

Article

# Chaos Control in Three Dimensional Cancer Model by State Space Exact Linearization Based on Lie Algebra

Mohammad Shahzad

Nizwa College of Applied Sciences, Ministry of Higher Education, Nizwa 611, Oman; dmsinfinite@gmail.com; Tel.: +968-99584197

Academic Editor: J. Alberto Conejero

Received: 23 December 2015; Accepted: 4 May 2016; Published: 10 May 2016

**Abstract:** This study deals with the control of chaotic dynamics of tumor cells, healthy host cells, and effector immune cells in a chaotic Three Dimensional Cancer Model (TDCM) by State Space Exact Linearization (SSEL) technique based on Lie algebra. A non-linear feedback control law is designed which induces a coordinate transformation thereby changing the original chaotic TDCM system into a controlled one linear system. Numerical simulation has been carried using *Mathematica* that witness the robustness of the technique implemented on the chosen chaotic system.

**Keywords:** SSEL; Lie bracket; Lie derivative; nonlinear feedback; TDCM

## 1. Introduction

Cancer pertains to a class of diseases characterized by out-of-control cell growth. Unsatisfactory performance of immune system against cancerous abnormal cells and consequently their chaotic growth leads to serious health damages and even death. So this chaotic nature of cancer needs to be controlled. The chaotic dynamics of cancer growth have been extensively studied in the literature to understand the mechanism of the disease and to predict its future behavior. Interactions of cancer cells with healthy host cells and immune system cells are the main components of these models and these interactions may yield different outcomes. Some important phenomena of cancer progression such as cancer dormancy, creeping through, and escape from immune surveillance have been investigated [1]. De Pillis and Radunskaya [2] included a normal tissue cell population in this model, performed phase space analysis, and investigated the effect of chemotherapy treatment by using optimal control theory whereas Kirschner and Panetta [3] examined the cancer cell growth in the presence of the effector immune cells and the cytokine IL-2 which has an essential role in the activation and stimulation of the immune system. They implied that antigenicity of the cancer cells plays an essential role in the recognition of cancer cells by the immune system. They observed oscillations in the cancer cell populations which is also demonstrated in the Kuznetsov's model and in addition, they obtained a stable limit cycle for some parameter range of the antigenicity. One can find many other models of the cancer-immune interactions with their dynamical analysis as well as investigations of optimal therapy effects. Although all these models include different cell populations, they share basic common characteristics such as existence of cancer free equilibria which is the main attention of investigating the therapy effects, coexisting equilibria where cancer and other cells are present in the body and in competition, and finally cancer escape and uncontrolled growth [4]. It has been observed that most of the interesting dynamics occur around coexisting equilibria which may yield oscillations in the cell populations, and converge to a stable limit cycle, as we mentioned before.

During the last decade, a lot of work based on different approaches has been done to control the chaos through the mathematical model representing cancer dynamics. Gohary and Alwasel [5] have

studied the chaos and optimal control of cancer model with completely unknown parameters together with the asymptotic stability analysis of biologically feasible steady-states whereas Gohary [6] studied the problem of optimal control of cancer self-remission and cancer unstable steady-states together with the stability analysis of biologically feasible equilibrium states using a local stability approach. Baghernia *et al.* [7] considered the nonlinear prey-predator model to show the natural interaction between cancer and immune cells. Furthermore, a controlling strategy is proposed based on sliding mode control to convert the unstable states to the desired chaotic status.

Motivated by the aforementioned studies, the author aims to control the chaotic dynamics of TDCM using SSEL technique based on Lie algebra. The main advantages of this approach are that it is not only robust but also in this approach the control is injected only on healthy host cells (*i.e.*,  $H(t)$ ) and effect of control can be seen on the rest of state variables (*i.e.*,  $T(t)$  &  $E(t)$ ).

Rest of the study has been organized as follows: In Section 2, a brief about the methodology has been described whereas Section 3 is on problem formulation. Section 4, contains the implementations of the technique on the considered system (TDCM). Section 5, is based on numerical simulations and lastly the whole study has been concluded in Section 6.

## 2. State Space Exact Linearization

It is a technique of controlling a chaotic system that involves transformation of a given non-linear system into a linear system by injecting a suitable control input [8]. Let us consider a non-linear dynamical system as:

$$\dot{x} = f(x) \tag{1}$$

After injecting control term it can be written as:

$$\dot{x} = f(x) = g(x)u(x) \tag{2}$$

where  $x \in \mathbb{R}^n$ , is the state vector; and  $u \in \mathbb{R}$ , is the control parameter,  $f : \mathbb{R}^n \rightarrow \mathbb{R}^n$  and  $g : \mathbb{R}^n \rightarrow \mathbb{R}^n$  are both smooth vector fields on  $\mathbb{R}^n$  and Equation (2) is called feedback linearizable in the domain  $\Omega \in \mathbb{R}^n$  if there exists a smooth reversible change of coordinates  $z \in T(x)$ ,  $x \in \Omega$  and a smooth transformation feedback  $v = \alpha(x) + \beta(x)u$ ,  $x \in \Omega$ , where  $v \in \mathbb{R}$  is the new control if the closed loop system is linear [9].

