

which implies that the tumor population cannot cross into negative values.

If  $C = 0$ , then

$$\left. \frac{dC}{dt} \right|_{C=0} = vT \geq 0,$$

since  $T(t) \geq 0$ . Hence,  $CD8^+$  T cells remain nonnegative.

If  $D = 0$ , then

$$\left. \frac{dD}{dt} \right|_{D=0} = \mu > 0,$$

which ensures that dendritic cells immediately re-enter the positive region.

Therefore, solutions cannot leave the nonnegative orthant, and all state variables remain non-negative for all  $t \geq 0$ .  $\square$

## 5.2. Boundedness of Solutions.

**Theorem 5.2.** *All solutions of system 4.1 with nonnegative initial conditions are uniformly bounded for  $t \geq 0$ .*

*Proof.* From the tumor equation, we have

$$\frac{dT}{dt} \leq \alpha T(1 - \beta T),$$

since all remaining terms contribute negatively to tumor growth. By comparison with the logistic equation, it follows that

$$0 \leq T(t) \leq \frac{1}{\beta} \quad \text{for all } t \geq 0.$$

Substituting this bound into equation  $\frac{dC}{dt}$  yields

$$\frac{dC}{dt} \leq \nu\beta^{-1} - (k + \tau_{128})C,$$

which implies that  $C(t)$  is bounded above by a finite constant.

Similarly, using the bound on  $T(t)$  in system 4.1 gives

$$\frac{dD}{dt} \leq \mu + \sigma\beta^{-1}D - (\omega + \zeta_{128})D,$$

which ensures boundedness of  $D(t)$  provided  $\omega + \zeta_{128} > \sigma\beta^{-1}$ , a condition that is biologically reasonable in post-treatment settings.

Hence, all state variables remain uniformly bounded for  $t \geq 0$ . □

The next table explained all the variables and parameters used, it was taken from [21].

## 6. FINDING SYSTEM STABILITY WITH SURGERY AND CHEMOTHERAPY

We shall analyze the equations of the system (4.1) to find all possible equilibrium points and hence test the stability of the system by Routh Hurwitz Criteria.

### 6.1. Equilibrium Analysis and steady state.

6.1.1. *Cancer-free Equilibrium.* By setting disease-related variables to zero in model (4.1), then

$$\begin{aligned} 0 &= \alpha T(1 - \beta T) - \gamma T - \phi CT - \xi_{100}T - \psi_{128}T \\ 0 &= \nu T - \eta CT - kC - \tau_{128}C \\ 0 &= \mu + \sigma DT - \rho CD - \omega D - \zeta_{128}D. \end{aligned} \tag{6.1}$$

Cancer-free equilibrium point,  $T = 0$  and  $C = 0$ , then

$$P_0 = \left(0, 0, \frac{\mu}{\omega + \zeta_{128}}\right)$$

The Jacobian matrix is

$$J = \begin{bmatrix} \alpha - 2\alpha\beta T - \gamma - \phi C - \xi_{100} - \psi_{128} & -\phi T & 0 \\ v - \eta C & -\eta T - k - \tau_{128} & 0 \\ \sigma D & -\rho D & \sigma T - \rho C - \omega - \zeta_{128} \end{bmatrix}. \quad (6.2)$$

Which at  $P_0$  is

$$J(P_0) = \begin{bmatrix} \alpha - \gamma - \xi_{100} - \psi_{128} & 0 & 0 \\ v & -k - \tau_{128} & 0 \\ \sigma D & -\rho D & -\omega - \zeta_{128} \end{bmatrix}. \quad (6.3)$$

Hence the characteristic polynomial

$$|J - \lambda I| = \begin{vmatrix} \alpha - \gamma - \xi_{100} - \psi_{128} - \lambda & 0 & 0 \\ v & -k - \tau_{128} - \lambda & 0 \\ \sigma D & -\rho D & -\omega - \zeta_{128} - \lambda \end{vmatrix}. \quad (6.4)$$

