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Darboux Integrability of the Biological System

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Abstract

In the given paper, we investigate the integrability of a mathematical model of a 3D biological system. Our results show that the system admits a polynomial first integral for some parameters, an invariant algebraic surface with an exponential factor, and Darboux first integral. The proof was realized with the help of weight homogeneous polynomials. A model combining virus therapy and chemotherapy holds promise for improving the efficacy of cancer treatments. Virus therapy can target and destroy cancer cells, while chemotherapy can enhance the immune response and sensitize the tumor to viral therapy.

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1. Introduction

Ordinary differential equation theory represents a key area in mathematics the fundamental instruments of mathematical science, it can be used Across numerous scientific disciplines covering areas like applied mathematics, physics, and more generally, the applied sciences. Throughout the last 50 years, we have witnessed a growing interest in understanding autonomous differential systems, owing to their numerous applications in the natural sciences. Conservation of biological systems is of first priority among scientists and researchers; however, their actual dynamical behaviour is hard to monitor and analyze. Below is the mathematical framework for viral therapy in conjunction with chemotherapeutic treatment for cancer, adopting chemotherapy features from the original model [1]. In this study, the components will virus-infected tumor cells, non-virus-infected tumor cells and medication levels denoted as x, y and z respectively. There is a lot of research on the effects of cancer cells on the virus [2, 3],. Within this framework, r_1 follows a logistic growth pattern for the tumor cells not affected by infection, d_1 represents the death rate of uninfected tumor cells, β represents the spread level of a virus, α represents the speed of expansion for the chemical-based therapy drug, r_2 rate of growth for logistic of tumor cells affected by infection, d_2 rate of deaths for infected tumor cell, κ maximum capacity that tumor cells occupied, ν is amount of medication, and γ the reduction rate of chemotherapy medication. Mathematically, the framework of viral treatment cancer treatment through chemotherapy may be stated in the formula below:

$$\begin{aligned} \dot{x} &= P(x,y,z) = r_1 x\left(1-\frac{x+y}{\kappa}\right) - d_1 x - \beta xy - \alpha z \\ \dot{y} &= Q(x,y,z) = r_2 y\left(1-\frac{x+y}{\kappa}\right) - d_2 y - \beta xy \\ \dot{z} &= R(x,y,z) = \nu - \gamma z. \end{aligned} \qquad (1.1)$$

In 1878, Darboux [4, 5]. Had shown the method for obtaining the first integrals of a 2D differential system may are created along with sufficient invariant algebraic curves. Particularly, he possessed demonstrated which an autonomous polynomial system of degree m that possesses a first integral should at least have a number $\left[\frac{m(m+1)}{2}+1\right]$ invariant algebraic curves, having a straightforward expression in conformity with its invariant algebraic curves. This study delivers an invariant of system (1.1), which includes the Darboux first integral and polynomial first integrals. Since our system has no first integral [6]. Reducing the reality of its dynamic behavior, the existence of Darboux first integrals completely resolves the problem of phase diagrams determination.

2. Preliminary Concepts

Recall some definitions, theorems, notions and tools as follow.

Definition 2.1. [7, 8]**:** The vector field χ associated to the differential system (1.1), is defined by

$$\chi = P(x,y,z)\frac{\partial}{\partial x} + Q(x,y,z)\frac{\partial}{\partial y} + R(x,y,z)\frac{\partial}{\partial z}, \quad (2.2)$$

$(x,y,z) \in \mathbb{R}^3$.

Definition 2.2. [9]: A Let W be an open subset of $\mathbb{R}^3$. A non-constant function $H: W \to \mathbb{R}$ is a first integral of the polynomial vector field χ on W if it is constant on all orbits $(x(t), y(t), z(t))$ of χ contained in W; i.e. $H(x(t), y(t), z(t)) =$ constant for all values of t. $H$is a first integral of χ on W if and only if

$$\frac{dH}{dt} = \chi H = P\frac{\partial H}{\partial x} + Q\frac{\partial H}{\partial y} + R\frac{\partial H}{\partial z} = 0 \quad (2.3)$$

On W.