For two vector fields,  $f(x)$  and  $g(x)$ , the different order Lie brackets are denoted by the symbols as follows:

$ad_f^k g(x) = [f, ad_f^{k-1}g](x)$  for  $k = 1, 2, 3, \dots$  with  $ad_f^0 g(x) = g(x)$ , and each of  $ad_f^k g(x) \in \mathbb{R}^n$  for  $k = 1, 2, 3, \dots$ . If we write  $ad_f^k g(x) = \left[ \begin{matrix} (ad_f^k g(x))_1 & (ad_f^k g(x))_2 & \dots & (ad_f^k g(x))_n \end{matrix} \right]^T$ ; then  $(ad_f^k g(x))_j$  is computed by the formula:

$$(ad_f^k g(x))_j = \sum_{i=1}^n \left[ f_i \frac{\partial}{\partial x_i} (ad_f^{k-1} g(x))_j - (ad_f^{k-1} g(x))_i \frac{\partial}{\partial x_i} f_j \right]$$

In some neighborhood  $N(x_0)$  of a point  $x_0$ , if the matrix,

$$M = \left[ \begin{matrix} g(x_0) & ad_f g(x_0) & ad_f^2 g(x_0) \dots & ad_f^{n-1} g(x_0) \end{matrix} \right]$$

has a rank  $n$  and  $S = \text{span} \{g, ad_f g, ad_f^2 g, \dots, ad_f^{n-2} g\}$  is involutive, then there exists a real valued function  $\lambda(x) \in N(x_0)$ , such that:

$L_g \lambda(x) = L_{ad_f g} \lambda(x) = L_{ad_f^2 g} \lambda(x) = \dots = L_{ad_f^{n-2} g} \lambda(x) = 0$ , and  $L_{ad_f^{n-1} g} \lambda(x) \neq 0$  where  $L_F \lambda(x)$  denotes the Lie derivative of the real valued function  $\lambda(x)$  with respect to the vector field  $F$ . If that happens there exists transformation in  $N(x_0)$ , given by:

$$\begin{aligned}
 z &= \begin{bmatrix} z_1 & z_2 & z_3 & \dots & z_n \end{bmatrix}^T = T(x) \\
 &= \begin{bmatrix} T_1(x) & T_2(x) & \dots & T_n(x) \end{bmatrix}^T \\
 &= \begin{bmatrix} \lambda(x) & L_f \lambda(x) & \dots & L_f^{n-1} \lambda(x) \end{bmatrix}^T
 \end{aligned}
 \tag{3}$$

and  $v = L_f^n \lambda(x) + L_g L_f^{n-1} \lambda(x) u$  that transforms the non-linear system into the linear controllable system [10–14]:

$$\begin{aligned}
 \dot{z}_1 &= z_2 \\
 \dot{z}_2 &= z_3 \\
 \dot{z}_{n-1} &= z_n \\
 \dot{z}_n &= v
 \end{aligned}
 \tag{4}$$

### 3. Problem Formulation

The simplicity and elusiveness of the TDCM in its various forms have attracted the attention of mathematicians for decades. The equations of motion of TDCM [1] are given by:

$$\begin{aligned}
 \frac{dT}{dt} &= r_1 T \left(1 - \frac{T}{k_1}\right) - a_{12} TH - a_{13} TE \\
 \frac{dH}{dt} &= r_2 H \left(1 - \frac{H}{k_2}\right) - a_{21} TH \\
 \frac{dE}{dt} &= \frac{r_3 TE}{T+k_3} - a_{31} TE - d_3 E
 \end{aligned}
 \tag{5}$$

where  $T(t)$  denotes the number of cancer cells;  $H(t)$  denotes the healthy host cells and  $E(t)$  denotes effector immune cells at the time  $t$ ;  $r_1$  is the growth rate of cancer cells in the absence of any effect from other cell populations with maximum carrying capacity  $k_1$ ,  $a_{12}$ , and  $a_{13}$  refers to the cancer cells killing rate by the healthy host cells and effector cells respectively;  $r_2$  is the growth rate of healthy host cells with maximum carrying capacity  $k_2$ ;  $a_{21}$  is the rate of inactivation of the healthy cells by cancer cells. The rate of recognition of the cancer cells by the immune system depends on the antigenicity of the cancer cells. Since this recognition process is very complex, in order to keep the model simple, assume the stimulation of the immune system depends directly on the number of cancer cells with positive constants  $r_3$  and  $k_3$ . The effector cells are inactivated by the cancer cells at the rate  $a_{31}$  as well as they die naturally at the rate  $d_3$ . We assume that the cancer cells proliferate faster than the healthy cells (*i.e.*,  $r_1 > r_2$ ) and all system parameters are being kept positive.

