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JACOBY LAST MULTIPLIER AND GROUP THEORETIC APPROACHES TO A MODEL DESCRIBING BREAST CANCER STEM CELLS

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Abstract. Despite the complexity of tumour cells population, which is well known as difficult to control. Mathematical modelling has been identified as a powerful tool to understand complex dynamics and integrations of tumour cells population. In this paper, the technique of Jacobi Last Multiplier is employed to build linear Lagrangians of cancer stem cells (CSC) which describe the development dynamic of CSC population in vitro as well as in vivo. Additionally, the use of Noether's theorem facilitate in achieving conservation laws of the reduced two dimensional nonlinear system. The technique of Lie Symmetry is applied to a model and helps to point out the correlation between parameters. As a result, the system has been linearized and the corresponding analytical as well as numerical solutions were provided.

Keywords: Lagrangian; Lie symmetry group; cancer stem cells.

2010 AMS Subject Classification: 34C14, 34M55.

1. INTRODUCTION

Breast cancer is mainly the familiar form of persistent cancer among women [21]. Cancer stem cells (CSCs) are expressed as an undersized compartment of cancer cells inside cancer that can restore and reproduce diverse families of cancer cells that contain the tumour. According to

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Liu et al. [10], CSCs are frequently resistant to chemotherapeutic drugs. Therefore, it may be considered as the main cause of tumour deterioration and metastasis [10]. To analytically study the involvedness of cancer development and response to treatment in breast malignancy [21, 1], mathematical modelling is utilized to provide a framework to investigate the vigorous, as well as cell invasion of breast cancer citeMichael. Moreover, responses to medical issues cannot always come from modern clinical and investigational equipment [1].

This paper investigates the linear lagrangian and closed-form solutions of a mathematical model of breast cancer stem cells. The model was formulated by Liu et al [10]. In their study, the authors computer-generated probable results of diverse therapeutic approaches for breast cancer. The population dynamics of the cell is divided into three different classes: The cancer stem cells (CSCs) phenotype denoted by $x_0(t)$; the progenitor cells (PCs) phenotype denoted by $x_1(t)$, and the terminally differentiated cells (TDCs) phenotype denoted by $x_2(t)$. The model flow diagram which represented the disease is given by [10]

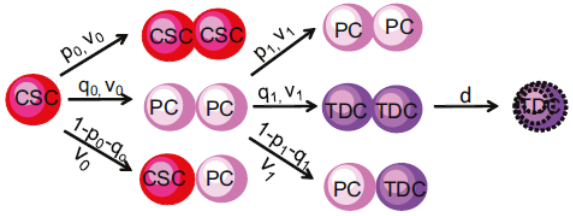

FIGURE 1. Cancer stem cells (CSC) describing the expansion of CSC population dynamics in vitro as well as in vivo.

The model is governed by the following system of nonlinear ordinary differential equations [10]

$$\frac{dx_0}{dt} = (p_0 - q_0)v_0x_0(t) - d_0x_0(t) \tag{1}$$

$$\frac{dx_1}{dt} = (1 - p_0 - q_0)v_0x_0(t) + (p_1 - q_1)v_1x_1(t) - d_1x_1(t) \tag{2}$$

$$\frac{dx_2}{dt} = (1 - p_1 - q_1)v_1x_1(t) - d_2x_2(t) \tag{3}$$

where p_0 and p_1 represent the probability that CSC and PC are divided into a pair of CSCs and PCs respectively, while the probability that CSC and PC is divided into PCs and TDCs is represented by q_0 and q_1. The rates of synthesis are denoted by v_0 and v_1. Furthermore,

$d_i, i = 0, 1, 2$, is the degradation rate of CSCs, PCs and TDCs, respectively.