Definition 2.3. [10]**:** Let $h(x,y,z) \in \mathbb{R}^3$a non-zero polynomial. The algebraic surface $h(x,y,z) = 0$ is an invariant algebraic surface of the polynomial differential system (1.1), if for some polynomial $K(x,y,z) \in \mathbb{R}^3$,we have

$$\chi h = P\frac{\partial h}{\partial x} + Q\frac{\partial h}{\partial y} + R\frac{\partial h}{\partial z} = Kh. \quad (2.4)$$

The polynomial $K(x,y,z)$ is called the cofactor of the invariant algebraic surface $h = 0$. Since the polynomial differential system has degree m, any cofactor has degree at most $m - 1$.

Definition 2.4. [11]: If $h, g \in \mathbb{R}^3$are coprime, then the function $E = e^{\frac{g}{h}}$ is an exponential factor of vector field χ if there exists a polynomial L_E of degree at most $m - 1$ such that

$$\chi E = P\frac{\partial E}{\partial x} + Q\frac{\partial E}{\partial y} + R\frac{\partial E}{\partial z} = EL_E. \quad (2.5)$$

The polynomials L_E called cofactor of the Exponential factor E.

Definition 2.5. [12]: we say that the polynomial differential system (1.1), is quasi(weight)-homogeneous, if there is $s = (s_1, s_2, s_3) \in \mathbb{Z}$ and $d \in \mathbb{Z}$ such that for arbitrary $\mu \in \mathbb{R}^+$,$P(\mu^{s_1}x, \mu^{s_2}y, \mu^{s_3}z) = \mu^{s_1-1+d}P(x,y,z)$, $Q(\mu^{s_1}x, \mu^{s_2}y, \mu^{s_3}z) = \mu^{s_2-1+d}Q(x,y,z)$ and $R(\mu^{s_1}x, \mu^{s_2}y, \mu^{s_3}z) = \mu^{s_3-1+d}R(x,y,z)$. We call $s = (s_1, s_2, s_3)$ the weight exponent of system (1.1), and d the weight degree with respect to the weight exponent s.

Proposition 2.6. [13]: If $E = e^{\frac{g}{h}}$ is an exponential factor of polynomial differential system (1.1), and h is a nonconstant polynomial then $h = 0$ is an invariant algebraic surface and finally, e^g can be exponential factor resulting of the multiplicity of the infinite invariant plane.

Lemma 2.7. [14]**:** Assume that $e^{\frac{g_1}{h_1}}, \dots, e^{\frac{g_j}{h_j}}$ are exponential factors of the polynomial differential system (1.1), with cofactors L_j for $j = 1, \dots, r$. Then $e^G = e^{\frac{g_1}{h_1} + \dots + \frac{g_r}{h_r}}$ is also an exponential factor of polynomial differential system (1.1), with cofactor $L = \sum_{j=1}^{r} L_j$.

Theorem 2.8. [15]: Suppose that a polynomial vector field χ of degree d in $\mathbb{R}^3$ admits p irreducible invariant algebraic surfaces $f_i = 0$ such that the f_i are pairwise relatively prime with cofactors K_i for $i = 1, \dots, p$ and q exponential factors $e^{\frac{g_j}{h_j}}$ with cofactors L_j for $j = 1, \dots, q$. There exist $\lambda_i, \mu_j \in \mathbb{R}$ not all zero such that

$$\sum_{i=1}^{p} \lambda_i K_i + \sum_{j=1}^{q} \mu_j L_j = 0. \quad (2.6)$$

If and only if function

$$f_1^{\lambda_1} \dots f_p^{\lambda_p} \left(\left[e^{\frac{g_1}{h_1}}\right]^{\mu_1} \dots \left[e^{\frac{g_q}{h_q}}\right]^{\mu_q} \right). \quad (2.7)$$

Is a first integral of system (1.1).