Expanding the determinant by the first row, we derive the characteristic equation

$$-(\alpha + \gamma + \xi_{100} + \psi_{128} + \lambda)(k + \tau_{128} + \lambda)(\omega + \zeta_{128} + \lambda) = 0 \quad (6.5)$$

or

$$\lambda^3 + \beta_1 \lambda^2 + \beta_2 \lambda + \beta_3 = 0. \quad (6.6)$$

where

$$\beta_1 = \tau_{128} + k + \zeta_{128} + \omega + \psi_{128} + \xi_{100} + \gamma + \alpha.$$

$$\beta_2 = \alpha\omega + \alpha\zeta_{128} + \alpha k + \alpha\tau_{128} + \gamma\omega + \gamma\zeta_{128} + \gamma k + \gamma\tau_{128} + \xi_{100}\omega + \xi_{100}\zeta_{128} + \xi_{100}k + \xi_{100}\tau_{128} \\ + \psi_{128}\omega + \psi_{128}\zeta_{128} + \psi_{128}k + \psi_{128}\tau_{128} + k\omega + \tau_{128}\omega + k\zeta_{128} + \tau_{128}\zeta_{128}.$$

$$\beta_3 = \alpha k\omega + \alpha\tau_{128}\omega + \alpha k\zeta_{128} + \alpha\tau_{128}\zeta_{128} + \gamma k\omega + \gamma\tau_{128}\omega + \gamma k\zeta_{128} + \gamma\tau_{128}\zeta_{128} + \xi_{100}k\omega + \xi_{100}\tau_{128}\omega + \\ \xi_{100}k\zeta_{128} + \xi_{100}\tau_{128}\zeta_{128} + \psi_{128}k\omega + \psi_{128}\tau_{128}\omega + \psi_{128}k\zeta_{128} + \psi_{128}\tau_{128}\zeta_{128}.$$

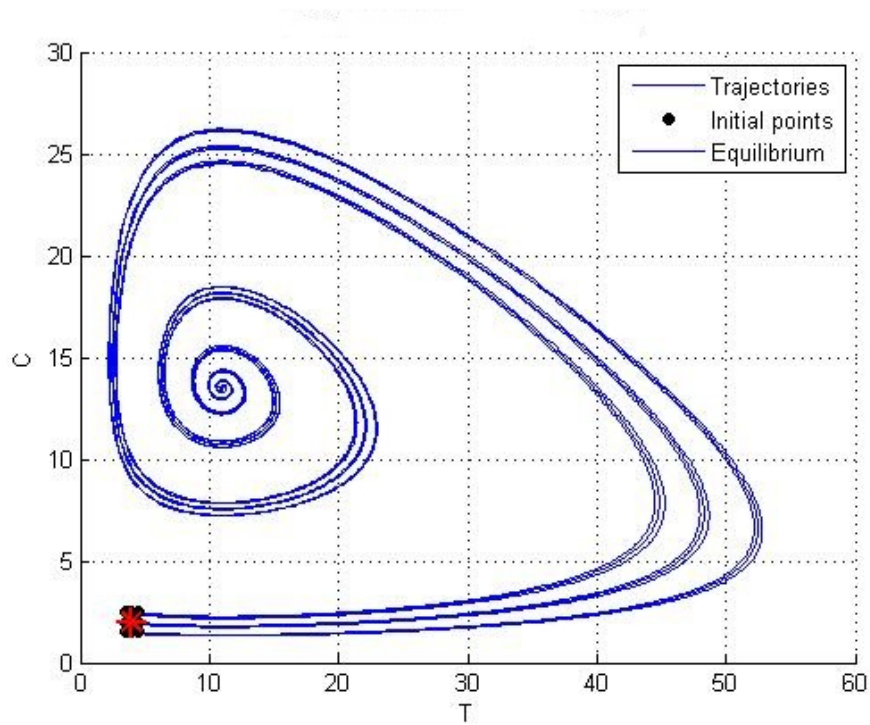
So if  $\beta_1 > 0$ ,  $\beta_2 > 0$  and  $\beta_1\beta_2 - \beta_3 > 0$ , then by Routh-Hurwitz method, the equilibrium point

$$P_0 = \left(0, 0, \frac{\mu}{\omega + \zeta_{128}}\right)$$

is asymptotically stable.