According to the theory of Lie symmetry, any system of first-order ordinary differential equations admits an infinite number of Lie point symmetries [12, 18]. Nevertheless, the reduction of the infinite number of transformations occurs in replacing the original system with a system containing at least one second-order differential equation [13, 18]. The discussion in the present paper is highlighted conservation laws for a nonlinear system of physical quantity describing breast cancer. However, to be able to assess the physical method requires the physical magnitude to be conserved in space and time. In [6], Ibragimov formulated a mathematical technique that lead to obtaining the laws of conservation for a physical system that is illustrated by a differential equation. In addition, the author develops the main conservation result for any well-defined system of differential equations. It is also argued that the method of Lie symmetry analysis can be used to unpack the conservation law theorem of nonlinear differential equations. In [19], Noether formulated a theorem that facilitates in acquiring local conservation laws for a system of differential equations that admit a variational principle. Furthermore, the scholar has shown that if a Lie point transformation is obtained, then one can achieve the change of a local conservation law by way of a direct formula that entails the infinitesimal Lie point symmetry and the Langrangian of the action function. In [2], Bluman et. al. shown how the local conservation laws for any given system of differential equations can be directly constructed.

In 1971, Kerner initiated the application of linear Lagrangians in the analysis of population dynamics [9]. The author's technique was restricted to interactions among even numbers of the group. His method was extended by Trubatch and Franco to odd numbers of interacting species (see [25]). In addition, They introduced a dummy variable as well as an extra equation of motion in case two of the equations of motion is integrated. As a result, one population can be represented in terms of the other. Later on, Wooley [26] explained the method with more clarity and clearly in a dissimilar circumstance. Nucci and Tamizhmani [20] demonstrated that the technique developed by Trubatch and Franco [25] and soon after by Paine [23] for

achieving Lagrangians of a biological classical models, is simply equivalent to the Jacobi Last Multiplier. Moreover, researchers showed how one can attain linear Lagrangians of systems of two-dimensional first-order ordinary differential equations. Above and beyond, the authors provide a technique of finding nonlinear Lagrangians of the corresponding single second-order equation.

This study is organised as follows. We provide some basic definitions and theorems which will be employed throughout the paper. we reduced the three-dimensional system (1)-(3) into a single ordinary differential equation of second-order. As a result, the Jacoby Last multiplier was performed for the solutions of nonlinear second-order differential equation and obtained linear lagrangian in Sections 2 and 3. We performed a Lie symmetry method of the reduced equations to obtain explicit along with numerical solutions in Section 4. The conclusion is provided in Section 5.

2. Fundamental Definitions and Theorems

In this Section, a comprehensive review of the Jacoby Last multiplier and group-theoretic approaches to the Solution of differential equations are given. The theory entails the tools necessary for after be employed throughout the paper. In [12, 14], Matadi provided fundamental definitions and theorems which can be found from the literature (see [20, 25]).

2.1. The Jacoby Last multiplier Method. In [16, 11], Matadi summarised the technique of Jacoby Last Multiplied due to Nucci and Tamizhmani [20] as follows. Given a system of two first-order ordinary differential [25]

$$\begin{aligned} \dot{u_1} &= \phi_1(t,u_1,u_2) \\ \dot{u_2} &= \phi_1(t,u_1,u_2), \end{aligned} \tag{4}$$

admits the following linear Lagrangian

$$L = U_1(t,u_1,u_2)\dot{u_1} + U_2(t,u_1,u_2)\dot{u_2} - V(t,u_1,u_2). \tag{5}$$

The most important step is to obtain a function W in such a way

$$W = -\frac{\partial U_1}{\partial u_2} = \frac{\partial U_2}{\partial u_1} \tag{6}$$

and

$$\frac{\mathrm{d}\log(W)}{\mathrm{d}t} + \frac{\partial \phi_1}{\partial u_1} + \frac{\partial \phi_2}{\partial u_2} = 0. \tag{7}$$

Nucci and Tamizhmani [20] claimed that (7) is equivalent to the Jacobi Last Multiplier for the system (4). Consequently, it was pointed out that the finding of a Jacobi Last Multiplier $M(t,u_1,u_2)$ leads to a Lagrangian of the system (4) which can be obtained by double integrations, i.e. [20]

$$L = \left(\int M du_1\right)\dot{u_2} - \left(\int M du_2\right)\dot{u_1} + g(t,u_1,u_2) + \frac{d}{dt}G(t,u_1,u_2), \tag{8}$$

with $g(t,u_1,u_2)$ satisfying a linear differential equations of first-order which has to be at all times integrated [20]. In order to correctly apply Noether's theorem [19], the arbitrary gauge function $G(t,u_1,u_2)$ needs to be taken into consideration. If a Noether's symmetry

$$\Gamma = \xi(t,u_1,u_2)\partial_t + \eta_1(t,u_1,u_2)\partial_{u_1} + \eta_2(t,u_1,u_2)\partial_{u_2} \tag{9}$$

exists for the Lagrangian L in (8) then a first integral of system (4) is [20]

$$-\xi L - \frac{\partial L}{\partial \dot{u_1}}(\eta_1 - \xi \dot{u_1}) - \frac{\partial L}{\partial \dot{u_2}}(\eta_2 - \xi \dot{u_2}) + G(t,u_1,u_2). \tag{10}$$