In order to make Equation (5) dimensionless, let us introduce:  $x_1 = \frac{T}{k_1}$ ,  $x_2 = \frac{H}{k_2}$ ,  $x_3 = \frac{E}{k_3}$ ,  $\tau = r_1 t$ ,  $A_{12} = \frac{a_{12} k_2}{r_1}$ ,  $A_{13} = \frac{a_{13} k_3}{r_1}$ ,  $R_2 = \frac{r_2}{r_1}$ ,  $A_{21} = \frac{a_{21} k_1}{r_1}$ ,  $R_3 = \frac{r_3}{r_1}$ ,  $K_3 = \frac{k_3}{k_1}$ ,  $A_{31} = \frac{a_{31} k_1}{r_1}$ ,  $D_3 = \frac{d_3}{r_1}$ , the non-dimensional form of the TDCM Equation (5), can be written as:

$$\text{TDCM : } \begin{cases} \dot{x}_1 = x_1(1 - x_1) - A_{12}x_1x_2 - A_{13}x_1x_3 \\ \dot{x}_2 = R_2x_2(1 - x_2) - A_{21}x_1x_2 \\ \dot{x}_3 = \frac{R_3x_1x_3}{x_1+K_3} - A_{31}x_1x_3 - D_3x_3 \end{cases}
 \tag{6}$$

### 4. Control of the Chaotic System

In order to apply the control technique, the above system of Equation (6) can be written as  $\dot{x} = f(x)$  where,  $x = \begin{bmatrix} x_1 & x_2 & x_3 \end{bmatrix}^T$ , and,

$$f(x) = \begin{bmatrix} x_1(1 - x_1) - A_{12}x_1x_2 - A_{13}x_1x_3 & R_2x_2(1 - x_2) - A_{21}x_1x_2 & \frac{R_3x_1x_3}{x_1+K_3} - A_{31}x_1x_3 - D_3x_3 \end{bmatrix}^T$$

Parametric entrainment control  $u(x_1, x_2, x_3)$  is applied to the parameter  $R_2$  in the second equation of the Equation (6) and one gets,

$$\dot{x} = f(x) + g(x)u \tag{7}$$

where  $g(x) = \begin{bmatrix} 0 & x_2 & 0 \end{bmatrix}^T$  and  $u \in \mathbb{R}$ .

Using Equations (6) and (7), and using Lie bracket,

$$ad_f g(x) = \begin{bmatrix} A_{12}x_1x_2 & 2R_2x_2^2 & 0 \end{bmatrix}^T \tag{8}$$

$$ad_f^2 g(x) = \begin{bmatrix} A_{12}x_1^2x_2 & A_{21}^2x_1x_2^2 + 2R_2x_2^2(R_2 - A_{21}x_1) & -A_{21}x_1x_2 \left\{ \frac{R_3K_3x_3}{(x_1+K_3)^2} - A_{31}x_3 \right\} \end{bmatrix}^T \tag{9}$$

**Lemma 1.** For any  $x_0 \in \mathbb{R}^3 \setminus \text{span}\{(1, 0, 0), (0, 0, 1)\} \cup \text{span}\{(0, 1, 0), (0, 0, 1)\}$ , there exists an open set  $N(x_0)$  containing  $x_0$  where the matrix  $M = \begin{bmatrix} g(x_0) & ad_f g(x_0) & ad_f^2 g(x_0) \end{bmatrix}$  has rank 3 and  $S = \text{span}\{g, ad_f g\}$  is involutive.

**Proof.** Let

$$|M| = \begin{vmatrix} 0 & A_{12}x_1x_2 & A_{12}x_1^2x_2 \\ x_2 & 2R_2x_2^2 & A_{21}^2x_1x_2^2 + 2R_2x_2^2(R_2 - A_{21}x_1) \\ 0 & 0 & -A_{21}x_1x_2 \left\{ \frac{R_3K_3x_3}{(x_1+K_3)^2} - A_{31}x_3 \right\} \end{vmatrix} = A_{12}^2x_1^2x_2^3x_3 \left( \frac{R_3K_3}{(x_1+K_3)^2} - A_{31} \right) \neq 0, \text{ for}$$

non-zero values of state variables involved in  $|M|$ . It is also confirmed by Figure 1.

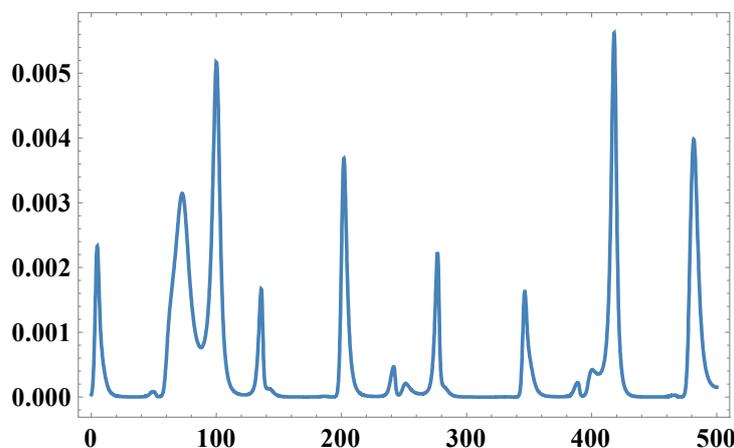


Figure 1. Time series of Det (M).

Therefore  $\rho(M) = 3$  or equal to the order of the system. With the help of Equations (7) and (8) one can show that:

$$\begin{bmatrix} g, ad_f g \end{bmatrix} = \begin{pmatrix} A_{12}x_1x_2 \\ 2R_2x_2^2 \\ 0 \end{pmatrix} = ad_f g(x) \tag{10}$$

which shows that  $\begin{bmatrix} g, ad_f g \end{bmatrix}$  belongs to  $S = \text{span}\{g, ad_f g\}$ . Hence,  $S$  is involutive.