Definition 2.9. [15]: A first integral is called Darboux first integral if it is of the form (2.6).

3. Main Results and Their Proofs of The Biological System

Proposition 3.1. System (3.1), has an invariant algebraic surface $h(x,y,z) = y + \frac{(d_2 - r_2)\kappa}{r_2}$ with cofactor $-\frac{r_2}{\kappa}y$, where $\beta = -\frac{r_2}{\kappa}$.

Proof. The system (1.1), after collecting it changes to biological system

$$\dot{x} = \left(-\frac{r_1}{\kappa} - \beta\right)xy - \frac{r_1 x^2}{\kappa} + (r_1 - d_1)x - \alpha z$$
$$\dot{y} = \left(-\frac{r_2}{\kappa} - \beta\right)xy - \frac{r_2 y^2}{\kappa} + (r_2 - d_2)y \quad (3.8)$$
$$\dot{z} = \nu - \gamma z.$$

Let $h(x,y,z) = \sum_{i=0}^{n} h_i(x,y)z^i$ be an invariant algebraic of system (3.1), where $h_i(x,y)z^i$ is a homogeneous polynomial of degree i, and we assume that $h_n \neq 0$ with $n \geq 1$. Since the system contains the quartic term, then the cofactor K of an invariant algebraic surface must be of the form $K = k_0 + k_1 x + k_2 y + k_3 z$, for some $k_j \in \mathbb{R}$, and $j = 0, \dots, 3$.

Then by Eq (2.3), we find that

$$\left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x-\alpha z\right)\left(\frac{\partial h}{\partial x}\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial h}{\partial y}\right)+(\nu-\gamma z)\left(\frac{\partial h}{\partial z}\right)=(k_0+k_1x+k_2y+k_3z)h. \quad (3.9)$$

Computing the coefficient of z^{n+1} in Eq (3.2),

$$(-\alpha)\left(\frac{\partial h}{\partial x}\right)=(k_3)h. \quad (3.10)$$

Then

$$h_n(x,y)=f_1(y)e^{-\frac{k_3x}{\alpha}}. \quad (3.11)$$

where $f_1(y)$ is any function in the variable y. Since $h_n(x,y)$ is a homogeneous polynomial, then we must have $k_3=0$. Now, we want to show that $k_0=k_1=0$ and $k_2=\frac{r_2}{\kappa}$ we apply the change of variables
$x=X,\quad y=\mu^{-1}Y,\quad z=\mu^{-1}Z,\quad t=\mu T$, where $\mu\in\mathbb{R}\backslash\{0\}$
Then system (3.1) becomes

$$\begin{aligned}\dot{X}&=-\frac{r_1}{\kappa}\mu X^2-\left(\frac{r_1}{\kappa}+\beta\right)XY+(r_1-d_1)\mu X-\alpha Z\\ \dot{Y}&=-\frac{r_2}{\kappa}Y^2-\left(\frac{r_2}{\kappa}+\beta\right)\mu XY+(r_2-d_2)\mu Y\\ \dot{Z}&=\mu^2\nu-\gamma\mu Z.\end{aligned} \quad (3.12)$$

where the dot indicates the variable's derivative.

Let $F(X,Y,Z)=\mu h(X,\mu Y,\mu Z)=\sum_{i=0}^{n}\mu^iF_i(X,Y,Z)$, where $F_i(X,Y,Z)$ is the weight homogeneous part with weight degree $n-i$ of F and n is the weight degree of F with weight exponent $s=(0,-1,-1)$.We also set $K(X,Y,Z)=\mu K(X,\mu Y,\mu Z)=\mu(k_1X+k_0)+k_2Y$.
Since $F(X,Y,Z)$ is an invariant algebraic surface of system (2.1), then Eq (2.3), we write as