Nucci and Tamizhmani [20] stated that for a given second-order equation

$$\ddot{x} = \phi(t,x,\dot{x}) \tag{11}$$

there exists a bijection between the Jacobi Last Multiplier and the Lagrangian, $L = L(t,x,\dot{x})$, as a result,

$$M = \frac{\partial^2 L}{\partial \dot{x}^2} \tag{12}$$

with $M = M(t,x,\dot{x})$ fulfilling the given equation

$$\frac{\mathrm{d}\log(M)}{\mathrm{d}t} + \frac{\partial \phi}{\partial \dot{x}} = 0. \tag{13}$$

In addition, equation (11) satisfies the Euler-Lagrangian equation:

$$-\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{\partial L}{\partial \dot{x}}\right)+\frac{\partial L}{\partial x}=0. \tag{14}$$

The authors claimed that the following Lagrangian L is found if and only if a Jacobi Last Multiplier is obtained

$$L=\int\left(\int M d\dot{x}\right)d\dot{x}+l_1(t,x)\dot{x}+l_2(t,x), \tag{15}$$

with l_1 and l_2 describing the gauge function $F=F(t,x)$ [20]

$$l_1 = \frac{\partial F}{\partial x}, \tag{16a}$$

$$l_2 = \frac{\partial F}{\partial t}+l_3. \tag{16b}$$

2.2. Lie Group Theory. The overall idea behind Lie's theory is to transform independent and dependant variables of a differential equation, such that the order of a differential equation gets reduced and easy to solve. If a differential equation admits the symmetry group, its order can be reduced by using what is called *Canonical Coordinates*.

Definition 1. The canonical coordinates $(r(x,y),s(x,y))$ of a differential equation are the coordinates in which the equation becomes separable [24].

According to Lie theory, the kth-order differential equation [14, **?**]

$$u_t-F(t,x,u,u_{(1)},u_{(2)},...,u_{(k)})=0, \tag{17}$$

admits the given Lie group of transformations of one-parameter

$$\begin{aligned}
\hat{t} &\approx t+a\xi^0(t,x,u,u_{(1)},u_{(2)},...,u_{(k)})\\
\hat{x}^i &\approx x^i+a\xi^i(t,x,u,u_{(1)},u_{(2)},...,u_{(k)})\\
\hat{u}^\alpha_i &\approx u^\alpha_i+a\eta^\alpha_i(t,x,u,u_{(1)},u_{(2)},...,u_{(k)})
\end{aligned}$$

with infinitesimal Lie generator [13, **?**]

$$X=\xi^0\frac{\partial}{\partial t}+\xi^i\frac{\partial}{\partial x^i}+\eta^\alpha\frac{\partial}{\partial u^\alpha}. \tag{18}$$

if

$$\hat{u}_t - F(\hat{t},\hat{x},\hat{u},\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}) = 0. \tag{19}$$

The group transformations $\hat{t}$, $\hat{x}$ and $\hat{u}$ are obtained by solving the following Lie equations [12]

$$\begin{aligned} \frac{d\hat{t}}{da} &= \xi^0(\hat{t},\hat{x},\hat{u},\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}) \\ \frac{d\hat{x}^i}{da} &= \xi^i(\hat{t},\hat{x},\hat{u},\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}) \\ \frac{d\hat{u}^\alpha_i}{da} &= \eta^\alpha_i(\hat{t},\hat{x},\hat{u},\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}) \end{aligned} \tag{20}$$

with initial conditions

$$\hat{t}\mid_{a=0} = t, \hat{x}^i\mid_{a=0} = x^i, \hat{u}^\alpha_i\mid_{a=0} = u^\alpha_i.$$