**Lemma 2.** For any thrice differentiable function  $\Psi(x_3)$ , there exists, a smooth transformation  $z = \begin{bmatrix} \Psi & L_f \Psi & L_f^2 \Psi \end{bmatrix}^T$  with a smooth inverse, defined on an open set  $N(x_0)$  where  $x_0 \in \mathbb{R}^3 \setminus \text{span}\{(1, 0, 0), (0, 0, 1)\} \cup \text{span}\{(0, 1, 0), (0, 0, 1)\}$  that reduces Equation (6) to a linear controllable form.

**Proof.** Since Lemma 1 holds, there exists a real valued function  $\lambda(x)$  such that  $L_g\lambda(x) = 0$  and  $L_{ad_f g}\lambda(x) = 0$  but,  $L_{ad_f^2 g}\lambda(x) \neq 0$ . Now,  $L_g\lambda(x) = 0$  implies  $\frac{\partial \lambda}{\partial x_2} = 0$  and  $L_{ad_f g}\lambda(x) = 0$  implies  $\frac{\partial \lambda}{\partial x_1} = 0$ . Hence  $\lambda(x)$  is independent of  $x_1$  and  $x_2$  but depends on  $x_3$ . Thus,

$$\lambda(x) = \Psi(x_3) \tag{11}$$

where simple calculations yield,  $L_{ad_f^2 g}\lambda(x) = -A_{12}x_1x_2x_3 \left\{ \frac{R_3K_3}{(x_1+K_3)^2} - A_{31} \right\} \Psi'(x_3) \neq 0$  as  $x_1, x_2$  &  $x_3 \neq 0$ .

With the help Equation (11) one can easily calculate the following Lie derivatives given as

$$\begin{aligned} L_f\lambda(x) &= x_3 \left( \frac{R_3x_1}{x_1+K_3} - A_{31}x_1 - D_3 \right) \Psi'(x_3) \\ L_f^2\lambda(x) &= x_3A^2\Psi'(x_3) + x_3x_1BC\Psi'(x_3) + x_3^2A^2\Psi''(x_3) \\ L_f^3\lambda(x) &= x_3 \left[ A^3 + 3x_1ABC + x_3A^3 + x_3x_1ABC^2 - \frac{2R_3K_3x_1^2C^2}{(x_1+K_3)^3} \right] \Psi'(x_3) \\ &\quad - x_3x_1B [x_1C + A_{12}R_2x_2(1-x_2) + A_{12}A_{21}x_1x_2 + A_{13}x_3A] \Psi'(x_3) \\ &\quad + x_3^2A [3x_1BC + 2A^2] \Psi''(x_3) + x_3^3A^3\Psi'''(x_3) \\ L_gL_f^2\lambda(x) &= -x_1x_2x_3A_{12}B\Psi'(x_3) \end{aligned} \tag{12}$$

where,  $A = \frac{R_3x_1}{x_1+K_3} - A_{31}x_1 - D_3$ ,  $B = \frac{R_3K_3}{(x_1+K_3)^2} - A_{31}$ ,  $C = 1 - x_1 - A_{12}x_2 - A_{13}x_3$ .

With the help of Equation (12), the transformation Equation (3) takes the form

$$z = \begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} = T(x) = \begin{bmatrix} T_1(x) \\ T_2(x) \\ T_3(x) \end{bmatrix} = \begin{bmatrix} \lambda(x) \\ L_f\lambda(x) \\ L_f^2\lambda(x) \end{bmatrix} = \begin{bmatrix} \Psi(x_3) \\ x_3A\Psi'(x_3) \\ x_3(A^2 + x_1BC)\Psi'(x_3) + x_3^2A^2\Psi''(x_3) \end{bmatrix} \tag{13}$$

Inverse transformation can be calculated from Equation (13) as

$$x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = T^{-1}(z) = \begin{bmatrix} T_1^{-1}(z) \\ T_2^{-1}(z) \\ T_3^{-1}(z) \end{bmatrix} \tag{14}$$

Controller  $u$  is obtained from the Equation (3) as

$$u = \frac{1}{L_gL_f^2\lambda(x)} \left[ v - L_f^3\lambda(x) \right] \tag{15}$$

These will change the TDCM given by Equation (6) into a linear controllable system:

$$\begin{aligned} \dot{z}_1 &= z_2 \\ \dot{z}_2 &= z_3 \\ \dot{z}_3 &= v \end{aligned} \tag{16}$$

where  $v$  is considered linear in  $z_1, z_2$ , and  $z_3$ . Without loss of generality, one may choose the linear form of  $v$  as  $v = a_1z_1 + a_2z_2 + a_3z_3$  where,  $a_1, a_2, a_3 \in \mathbb{R}$ .

**Theorem 1 [8].** (Stabilization at a point): The controller  $v = a_1z_1 + a_2z_2 + a_3z_3$  stabilizes the equilibrium point  $z = (0, 0, 0)$  iff  $a_1, a_2, a_3 < 0$  and  $a_1 + a_2a_3 > 0$ .