In figure 1 we observe the stability of the point  $P_0$  during the normal growth of the dendritic cells  $D$ .

**Mathematical and Biological Interpretation at  $P_0$ :** If  $P_0$  stable, mathematically must the cells  $\mu$  grow at a normal rate; any abnormal proliferation or increase in their number indicates the beginning of tumor cell growth, so at this stable point, any minor disruption (a few remaining tumor cells following surgery) will eventually disappear on its own, signifying a superior clinical result: permanent remission or clinical remission.

FIGURE 1. A simulation model of  $P_0$  without  $T$  cells and  $C$  cells.

6.1.2. *Immune-deficient (CD8+ $T$ -free) equilibrium.* Here CD8 +  $T$ -free equilibrium point will be  $P_1 = (T_1, 0, D_1)$ , where  $T_1 = \frac{\alpha - \gamma - \xi_{100} - \psi_{128}}{\alpha\beta}$ ,  $D_1 = \frac{\mu}{\omega - \sigma T_1 + \zeta_{128}}$ , which will be positive if  $\alpha - \gamma > \xi_{100} + \psi_{128}$ , and  $\omega > \sigma T_1 - \zeta_{128}$ .

The Jacobian at  $P_1$  is

$$J(P_1) = \begin{bmatrix} \alpha - 2\alpha\beta T_1 - \gamma - \xi_{100} - \psi_{128} & -\phi T_1 & 0 \\ v & -\eta T_1 - k - \tau_{128} & 0 \\ \sigma D_1 & -\rho D_1 & \sigma T_1 - \omega - \zeta_{128} \end{bmatrix} \quad (6.7)$$

and the characteristic equation is

$$(\gamma - \alpha + 2\alpha\beta T_1 + \xi_{100} + \psi_{128} + \lambda)(\eta T_1 + k + \tau_{128} + \lambda)(\omega + \zeta_{128} - \sigma T_1 + \lambda) - (\phi T_1)(v)(\omega + \zeta_{128} - \sigma T_1 + \lambda) = 0 \quad (6.8)$$

or

$$\lambda^3 + \beta_1 \lambda^2 + \beta_2 \lambda + \beta_3 = 0. \quad (6.9)$$

Where

$$\beta_1 = (\gamma - \alpha) + \omega + \zeta_{128} + \eta T_1 + k + \tau_{128} + 2\alpha\beta T_1 + \xi_{100} + \psi_{128} - \sigma T_1.$$

$$\beta_2 = (\gamma - \alpha)(\omega + \zeta_{128} + \eta T_1 + k + \tau_{128} - \sigma T_1) + (\omega + \zeta_{128})\eta T_1 + (\omega + \zeta_{128})k + (\omega + \zeta_{128})\tau_{128} +$$

$$\begin{aligned}
& (\omega + \zeta_{128})2\alpha\beta T_1 + (\omega + \zeta_{128})\xi_{100} + (\omega + \zeta_{128})\psi_{128} + 2\alpha\beta T_1^2\eta + \xi_{100}\eta T_1 + \psi_{128}\eta T_1 + 2k\alpha\beta T_1 \\
& + k\xi_{100} + k\psi_{128} + 2\alpha\beta\tau_{128}T_1 + \xi_{100}\tau_{128} + \psi_{128}\tau_{128} - (\sigma\eta T_1^2 + k\sigma T_1 + \tau_{128}\sigma T_1 + 2\sigma\alpha\beta T_1^2 + \xi_{100}\sigma T_1 \\
& + \psi_{128}\sigma T_1 + \phi T_1 v).
\end{aligned}$$