The infinitesimal form of $\hat{u}_{\bar{t}},\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}$ are found by the given formulas [16]:

$$\begin{aligned} \hat{u}^\alpha_i &\approx u^\alpha_i + a\eta^\alpha_i(x,u,u_1) \\ \hat{u}^\alpha_{ij} &\approx u^\alpha_{ij} + a\eta^\alpha_{ij}(x,u,u_1,u_2) \\ &... \\ \hat{u}^\alpha_{i_1...i_k} &\approx u^\alpha_{i_1...i_k} + a\eta^\alpha_{i_1...i_k}(x,u,u_1,...,u_k). \end{aligned} \tag{21}$$

The functions $\eta^\alpha_i(x,u,u_1)$, $\eta^\alpha_{ij}(x,u,u_1,u_2)$, and $\eta^\alpha_{i_1...i_k}(x,u,u_1,...,u_k)$ are obtained from the following prolongation formulas [24]

$$\begin{aligned} \eta^\alpha_i &= D_i(\eta^\alpha) - u^\alpha_j D_i(\xi^j) \\ \eta^\alpha_{ij} &= D_j(\eta^\alpha_i) - u^\alpha_{il} D_j(\xi^l) \\ &... \\ \eta^\alpha_{i_1...i_k} &= D_{i_k}(\eta^\alpha_{i_1...i_{k-1}}) - u^\alpha_{i_1...i_{k-1}l} D_{i_k}(\xi^l). \end{aligned} \tag{22}$$

where D_i denotes the operator of total differentiation with respect to $(x_1,x_2...x_n)$, then

$$D_i = \frac{\partial}{\partial x_i} + u^\alpha_i \frac{\partial}{\partial u^\alpha} + u^\alpha_{ij}\frac{\partial}{\partial u^\alpha_j}. \tag{23}$$

The transformed derivatives $\hat{u}_{(1)},\hat{u}_{(2)},...,\hat{u}_{(k)}$ can be computed from the formulae

$$D_i = D_i(f^i)\hat{D}_j. \tag{24}$$

The generators are therefore given by

$$\begin{aligned} X^{[1]} &= X+\eta_i^{\alpha}(x,u,u_1)\frac{\partial}{\partial u_i^{\alpha}} \\ &\ldots \\ X^{[k]} &= X^{[1]}+\ldots+\eta^{\alpha}_{i_1\ldots i_k}(x,u,\ldots,u_k)\frac{\partial}{\partial u^{\alpha}_{i_1\ldots i_k}}. \end{aligned} \tag{25}$$

Theorem 1. *A function $F(x,u,\cdots,u_k)$ is invariant under the prolonged group G, if and only if* [13]

$$X^{[k]}F=0, \tag{26}$$

where $X^{[k]}$ is the generator of G.

Theorem 2. *Every one-parameter group of transformations $(\hat{x}=f(x,y,\varepsilon),\hat{y}=g(x,y,\varepsilon))$ is reduced to a group of translations $\hat{t}=t+\varepsilon$, $\hat{u}=u$ with the generator* [13]

$$X=\frac{\partial}{\partial t}$$

by suitable change of variables

$$t=t(x,y), \quad u=u(x,y).$$

Theorem 3. ***(Noether's Theorem)***

Given a Euler-Lagrange equations [6]

$$\frac{\partial L}{\partial u^{\alpha}}-D_i\frac{\partial L}{\partial u_i^{\alpha}}=0,\ \alpha=1....m \tag{27}$$

with $L(x,u,u_{(1)})$ be a Lagrangian of first-order involving with the independent variables $x=(x^1,\ldots,x^n)$, dependent variables $u=(u,\ldots,u^m)$ as well as the first-order derivatives $u_{(1)}=\{u_i^{\alpha}\}$. According to Noether's theorem, in as much as the variational integral through Lagrangian $L(x,u,u_{(1)})$ is invariant under the group X generator given by

$$X=\xi^i(x,u,u_{(1)},\ldots)\frac{\partial}{\partial x^i}+\eta^{\alpha}(x,u,u_{(1)},\ldots)\frac{\partial}{\partial u^{\alpha}}. \tag{28}$$

The given vector field $T^i = (T^1, ..., T^n)$

$$T^i = L\xi^i + (\eta^\alpha - \xi^j u_j^\alpha)\frac{\partial L}{\partial u_j^\alpha} \tag{29}$$

admits a law of conservation for the Euler-Lagrange equations (27).

The proof of Theorem 3 is sketch out in [6].