**Theorem 2 [8].** (Stabilization onto a limit cycle—Hopf bifurcation): The controller  $v = a_1z_1 + a_2z_2 + a_3z_3$  stabilizes the system on to a stable limit cycle if  $a_1, a_2, a_3 < 0$  and  $a_1 + a_2a_3 > 0$ .

Now, using Equations (12) and (15), the controller  $u$  can be written as:

$$u = \frac{-1}{x_1 x_2 x_3 A_{12} B} \begin{bmatrix} a_1 \Psi(x_3) + (a_2 x_3 A + a_3 x_3 A^2 + a_3 x_3 x_1 BC) \Psi'(x_3) + a_3 x_3^2 A^2 \Psi''(x_3) \\ -x_3 \left[ A^3 + 3x_1 ABC + x_3 x_1 ABC^2 - \frac{2R_3 K_3 x_1^2 C^2}{(x_1 + K_3)^3} \right] \Psi'(x_3) \\ -x_3 x_1 B [x_1 C + A_{12} R_2 x_2 (1 - x_2) + A_{12} A_{21} x_1 x_2 + A_{13} x_3 A] \Psi'(x_3) \\ + x_3^2 A [3x_1 BC + 2A^2] \Psi''(x_3) + x_3^3 A^3 \Psi'''(x_3). \end{bmatrix} \quad (17)$$

Equation (6) with an output function  $\Psi(x_3)$  becomes a controlled one when the control loop is closed with control input given by Equation (17).

Now the problem is studied for the particular forms of  $\Psi(x_3)$ . However, there are many choices for  $\Psi(x_3)$  (i.e., linear, quadratic, etc. in  $x_3$ ). Here we choose only linear because the other forms will give more complicated forms of  $u$  after tedious calculations.

Let, a linear output  $\Psi(x_3) = x_3 - x_g$  will give control law:

$$u = \frac{-1}{x_1 x_2 x_3 A_{12} B} \begin{bmatrix} a_1(x_3 - x_g) + (a_2 x_3 A + a_3 x_3 A^2 + a_3 x_3 x_1 BC) \\ -x_3 \left[ A^3 + 3x_1 ABC + x_3 x_1 ABC^2 - \frac{2R_3 K_3 x_1^2 C^2}{(x_1 + K_3)^3} \right] \\ -x_3 x_1 B [x_1 C + A_{12} R_2 x_2 (1 - x_2) + A_{12} A_{21} x_1 x_2 + A_{13} x_3 A] \end{bmatrix} \quad (18)$$

stabilizes Equation (6) to the control goal  $\vec{x}_{g1} = (18.87 \quad -17.87 + 2.5x_g \quad x_g)^T$  or  $\vec{x}_{g2} = (0.13 \quad 0.87 + 2.5x_g \quad x_g)^T$  where  $x_g$  is the parameter that determines the control goal.

Let  $\Psi(x_3) = x_3 + K$ , where  $K$  is arbitrary constant to be determined later. Controlling Equation (17) to the origin and changing the values of  $K$ , one can control  $x$  to the control goal  $x_g$ . In this case control law takes the form:

$$u = \frac{-1}{x_1 x_2 x_3 A_{12} B} \begin{bmatrix} a_1(x_3 + K) + (a_2 x_3 A + a_3 x_3 A^2 + a_3 x_3 x_1 BC) \\ -x_3 \left[ A^3 + 3x_1 ABC + x_3 x_1 ABC^2 - \frac{2R_3 K_3 x_1^2 C^2}{(x_1 + K_3)^3} \right] \\ -x_3 x_1 B [x_1 C + A_{12} R_2 x_2 (1 - x_2) + A_{12} A_{21} x_1 x_2 + A_{13} x_3 A] \end{bmatrix} \quad (19)$$

for the transformations, from linear to nonlinear and *vice versa*, we have the following relations respectively,

$$\begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} = \begin{bmatrix} x_3 + K \\ x_3 A \\ x_3 A^2 + x_3 x_1 BC \end{bmatrix} \quad (20)$$

Similarly, using reverse transformation, someone can find  $x$  in terms of  $z$ . Below the same has been written using *Mathematica*:

$$\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} -2.5(D \pm E) \\ \frac{2 \left( K - z_1 + z_3 + \frac{z_1^2}{z_1 - K} \right)}{5(z_1 - K)(D \pm E) \left( \frac{18}{25(D \pm E)^2} - \frac{1}{5} \right)} + 2.5(D \pm E - z_1 + K + 0.4) \\ (z_1 - K) \end{bmatrix} \quad (21)$$

where  $D = -3.8 - \frac{z_2}{z_1 - K}$  and  $E = \sqrt{14.04 + \frac{8.4z_2}{K - z_1} + \frac{z_2^2}{(K - z_1)^2}}$ .

Since the feedback control law stabilizes the equilibrium point of Equation (16), then using Equation (21) and changing the value of  $K$ , one can control  $x_3$  to the goal  $x_g$  and the variation of  $K$  is given by the formula:

$$K = -x_g \quad (22)$$

As  $x_3$  goes to the goal  $x_g$ , the state vector  $x$  goes to  $\vec{x}_{g1} = \left( 18.87 \quad -17.87 + 2.5x_g \quad x_g \right)^T$  or  $\vec{x}_{g2} = \left( 0.13 \quad 0.87 + 2.5x_g \quad x_g \right)^T$ .