$$\begin{aligned}
\beta_3 = & (\gamma - \alpha)[(\omega + \zeta_{128})\eta T_1 + (\omega + \zeta_{128})k + (\omega + \zeta_{128})\tau_{128} - (\eta\sigma T_1^2 + k\sigma T_1 + \tau_{128}\sigma T_1)] \\
& + 2\alpha\beta\zeta_{128}T_1^2\eta + \zeta_{128}\xi_{100}\eta T_1 + \zeta_{128}\psi_{128}\eta T_1 + 2k\alpha\beta\zeta_{128}T_1 + k\zeta_{128}\xi_{100} + k\zeta_{128}\psi_{128} + 2\alpha\beta\zeta_{128}\tau_{128}T_1 \\
& + \zeta_{128}\xi_{100}\tau_{128} + \zeta_{128}\psi_{128}\tau_{128} + 2\omega\alpha\beta T_1^2\eta + \omega\xi_{100}\eta T_1 + \omega\psi_{128}\eta T_1 + 2\omega k\alpha\beta T_1 + k\xi_{100}\omega + \\
& \omega k\psi_{128} + 2\omega\alpha\beta\tau_{128}T_1 + \omega\xi_{100}\tau_{128} + \omega\psi_{128}\tau_{128} + \sigma\phi T_1^2 v - (2\alpha\beta\sigma T_1^3\eta + \xi_{100}\sigma\eta T_1^2 + \psi_{128}\sigma\eta T_1^2 + \\
& 2k\alpha\beta\sigma T_1^2 + k\xi_{100}\sigma T_1 + k\psi_{128}\sigma T_1 + 2\alpha\beta\sigma\tau_{128}T_1^2 + \xi_{100}\tau_{128}\sigma T_1 + \psi_{128}\tau_{128}\sigma T_1 + \omega\phi T_1 v + \\
& \zeta_{128}\phi T_1 v).
\end{aligned}$$

According to the Routh-Hurwitz stability criterion, the equilibrium point

$$P_1 = \left( \frac{\alpha - \gamma - \xi_{100} - \psi_{128}}{\alpha\beta}, 0, \frac{\mu}{\omega - \sigma T + \zeta_{128}} \right)$$

is asymptotically stable.

In figure 2 we observe the stabilization of the point  $P_1$  through the activation of dendritic cells  $C$  to limit cell growth  $T$ .

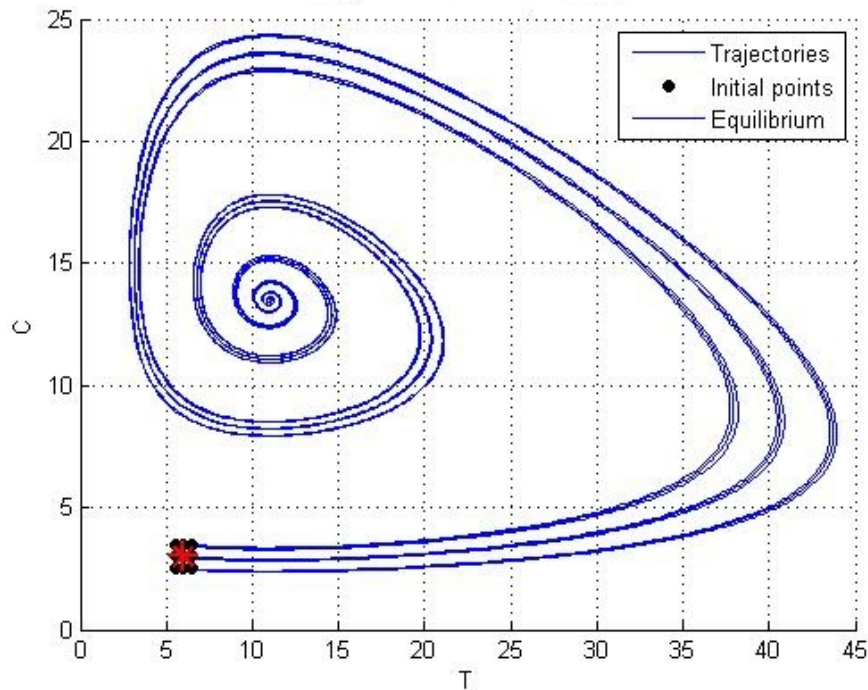


FIGURE 2. A simulation model of  $P_1$  without  $C$  cells.