Definition 2. *A vector* $T^i = (T^1 ... T^n)$ *is a conserved vector if* [6]

$$D_i(T^i) = 0 \tag{30}$$

3. Finding Lagrangian of the System (1)-(3)

In this section, Lagrangian of the two-dimensional system of first-order differential equations and one-dimensional second equation is found.

Given that the first equation of the system is independent on $x_1(t)$ and $x_2(t)$, the cancer stem cells (CSCs) phenotype, $x_0(t)$ can be found as follows

$$x_0(t) = A\exp[(pv_0 - d_0)t]. \tag{31}$$

Hence, the system (1)-(3) is reduced to

$$\frac{dx_1}{dt} = A(1-p)v_0\exp[(pv_0 - d_0)t] + (qv_1 - d_1)x_1(t) \tag{32}$$

$$\frac{dx_2}{dt} = (1-q)v_1x_1(t) - d_2x_2(t) \tag{33}$$

with

$$p = p_0 - q_0$$

and

$$q = p_1 - q_1.$$

Subsequent Jacobi Last Multiplier of the system (32)-(33) is found by using equation (7) above

$$M = \exp\{[d_1 + d_2 - qv_1]t\}. \tag{34}$$

By using equation (8), we obtain a linear Lagrangian of system (32)-(33):

$$\begin{aligned} L &= \exp\{[d_1 + d_2 - qv_1]t\}x_1(t)(1-q)v_1x_1(t) - d_2x_2(t) \\ &\quad - \exp\{[d_1 + d_2 - qv_1]t\}x_1(t)[A(1-p)v_0\exp[(pv_0 - d_0)t] + (qv_1 - d_1)x_1(t)] \\ &\quad \frac{2}{3}(1-q)v_1x_1^2 - d_2x_2x_1^2 + x_1x_2[A(1-p)v_0\exp[(pv_0 - d_0)t] + (qv_1 - d_1)x_1(t)] \\ &\quad + \frac{d}{d\tau}G(\tau, x_1, x_2). \end{aligned}$$

From equation (33), we obtain

$$x_1(t) = \frac{1}{(1-q)v_1}\frac{dx_2}{dt} + \frac{d_2}{(1-q)v_1}x_2 \tag{35}$$

The substitution of equation (35) into (32) gives

$$\frac{d^2x_2}{dt^2} + (d_2 - k_2)\frac{dx_2}{dt} - d_2k_2x_2(t) - k_3\exp[k_4t] = 0 \tag{36}$$

where

$$\begin{aligned} k_2 &= \frac{qv_1 - d_1}{1 - qv_1} \\ k_3 &= (1-p)v_0 \\ k_4 &= pv_0 - d_0. \end{aligned} \tag{37}$$

Applying the technique due to Nucci (see [20]) as summarized above, the Jacobi Last Multiplier is given by

$$M = \exp[(k_2 - d_2)t]. \tag{38}$$

Hence applying equation (15), we obtain the given Lagrangian

$$L_1 = \frac{\exp\{[k_2 - d_2)t]\}\dot{x}^2}{2} + \dot{x} + \frac{d}{d\tau}F(\tau, x) \tag{39}$$

The Lagragian equation (39) suggests that the case $k_2 \neq d_2$, provides the efficiency of chemotherapy agent on cancer stem cells (CSCs). In addition, the model equations (1)-(3) reaches the global tumour clearance state in the case $k_2 = d_2$.

4. Results and Discussion

In this section, the method of Lie symmetry analysis is used to find the analytical solution of the model. Furthermore, numerical simulations of treatment protocols are examined. In addition, simulations confirmed the theoretical approach and are performed using Python.