### 5. Numerical Simulations

The system parameters involved in Equation (6) have been chosen as:  $A_{12} = 1$ ;  $A_{13} = 2.5$ ;  $A_{21} = 1.5$ ;  $R_2 = 0.6$ ;  $A_{31} = 0.2$ ;  $R_3 = 4.5$ ;  $k_3 = 1$ ;  $D_3 = 0.5$  with the initial conditions:  $T(0) = 0.1$ ;  $H(0) = 0.1$ ;  $E(0) = 0.1$ , and for  $K = -1$ ;  $a_1 = -0.1$ ;  $a_2 = -0.9$ ;  $a_3 = -0.6$ , a controller given by Equation (19) is evaluated. Using *Mathematica*, the following different graphs have been plotted to show the robustness as well as effectiveness of the implemented technique. Figures 2 and 3 depict the uncontrolled and controlled time series of the state variables of the system Equation (6), respectively whereas the phase plots (a graph between state vector & its derivative) of three state vectors are shown in Figures 4–6 for controlled and uncontrolled one, respectively. Someone can observe that chaotic attractors are being replaced by regular ones as the controller is injected. Comparative parametric plots of controlled and uncontrolled state vectors pairwise and 3D have been sketched (Figures 7–11).

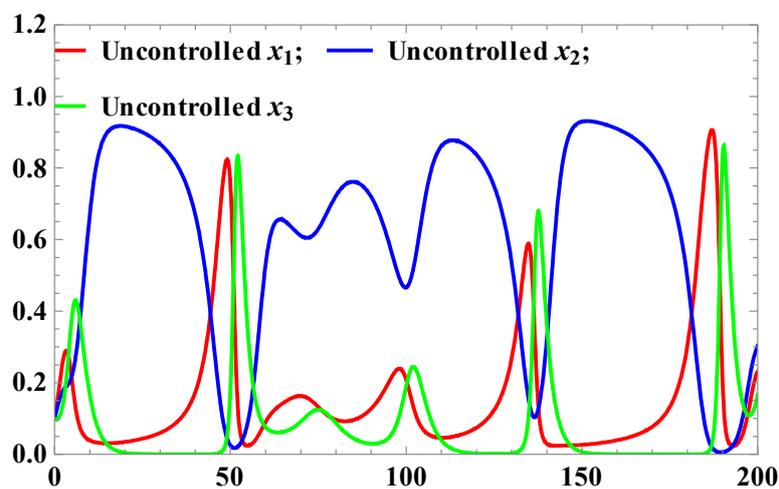


Figure 2. Time series of uncontrolled  $x_1, x_2$ , and  $x_3$ .

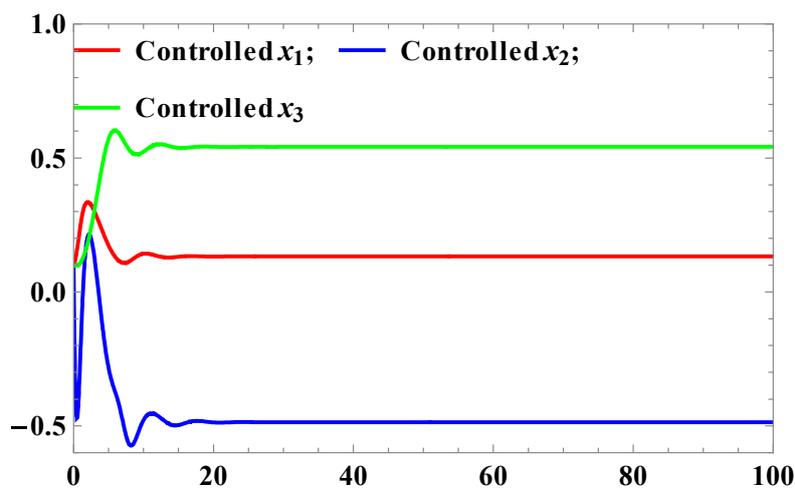


Figure 3. Time series of controlled  $x_1, x_2$ , and  $x_3$ .

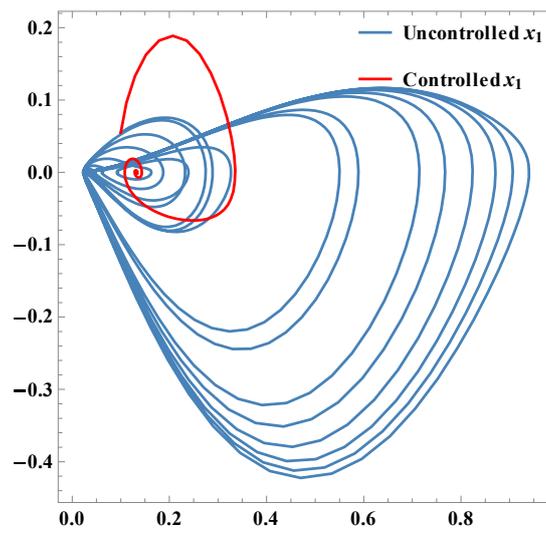


Figure 4. Phase plots of  $x_1$ .