**Mathematical and Biological Interpretation at  $P_1$ :** If  $P_1$  is stable then, mathematically must  $\alpha < \gamma + \xi_{100} + \psi_{128}$  and  $\sigma T > \omega + \zeta_{128}$  so that we can achieve stability. Biological the tumor remains at a positive level while immune cells  $C$  is zero (or very low). If stable: This represents immune relapse/failure – even if a large portion of the tumor is removed with surgery, the immune system is not activated enough to control the remnants, and the tumor will be an ongoing problem. Clinical indications: Stabilization in this case can be achieved by boosting the patient's immunity through (immunotherapy) or chemical modification that reduces the toxicity of the treatment on immune cells (reduce  $\psi_{128}$ ,  $\tau_{128}$ , Or reduce immune exhaustion  $\eta$ ).

6.1.3. *Endemic (coexistence) equilibrium.* There is an equilibrium point  $P = (T, C, D)$  with  $C > 0$ , namely

$$T = \frac{\alpha - \gamma - \phi C - \xi_{100} - \psi_{128}}{\alpha\beta}, C = \frac{vT}{\eta T + k + \tau_{128}} \text{ and } D = \frac{\mu}{\rho C - \sigma T + \omega + \zeta_{128}}.$$

By substitution  $C$  in  $T$  above, we have

$$\alpha\beta\eta T^2 + [\gamma\eta - \alpha\beta k - \alpha\beta\tau_{128} - \alpha\eta + \phi v - \psi_{128}\eta + \xi_{100}\eta]T + \alpha k + \alpha\tau_{128} - \gamma k - \gamma\tau_{128} + k\psi_{128} + \psi_{128}\tau_{128} - k\xi_{100} - \tau_{128}\xi_{100} = 0.$$

Then

$$xT^2 + yT + z = 0$$

where

$$x = \alpha\beta\eta$$

$$y = \gamma\eta - \alpha\beta k - \alpha\beta\tau_{128} - \alpha\eta + \phi v - \psi_{128}\eta + \xi_{100}\eta$$

$$z = \alpha k + \alpha\tau_{128} - \gamma k - \gamma\tau_{128} + k\psi_{128} + \psi_{128}\tau_{128} - k\xi_{100} - \tau_{128}\xi_{100}.$$

So we have

$$T^* = \frac{-y \pm \sqrt{(y^2 - 4xz)}}{2x}$$

$$C^* = \frac{vT^*}{\eta T^* - k - \tau_{128}}$$

$$D^* = \frac{\mu}{\rho C^* - \sigma T^* + \omega + \zeta_{128}}$$

hence endemic equilibrium point is

$$P^* = (T^*, C^*, D^*) = \left( T^*, \frac{vT^*}{\eta T^* - k - \tau_{128}}, \frac{\mu}{\rho C^* - \sigma T^* + \omega + \zeta_{128}} \right)$$

where  $T^*, C^*, D^*$  are positives under conditions  $\frac{\sqrt{y^2 - 4xz}}{2x} > \frac{y}{2x}$ ,  $\eta T^* > k + \tau_{128}$ ,  $\rho C^* > \sigma T^* - \omega - \zeta_{128}$ , respectively.

The Jacobian matrix at  $P^*$  is

$$J(p^*) = \begin{bmatrix} \alpha - 2\alpha\beta T^* - \gamma - \phi C^* - \xi_{100} - \psi_{128} & -\phi T^* & 0 \\ v - \eta C^* & -\eta T^* - k - \tau_{128} & 0 \\ \sigma D^* & -\rho D^* & \sigma T^* - \rho C^* - \omega - \zeta_{128} \end{bmatrix}. \quad (6.10)$$

And hence the characteristic equation is

$$(\gamma - \alpha + 2\alpha\beta T^* + \phi C^* + \xi_{100} + \psi_{128} + \lambda)(\eta T^* + k + \tau_{128} + \lambda)(\rho C^* + \omega + \zeta_{128} - \sigma T^* + \lambda) - (\phi T^*)(v - \eta C^*)(\rho C^* + \omega + \zeta_{128} - \sigma T^* + \lambda) = 0 \quad (6.11)$$