4.1. Symmetry Analysis of equation (36). As stated in the introduction, a system (1)-(3) admits an infinite number of Lie point symmetries. In this section Lie symmetry of the reduced equation (36) is performed. Using SYM packages ([3], [4], [5]) and we obtain an eight-dimensional Lie symmetry algebra, namely

$$\begin{aligned}
G_1 &= (d_2-k_2)\Big[\partial_t + \exp(k_4 t)\partial_{x_2}\Big] \\
G_2 &= \frac{d_2}{k_4}\Big[\partial_t + (d_2-k_3)\partial_{x_2}\Big] \\
G_3 &= \partial_t \\
G_4 &= x_2\partial_t + t x_2 \exp(k_4 t)\partial_x \\
G_5 &= d_2 \exp(k_4 t)\partial_t \\
G_6 &= \exp[-t(d_2-k_2)]x_2\partial_{x_2} \\
G_7 &= x_2^2\partial_{x_2} \\
G_8 &= \exp[-t(d_2-k_2)]\partial_t .
\end{aligned} \tag{40}$$

The above Lie symmetry algebra is isomorphic to $Sl(3,\Re)$, which means that equation (36) is linearizable by means of a point transformation. The case $d_2 = \frac{1-d_1}{1-qv_1}$ and $p_0 = 1+q_0$ gives the following

$$\frac{d^2x_2}{dt^2} + \frac{dx_2}{dt} - x_2(t) - k_3\exp[k_4 t] = 0. \tag{41}$$

Hence, the complementary function is given by

$$x_2^c = c_1 \exp[\frac{-(1+\sqrt{5})t}{2}] + c_2 \exp[\frac{(-1+\sqrt{5})t}{2}]. \tag{42}$$

Correspondingly, the superposition principle for nonhomogeneous differential equations suggests that we seek a particular solution $x_2^p = E\exp(k_4 t)$. Hence, replacing the values of k_3 and k_4 (see equation (3)), we obtain the number of terminally differentiated cells (TDCs) phenotype

$$x_2(t) = c_1 e^{[\frac{-(1+\sqrt{5})t}{2}]} + c_2 e^{[\frac{(-1+\sqrt{5})t}{2}]} + (1-p)v_0 e^{[(pv_0-d_0)t]}. \tag{43}$$

The progenitor cells (PCs) is found by substituting equation (43) into (35)

$$\begin{aligned} x_1(t) &= \tfrac{1}{(1-q)v_1}\left[\tfrac{-c_1(1+\sqrt{5})}{2} e^{[\frac{-(1+\sqrt{5})t}{2}]} + \tfrac{c_2(-1+\sqrt{5})}{2} e^{[\frac{(-1+\sqrt{5})t}{2}]} + v_0(1-p)(pv_0-d_0)e^{[(pv_0-d_0)t]}\right] \\ &+ \tfrac{d_2}{(1-q)v_1}\left[c_1 e^{[\frac{-(1+\sqrt{5})t}{2}]} + c_2 e^{[\frac{(-1+\sqrt{5})t}{2}]} + (1-p)v_0 e^{[(pv_0-d_0)t]}\right]. \end{aligned}$$

In the case $d_2 \neq \frac{1-d_1}{1-qv_1}$ and $p_0 \neq 1+q_0$ the number of terminally differentiated cells (TDCs) and progenitor cells (PCs) phenotypes are obtained as follows

$$x_2(t) = \frac{(1-p)v_0 e^{(p-v_0-d_0)t}\left[\frac{d_2 - v_1(pv_0-d_0)(1-q)}{(1-q)v_1} + e^{-d_2 t}(v_0-d_0)\right]}{(pv_0-d_0+d_2)\left(\frac{v_1(pv_0-d_0)(1-q)-d_2}{(1-q)v_1}\right)\frac{d_2(v_1-qv_1+1)}{(1-q)v_1}} + c_1 e^{-d_2 t} + c_2 e^{\frac{d_2}{(1-q)v_1}t}.$$

and

$$\begin{aligned} x_1(t) &= \tfrac{1}{(1-q)v_1}\left[\frac{(1-p)v_0 e^{(pv_0-d_0)t}\left[\frac{(pv_0-d_)(d_2-v_1(pv_0-d_0)(1-q)))}{(1-q)v_1} + e^{-d_2 t}(v_0-d_0)(pv_0-d_0-d_2)\right]}{(pv_0-d_0+d_2)\left(\frac{v_1(pv_0-d_0)(1-q)-d_2}{(1-q)v_1}\right)\frac{d_2(v_1-qv_1+1)}{(1-q)v_1}} + c_1 e^{-d_2 t} + c_2 e^{\frac{d_2}{(1-q)v_1}t}\right] \\ &+ \tfrac{d_2}{(1-q)v_1}\left[\frac{(1-p)v_0 e^{(p-v_0-d_0)t}\left[\frac{d_2-v_1(pv_0-d_0)(1-q)}{(1-q)v_1} + e^{-d_2 t}(v_0-d_0)\right]}{(pv_0-d_0+d_2)\left(\frac{v_1(pv_0-d_0)(1-q)-d_2}{(1-q)v_1}\right)\frac{d_2(v_1-qv_1+1)}{(1-q)v_1}} + c_1 e^{-d_2 t} + c_2 e^{\frac{d_2}{(1-q)v_1}t}\right]. \end{aligned}$$