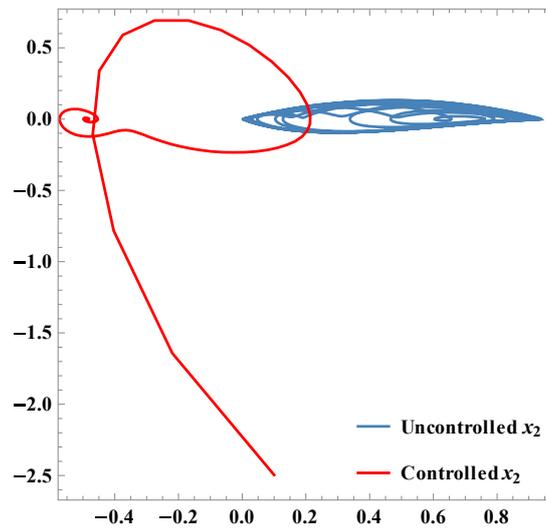


Figure 5. Phase plots of  $x_2$ .

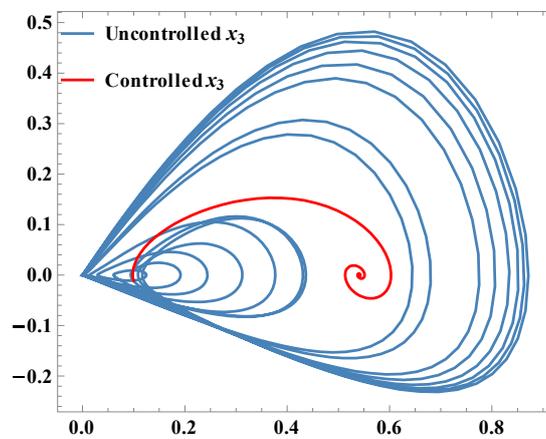


Figure 6. Phase plots of  $x_3$ .

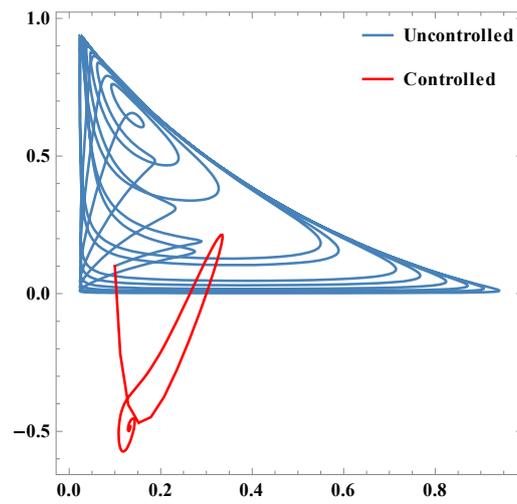


Figure 7. Parametric plots between  $x_1$  &  $x_2$ .

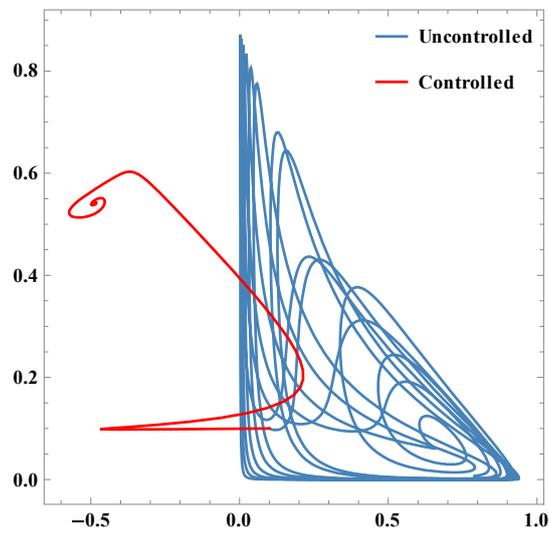


Figure 8. Parametric plots between  $x_2$  &  $x_3$ .

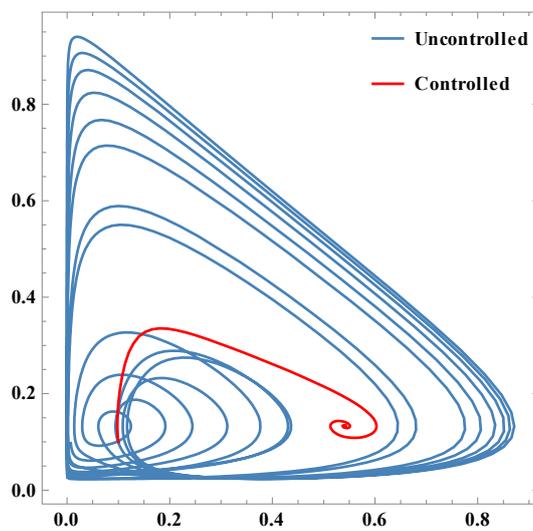


Figure 9. Parametric plots between  $x_3$  &  $x_1$ .