or

$$\lambda^3 + \beta_1 \lambda^2 + \beta_2 \lambda + \beta_3 = 0. \quad (6.12)$$

where

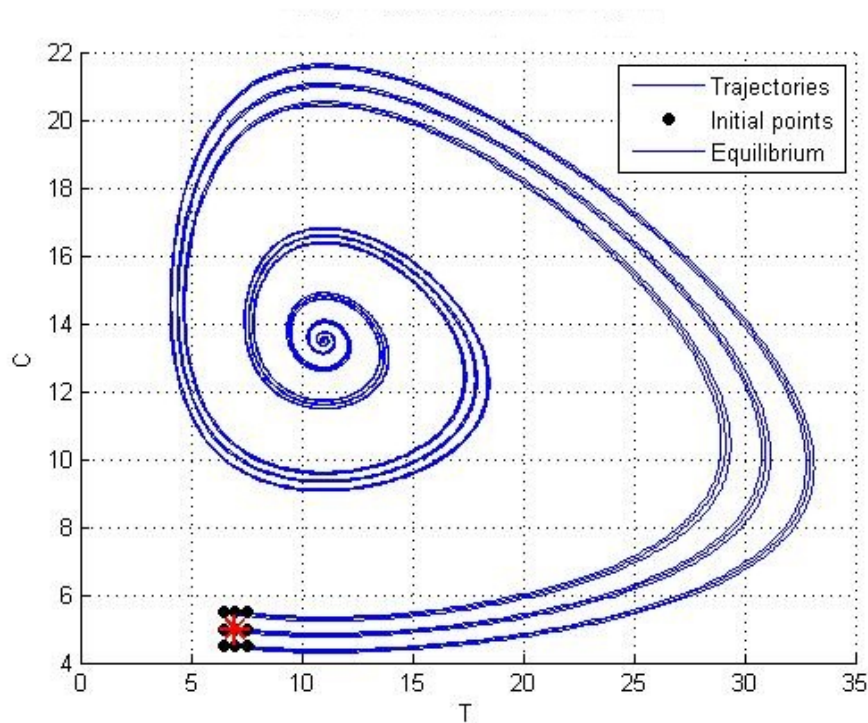
$$\beta_1 = (\gamma - \alpha) + 2\alpha\beta T^* + \phi C^* + \xi_{100} + \psi_{128} + \tau_{128} + k + \eta T^* + \rho C^* + \omega + \zeta_{128} - \sigma T^*.$$

$$\begin{aligned} \beta_2 = & (\gamma - \alpha)[\eta T^* + k + \tau_{128} + \rho C^* + \omega + \zeta_{128} - \sigma T^*] + 2\alpha\beta\eta T^{*2} + \eta\phi C^* T^* + \eta\xi_{100} T^* + \\ & \psi_{128}\eta T^* + 2\alpha\beta k T^* + \phi k C^* + k\xi_{100} + k\psi_{128} + 2\alpha\beta\tau_{128} T^* + \phi\tau_{128} C^* + \tau_{128}\xi_{100} + \\ & \psi_{128}\tau_{128} + \phi v T^* + 2\alpha\beta\rho T^* C^* + \rho\phi C^{*2} + \rho\xi_{100} C^* + \rho\psi_{128} C^* + \rho\tau_{128} C^* + \\ & \rho k C^* + \rho\eta C^* T^* + 2\alpha\beta\omega T^* + \omega\phi C^* + \omega\xi_{100} + \omega\phi_{128} + \tau_{128}\omega + k\omega + \eta\omega T^* + \\ & 2\alpha\beta\zeta_{128} T^* + \phi\zeta_{128} C^* + \xi_{100}\zeta_{128} + \psi_{128}\zeta_{128} + \tau_{128}\zeta_{128} + k\zeta_{128} + \eta\zeta_{128} T^* - \\ & (2\alpha\beta\sigma T^{*2} + \phi\sigma T^* C^* + \xi_{100}\sigma T^* + \psi_{128}\sigma T^* + \tau_{128}\sigma T^* + k\sigma T^* + \eta\sigma T^{*2}) - (\eta\phi T^* C^*). \end{aligned}$$