$$\left(-\frac{r_1}{\kappa}\mu X^2-\left(\frac{r_1}{\kappa}+\beta\right)XY+(r_1-d_1)\mu X-\alpha Z\right)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial X}\right)+\left(-\frac{r_2}{\kappa}Y^2-\left(\frac{r_2}{\kappa}+\beta\right)\mu XY+(r_2-d_2)\mu Y\right)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial Y}\right)+(\mu^2\nu-\gamma\mu Z)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial Z}\right)=(\mu(k_1X+k_0)+k_2Y)(\sum_{i=0}^{n}\mu^iF_i). \quad (3.13)$$

Computing the coefficient of μ^0 in the Eq (3.6), we obtain

$$\left(-\frac{r_1}{\kappa}XY-\beta XY-\alpha Z\right)\left(\frac{\partial F_0}{\partial X}\right)-\left(\frac{r_2}{\kappa}Y^2\right)\left(\frac{\partial F_0}{\partial Y}\right)-k_0YF_0. \quad (3.14)$$

The above differential equation has a solution

$$F_0(X,Y,Z)=f_1\left(Z,\frac{(\beta\kappa XY+r_1XY+r_2XY+\alpha\kappa Z)Y^{-\frac{\beta\kappa+r_1+r_2}{r_2}}}{\beta\kappa+r_1+r_2}\right)Y^{-\frac{k_2\kappa}{r_2}}. \quad (3.15)$$

In the biological system must be the power of variable is positive, then $k_2=-\frac{r_2}{\kappa}$ and $\beta=-\frac{r_2}{\kappa}$, then $F_0(X,Y,Z)=G_0(Z)Y$, Now computing the coefficient of μ^1 in the Eq (3.6), and substitution $k_2=-\frac{r_2}{\kappa}$, $\beta=-\frac{r_2}{\kappa}$ and $F_0(X,Y,Z)=G_0(Z)Y$, we obtain

$$-\frac{1}{\kappa}\left(\left(\frac{\partial}{\partial X}G_0(Z)Y\right)X\big((d_1-r_1)\kappa+r_1X\big)+\left(\frac{\partial}{\partial X}F_1(X,Y,Z)\right)\big((r_1-r_2)XY+\alpha\kappa Z\big)\right)-\frac{r_2}{\kappa}Y^2\left(\frac{\partial}{\partial Y}F_1(X,Y,Z)\right)-\frac{Y}{\kappa}\left(\left(\left(-\frac{r_2X}{\kappa}+d_2-r_2\right)\kappa+r_2X\right)\left(\frac{\partial}{\partial Y}G_0(Z)Y\right)\right)-\gamma Z\left(\frac{\partial}{\partial Z}G_0(Z)Y\right)+\frac{r_2}{\kappa}YF_1(X,Y,Z)-(k_1X+k_0)(G_0(Z)Y). \quad (3.16)$$

The above differential equation has a solution

$$F_1(X,Y,Z)=-\frac{k_1\kappa G_0(Z)X}{r_1-2r_2}+f_1\left(Z,\frac{(r_1XY+\alpha\kappa Z)Y^{-\frac{r_1}{r_2}}}{r_1}\right)Y+\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2}+\left(\frac{-\frac{\alpha\kappa^2G_0(Z)}{r_1(r_1-2r_2)}-\frac{\kappa^2G_0(Z)}{2r_1r_2}}{Y}\right)k_1Z. \quad (3.17)$$