The case $pv_0 = 1+d_0$ and $v_1 = \frac{1}{1-q}$ gives the following solutions:

$$x_2(t) = c_1 e^{[\frac{-(1+\sqrt{5})t}{2}]} + c_2 e^{[\frac{(-1+\sqrt{5})t}{2}]} + e^t.$$

$$\begin{aligned} x_1(t) &= \tfrac{-c_1(1+\sqrt{5})}{2} e^{[\frac{-(1+\sqrt{5})t}{2}]} + \tfrac{c_2(-1+\sqrt{5})}{2} e^{[\frac{(-1+\sqrt{5})t}{2}]} + 2e^t \\ &+ [c_1 e^{[\frac{-(1+\sqrt{5})t}{2}]} + c_2 e^{[\frac{(-1+\sqrt{5})t}{2}]}]. \end{aligned}$$

4.2. Numerical results. Recall that the parameter $d_i, i = 0,1,2$, is the degradation rate of CSCs, PCs and TDCs, respectively. However, it is known that cancer stem cells (CSCs) are resistant to some chemotherapy drugs, such as Irinotecan, up to date the degree of drug-resistant remained unknown. Regarding this model, it can be argued that should chemotherapy be ineffective on cancer stem cells (CSCs). Subsequently, tumour clearance relies on the efficiency of immunotherapy. However, when the efficacy of chemotherapy on CSCs upsurges, the amount of immunotherapy required for tumour clearance decreases. Figure 2 shown that chemotherapy is as efficient on CSCs as on tumour cells. In figure 3, the model estimates the time evolution of CSCs with different values of d_0.

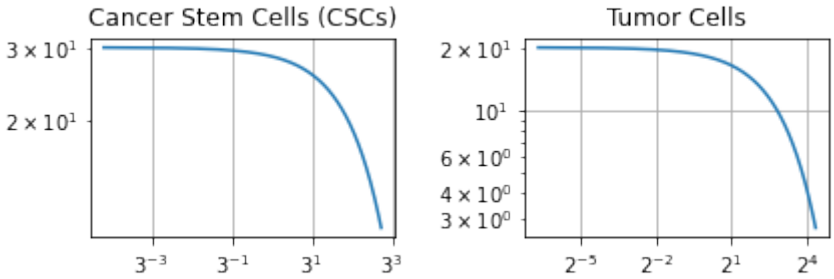

FIGURE 2. Numerical Solution of cancer stem and tumor cells.

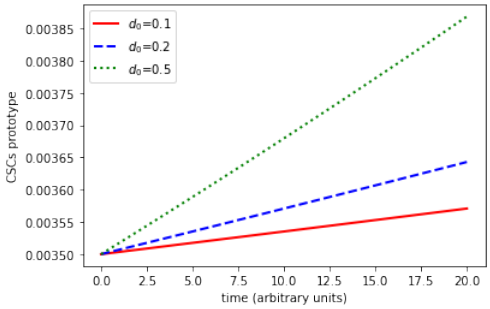

FIGURE 3. Numerical Solution of cancer stem cells with $d_0 = 0.1$, $d_0 = 0.2$ and $d_0 = 0.5$.

5. CONCLUSION

The analysis of nonlinear differential equations plays an essential role to comprehend physical models. Ove [22] stated that to find a closed-form solution of a nonlinear differential, one needs a complete understanding of the phenomena which are modelled. In this paper, linear lagrangian and closed-form solutions of a mathematical model of breast cancer stem cells are found by the mean of the Lie symmetry technique. The result revealed that under parameters values $d_2 \neq \frac{1-d_1}{1-qv_1}$ and $p_0 \neq 1+q_0$, the reduced second-order differential equation leads to the possibility of the linearization of the system and provide the corresponding solutions.

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CONFLICT OF INTERESTS

The author declares that there is no conflict of interests.

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