$$\begin{aligned} \beta_3 = & (\gamma - \alpha)(\eta T^* + k + \tau_{128} + \rho\eta C^* T^* + k\rho C^* + \tau_{128}\rho C^* + \eta\omega T^* + k\omega + \tau_{128}\omega + \eta\zeta_{128} T^* + k\zeta_{128} + \\ & \tau_{128}\zeta_{128} - k\sigma T^* - \tau\sigma T^* - \eta\sigma T^{*2}) + 2\alpha\beta\eta T^{*2} + \eta\phi C^* T^* + 2\alpha\beta\tau_{128} T^* + \phi\tau_{128} C^* + \tau_{128}\xi_{100} + \psi_{128}\tau_{128} + \\ & \phi v T^* + 2\alpha\beta\eta\rho C^* T^{*2} + \eta\phi\rho C^{*2} T^* + \eta\rho\xi_{100} C^{*2} T^* + \psi_{128}\eta\rho C^* T^* + 2\alpha\beta k\rho C^* T^* + \phi k\rho C^{*2} + k\xi_{100}\rho C^* + \\ & k\rho\psi_{128} C^* + 2\alpha\beta\tau_{128}\rho C^* T^* + \phi\tau_{128}\rho C^{*2} + \tau_{128}\xi_{100}\rho C^* + \tau_{128}\psi_{128}\rho C^* + \phi v\rho C^* T^* + 2\alpha\beta\eta\omega T^{*2} + \\ & \eta\phi\omega C^* T^* + \eta\omega\xi_{100} T^* + \omega\psi_{128}\eta T^* + 2\alpha\beta k\omega T^* + \phi k\omega C^* + k\omega\xi_{100} + \omega k\psi_{128} + 2\alpha\beta\tau_{128}\omega T^* + \\ & \phi\tau_{128}\omega C^* + \tau_{128}\xi_{100}\omega + \tau_{128}\psi_{128}\omega + \omega\phi v T^* + 2\alpha\beta\eta\zeta_{128} T^{*2} + \eta\phi\zeta_{128} C^* T^* + \eta\zeta_{128} T^* + \psi_{128}\eta\zeta_{128} T^* + \\ & 2\alpha\beta k\zeta_{128} T^* + \phi k\zeta_{128} C^* + k\xi_{100}\zeta_{128} + k\psi_{128}\zeta_{128} + 2\alpha\beta\tau_{128}\zeta_{128} T^* + \phi\tau_{128}\zeta_{128} C^* + \tau_{128}\xi_{100}\zeta_{128} + \\ & \psi_{128}\tau_{128}\zeta_{128} + \phi v\zeta_{128} T^* - \eta\phi T^*(\zeta_{128} C^* + \sigma T^* C^* + C^* + \rho C^{*2} + \omega C^*) - (2\alpha\beta\eta T^{*3} + \eta\sigma\phi C^* T^{*2} + \\ & \eta\xi_{100}\sigma T^{*2} + \psi_{128}\eta\sigma T^{*2} + 2\alpha\beta k\sigma T^{*2} + \phi k\sigma C^* T^* + k\sigma\xi_{100} T^* + k\sigma\psi_{128} T^* + 2\alpha\beta\tau_{128}\sigma T^{*2} + \phi\sigma\tau_{128} C^* T^* + \\ & \tau_{128}\sigma\xi_{100} T^* + \psi_{128}\tau_{128}\sigma T^* + \phi v\sigma T^{*2} - \eta\phi\sigma T^{*2} C^*). \end{aligned}$$

Thus  $\beta_1 > 0$ ,  $\beta_2 > 0$ , and  $\beta_1\beta_2 - \beta_3 > 0$ . From the principle of Routh-Hurwitz stability criterion, the equilibrium point  $P^* = (T^*, C^*, D^*) = \left(T^*, \frac{vT^*}{\eta T^* - k - \tau_{128}}, \frac{\mu}{\rho C^* - \sigma T^* + \omega + \zeta_{128}}\right)$  is asymptotically stable.

In figure 3 we observe that the immune system, with the presence of  $C$  and  $D$  cells, limits the spread of the tumor  $T$  cells.

FIGURE 3. A simulation model of endemic point  $P^*$ .