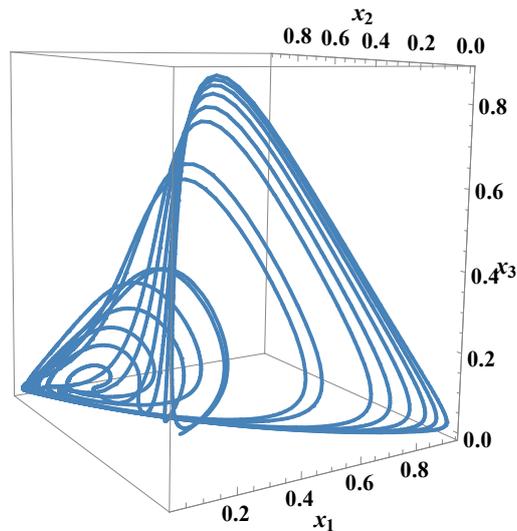


Figure 10. Parametric 3D plot of uncontrolled state vectors.

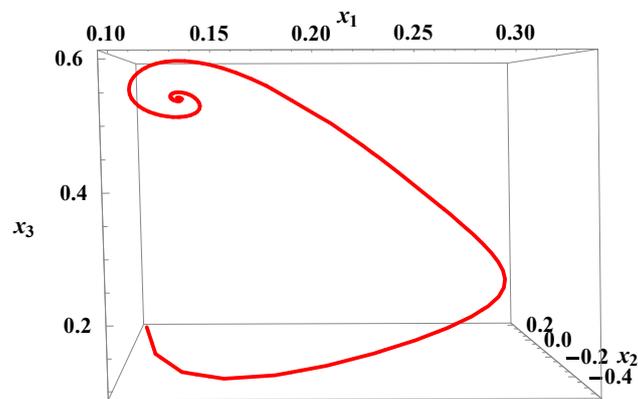


Figure 11. Parametric 3D plot of controlled state vectors.

## 6. Conclusions

In this paper, we have controlled the chaotic dynamics of TDCM using the SSEL method based on Lie algebra. Without the loss of generality, an equivalent linear system to the considered chaotic system has been obtained using Lie algebra. Also, a single control term has been injected to the chaotic system and the control has been observed in all three state vectors representing the number of cancer cells  $T(t)$ ; the healthy host cells  $H(t)$ ; and the effector immune cells  $E(t)$  in a very short time. The robustness of the technique in controlling the chaotic behavior can be observed through the presented plots.

**Conflicts of Interest:** The author declares no conflict of interest.

## References

1. Itik, M.; Banks, S.P. Chaos in a three dimensional cancer model. *IJBC* **2010**, *20*, 71–79. [[CrossRef](#)]
2. De Pillis, L.G.; Radunskaya, A. The dynamics of an optimally controlled tumor model: A case study. *Math. Comput. Model.* **2003**, *37*, 1221–1244. [[CrossRef](#)]
3. Kirschner, D.; Panetta, J.C. Modeling immunotherapy of the tumor-immune interaction. *J. Math. Biol.* **1998**, *37*, 235–252. [[CrossRef](#)] [[PubMed](#)]
4. D’Onofrio, A. A general framework for modeling tumor-immune system competition and immunotherapy: Mathematical analysis and biomedical inferences. *Phys. D Nonlinear Phenom.* **2005**, *208*, 220–235. [[CrossRef](#)]

5. El-Gohary, A.; Alwasel, I.A. The chaos and optimal control of cancer model with complete unknown parameters. *Chaos Solitons Fractals* **2009**, *42*, 2865–2874. [[CrossRef](#)]
6. El-Gohary, A. Chaos and optimal control of cancer self-remission and tumor system steady states. *Chaos Solitons Fractals* **2008**, *37*, 1305–1316. [[CrossRef](#)]
7. Baghernia, P.; Moghaddam, R.K.; Kobravi, H. Cancer sliding mode control considering to chaotic manners of system. *J. Med. Imaging Health Inform.* **2015**, *5*, 448–457. [[CrossRef](#)]
8. Islam, M.; Islam, B.; Islam, N. Chaos control in Shimizu Morioka system by Lie algebraic exact linearization. *Int. J. Dyn. Control* **2014**, *2*, 386–394. [[CrossRef](#)]
9. Andrievskii, B.R.; Fradkov, A.L. Control of chaos: Methods and applications. *Autom. Remote Control* **2003**, *64*, 673–713. [[CrossRef](#)]
10. Chen, L.Q.; Liu, Y.Z. A modified exact linearization control for chaotic oscillators. *Nonlinear Dyn.* **1999**, *20*, 309–317. [[CrossRef](#)]
11. Liqun, C.; Yanzhu, L. Control of Lorenz chaos by the exact linearization. *Appl. Math. Mech.* **1998**, *19*, 67–73. [[CrossRef](#)]
12. Tsagas, G.R.; Mazumdar, H.P. On the control of a dynamical system by a linearization method via Lie Algebra. *Rev. Bull. Calcutta Math. Soc.* **2000**, *8*, 25–32.
13. Alvarez-Gallegos, J. Non-linear regulation of a Lorenz system by feedback linearization techniques. *Dyn. Control* **1994**, *4*, 272–289.
14. Shinbrot, T.; Grebogi, C.; Ott, E.; Yorkee, J.A. Using small perturbation to control chaos. *Nature* **1993**, *363*, 411–474. [[CrossRef](#)]



© 2016 by the author; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (<http://creativecommons.org/licenses/by/4.0/>).