We must the power of Y is positive, then $G_0(Z)=0$ or $k_1=0$, if $G_0(Z)=0$ is a contradiction, then must be $k_1=0$.
Again, computing the coefficient of μ^2 in the Eq (3.6), and substitution $k_2=-\frac{r_2}{\kappa}$, $\beta=-\frac{r_2}{\kappa}$,
$F_0(X,Y,Z)=G_0(Z)Y$,$k_1=0$ and $F_1(X,Y,Z)=$

$$+f_1\left(Z,\frac{(r_1XY+\alpha\kappa Z)Y^{-\frac{r_1}{r_2}}}{r_1}\right)Y+\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2},$$

we obtain

$$-\frac{1}{\kappa}\left(\left(\frac{\partial}{\partial X}\left(G_1(Z)Y+\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2}\right)\right)X\big((d_1-r_1)\kappa+r_1X\big)\right)$$

$$-\frac{1}{\kappa}\left(\left(\frac{\partial}{\partial X}F_1(X,Y,Z)\right)\big((r_1-r_2)XY+\alpha\kappa Z\big)\right)-\frac{r_2\left(\frac{\partial}{\partial Y}F_2(X,Y,Z)\right)Y^2}{\kappa}$$

$$-\frac{Y\left(\left(-\frac{r_2}{\kappa}X+d_2-r_2\right)\kappa+r_2X\right)\left(\frac{\partial}{\partial Y}\left(G_1(Z)Y+\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2}\right)\right)}{\kappa}$$

$$-\gamma Z\left(\frac{\partial}{\partial Z}\left(G_1(Z)Y+\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2}\right)\right)$$

$$+\nu\left(\frac{\partial}{\partial Z}G_0(Z)Y\right)-k_0\left(G_1(Z)Y+\right.$$

$$\frac{\kappa\gamma\left(\frac{d}{dZ}G_0(Z)\right)Z}{r_2}+\frac{\kappa(d_2-r_2+k_0)G_0(Z)}{r_2}\Bigg). \quad (3.18)$$

The above differential equation has a solution

$$F_2(X,Y,Z)=f_1\left(Z,\frac{(r_1XY+\alpha\kappa Z)Y^{-\frac{r_1}{r_2}}}{r_1}\right)Y+\frac{\kappa\gamma\left(\frac{Z}{dZ}G_1(Z)\right)Z}{r_2}$$
$$+\frac{(\kappa d_2r_2-\kappa r_2^2+\kappa r_2k_0)G_1(Z)+\kappa\nu r_2\left(\frac{d}{dZ}G_0(Z)\right)}{r_2^2}$$
$$+\frac{1}{Y}\left(\frac{(\gamma^2\kappa^2+\gamma\kappa^2d_2-\gamma\kappa^2r_2+2\gamma\kappa^2k_0)\left(\frac{d}{dZ}G_0(Z)\right)}{2r_2}\right)$$
$$+\frac{1}{Y}\left(\frac{\gamma^2\kappa^2\left(\frac{d^2}{dZ^2}G_0(Z)\right)Z^2+(k_0d_2\kappa-k_0r_2\kappa^2+k_0^2\kappa^2)G_0(Z)}{2r_2}\right). \quad (3.19)$$

We must the power of Y is positive, then must be

$$+\frac{1}{Y}\left(\frac{(\gamma^2\kappa^2+\gamma\kappa^2d_2-\gamma\kappa^2r_2+2\gamma\kappa^2k_0)\left(\frac{d}{dZ}G_0(Z)\right)}{2r_2}\right)+$$
$$\frac{1}{Y}\left(\frac{\gamma^2\kappa^2\left(\frac{d^2}{dZ^2}G_0(Z)\right)Z^2+(k_0d_2\kappa-k_0r_2\kappa^2+k_0^2\kappa^2)G_0(Z)}{2r_2}\right)=0.$$

After Solving the above ordinary differential equation, we get

$$G_0(Z)=c_1Z^{-\frac{k_0}{\gamma}}+c_2Z^{\frac{d_2-r_2+k_0}{\gamma}}. \quad (3.20)$$

We must the power of Z is positive, then $k_0=0$ and $c_2=0$, then $G_0(Z)=c_1$.