**Mathematical and Biological Interpretation at  $P^*$ :** To be  $P^*$  stable, mathematically must  $\phi v - \alpha\eta > 0$  and  $\alpha - \gamma < 0$  in  $T^*$ , to control tumor growth. Biologically the tumor is present, but the immune system is limiting its growth; a state of partial control. At this stage, the condition becomes chronic but controlled—the tumor does not disappear, but it does not increase. Clinical management involves "active surveillance" and interventions to lower  $T$  and (increase  $\phi$  improving immune efficacy, or decrease  $\alpha$ —inhibiting cell growth, or increase  $\beta$ —reducing amplitude). This is how the patient is considered to be in a state of "controlled disease." Thus, requiring ongoing monitoring and immune-therapy, as well as the addition of chemotherapy doses at specific intervals to keep the tumor under control.

## 7. ILLUSTRATION AND DISCUSSION

The simulations are not intended for prediction or optimization, but rather to demonstrate consistency between the theoretical stability analysis and the qualitative behavior of the system. Figure 3 depicts the time evolution of tumor cells  $T(t)$ ,  $CD8 + T$  lymphocytes  $C(t)$ , and dendritic cells  $D(t)$  under post-treatment conditions. Starting from biologically feasible initial conditions, all state variables converge toward the endemic equilibrium  $P^*$ . This behavior confirms the local asymptotic stability derived analytically and illustrates a controlled disease state in which immune activity suppresses tumor growth without complete eradication. The phase-plane trajectories shown in Figure 1 provide further insight into the dynamical structure of the model.

Trajectories originating from different initial tumor and immune levels converge toward the same equilibrium point, indicating that the stability of the post-treatment equilibrium is robust with respect to variations in initial conditions with case of tumor disappearance. Figure 2 illustrates the sensitivity of long-term tumor burden to chemotherapy-induced tumor killing and immune toxicity parameters. Increasing the tumor cell killing rate reduces the steady-state tumor level, whereas elevated immune toxicity weakens tumor control with the absence of  $CD8 + T$  cells. Overall, the illustrations are fully consistent with the analytical results and reinforce the biological interpretation of post-treatment stability regimes corresponding to remission, immune failure, and controlled chronic disease.

### CONCLUSION

In this work, we examined a mathematical model that mimics the course of non-small-cell lung cancer (NSCLC) following chemotherapy and surgery where it was added various treatment initiation dates, during which three chemotherapy dosages and surgery were employed as the therapeutic approach. The aim of our study is to find the stability of the system (4.1) where we found three equilibrium points, and we tested their stability using Routh Hurwitz Criteria. We analyzed the effect of stability points and we studied its effects mathematically and biologically, and we concluded that,  $P_0$  is stable, mathematically must the cells  $\mu$  grow at a normal rate,  $P_1$  is stable under conditions  $\alpha < \gamma + \xi_{100} + \psi_{128}$  and  $\sigma T > \omega + \zeta_{128}$  so that we can achieve stability.  $T^*$  is stable, mathematically must  $\phi v - \alpha \eta > 0$  and  $\alpha - \gamma < 0$ , to control tumor growth. Biologically found that caution is advised when using immunosuppressive chemotherapy: if analysis indicates that  $\tau_{128}$  or  $\psi_{128}$  shifts the regimen from  $P_0$  to  $P_1$ , adjusting doses or their timing (e.g., delaying/splitting doses) or adding immunomodulatory support (G-CSF or targeted immunotherapy) should be considered. It's also important to remember that immune enhancement can reverse the equation: raising  $\phi$  or  $v$  (using immunotherapies such as checkpoint inhibitors or personalized cancer vaccines) may shift the balance to  $P_0$ . Dynamic monitoring: using repeated tests of immune and tumor markers to identify any shift to balance early and intervene quickly. Personalized treatment can be designed, as the model allows for simulating the "what if we increase/decrease" of any parameter—use it to tailor doses to each patient based on their initial parameters. From here we find the importance of finding the stability of mathematical systems that simulate cancer diseases with added the treatment plan, and its direct impact on the stability of the patient's life in terms of determining the time period for starting treatment and using appropriate doses for a period determined by the therapist that is compatible with the patient's clinical condition in order to reduce the chance of losing his life.

**Conflicts of Interest:** The authors declare that there are no conflicts of interest regarding the publication of this paper.

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