Theorem 3.2. The next two statements hold for system (3.1).

i. For $\alpha\neq 0$, the exponential factor of polynomial differential system (3.1), is e^z, with the cofactor $\nu c_1-\gamma c_1 z$.

ii. For $\alpha=0$, the exponential factor of polynomial differential system (3.1), is e^{xy+z}, with the cofactor $\nu-\gamma z$.

Proof. Let $F=e^{g(x,y,z)}$ and $g(x,y,z)$ satisfies the equation (2.4)

$$\left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x-\alpha z\right)\left(\frac{\partial e^{g(x,y,z)}}{\partial x}\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial e^{g(x,y,z)}}{\partial y}\right)+(\nu-\gamma z)\left(\frac{\partial e^{g(x,y,z)}}{\partial z}\right)=Le^{g(x,y,z)}. \quad (3.21)$$

The above equation becomes

$$\left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x-\alpha z\right)\left(\frac{\partial g(x,y,z)}{\partial x}\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial g(x,y,z)}{\partial y}\right)+(\nu-\gamma z)\left(\frac{\partial g(x,y,z)}{\partial z}\right)=L. \quad (3.22)$$

where $L=\lambda_0+\lambda_1x+\lambda_2y+\lambda_3z$.

Now, we want to show that for $n\geq 2$, has no exponential factor of polynomial differential system (3.1).

We apply the change of variables

$x=\mu^{-1}X$, $y=\mu Y$, $z=\mu^{-1}Z$, $t=\mu T$, where $\mu\in\mathbb{R}\backslash\{0\}$

Then the system (3.1), becomes

$$\dot{X}=-\frac{r_1X^2}{\kappa}+(r_1-d_1)\mu X-\left(\frac{r_1}{\kappa}+\beta\right)\mu^2XY-\alpha\mu Z$$
$$\dot{Y}=-\frac{r_2\mu^2}{\kappa}Y^2+(r_2-d_2)\mu Y-\left(\frac{r_2}{\kappa}+\beta\right)XY \quad (3.23)$$
$$\dot{Z}=\nu\mu^2-\gamma\mu Z.$$

where the dot indicates the variable's derivative.

Let $F(X,Y,Z)=\mu h(\mu^{-1}X,\mu Y,\mu^{-1}Z)=\sum_{i=0}^{n}\mu^iF_i(X,Y,Z)$, where $F_i(X,Y,Z)$ is the weight homogeneous part with weight degree $n-i$ of F and n is the weight degree of F with weight exponent $s=(0,-1,-1)$.We also set $K(X,Y,Z)=\mu^2K(\mu^{-1}X,\mu Y,\mu^{-1}Z)=\mu\lambda_0+\lambda_1X+\mu^2\lambda_2Y+\lambda_3Z$.

Since $F(X,Y,Z)$ is an invariant algebraic surface of system (3.1), then Eq (3.15), can be written as

$$\left(-\frac{r_1X^2}{\kappa}+(r_1-d_1)\mu X-\left(\frac{r_1}{\kappa}+\beta\right)\mu^2XY-\alpha\mu Z\right)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial X}\right)+\left(-\frac{r_2\mu^2}{\kappa}Y^2+(r_2-d_2)\mu Y-\left(\frac{r_2}{\kappa}+\beta\right)XY\right)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial Y}\right)+(\nu\mu^2-\gamma\mu Z)\left(\sum_{i=0}^{n}\mu^i\frac{\partial F_i}{\partial Z}\right)=(\mu\lambda_0+\lambda_1X+\mu^2\lambda_2Y+\lambda_3Z)\sum_{i=0}^{n}\mu^iF_i. \quad (3.24)$$

Calculate the coefficients of μ^0 in the Eq (3.17), we obtain

$$-\frac{r_1\left(\frac{\partial}{\partial X}F_0(X,Y,Z)\right)X^2}{\kappa}-\frac{(\beta\kappa+r_2)\left(\frac{\partial}{\partial Y}F_0(X,Y,Z)\right)XY}{\kappa}-\lambda_1X-\lambda_3Z=0. \quad (3.25)$$

The above differential equation has a solution

$$F_0(X,Y,Z)=-\frac{\kappa\lambda_1\ln(X)-f_1\left(YX^{-\frac{\beta\kappa+r_2}{r_1}},Z\right)r_1}{r_1}+\frac{\lambda_3\kappa Z}{r_1X}. \quad (3.26)$$

Since $F_0(X,Y,Z)$ is a weight homogeneous then we must $\lambda_1=0$, $\lambda_3=0$ and $\beta=-\frac{r_1+r_2}{\kappa}$.

Now calculate the coefficients of μ^1 in the equation (3.17) and substitution $\lambda_1=0$, $\lambda_3=0$, $\beta=-\frac{r_1+r_2}{\kappa}$ and $F_0(X,Y,Z)=f_1(Z)$, we obtain

$$-\frac{\kappa\left((d_1-r_1)X+\alpha Z\right)\left(\frac{\partial}{\partial X}f_1(Z)\right)+r_1\left(\frac{\partial}{\partial X}F_1(X,Y,Z)\right)X^2}{\kappa}-\frac{\kappa\left((d_1-r_1)\right)\left(\frac{\partial}{\partial Y}f_1(Z)\right)+r_1\left(\frac{\partial}{\partial X}F_1(X,Y,Z)\right)Y}{\kappa}-\gamma\left(\frac{d}{dZ}f_1(Z)\right)-\lambda_0=0. \quad (3.27)$$

The above differential equation has a solution

$$F_1(X,Y,Z)=f_2(XY,Z)+\frac{\kappa\gamma\left(\frac{d}{dZ}f_1(Z)\right)+\lambda_0}{r_1X}. \quad (3.28)$$

Since $F_1(X,Y,Z)$ is a weight homogeneous then we must $\lambda_0=0$ and since $\kappa\neq 0$ and $\gamma\neq 0$, then $\frac{d}{dZ}f_1(Z)=0$, and we can say that $f_1(Z)=c_1$,then which is contradiction. Then the polynomial differential system (3.1), has an exponential factor of $n<2$.

Therefore $g(x,y,z)=g_0(x,y)+g_1(x,y)z$, the Eq (3.15) becomes

$$\left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x-\alpha z\right)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial x}\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial y}\right)+(\nu-\gamma z)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial z}\right)=\lambda_0+\lambda_1x+\lambda_2y+\lambda_3z. \quad (3.29)$$

Case (i) In this case $\alpha\neq 0$ and the Eq (3.22), becomes

$$\left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x-\alpha z\right)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial x}\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial y}\right)+(\nu-\gamma z)\left(\frac{\partial(g_0(x,y)+g_1(x,y)z)}{\partial z}\right)=\lambda_0+\lambda_1x+\lambda_2y+\lambda_3z. \quad (3.30)$$

Calculate the coefficients of $z^i, i=0,1,2$, the following equations will obtain:

$$i=2: \qquad -\alpha\left(\frac{\partial}{\partial x}g_1(x,y)\right)=0. \quad (3.31)$$

$$i=1: \left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x\right)\left(\frac{\partial}{\partial x}g_1(x,y)\right)-\alpha\left(\frac{\partial}{\partial x}g_0(x,y)\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial}{\partial y}g_1(x,y)\right)-\gamma g_1(x,y)-\lambda_3=0. \quad (3.32)$$

$$i=0: \left(\left(-\frac{r_1}{\kappa}-\beta\right)xy-\frac{r_1x^2}{\kappa}+(r_1-d_1)x\right)\left(\frac{\partial}{\partial x}g_0(x,y)\right)+\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial}{\partial y}g_0(x,y)\right)+\nu g_1(x,y)-\lambda_1x-\lambda_2y-\lambda_0=0. \quad (3.33)$$

From Eq (3.24), results

$$g_1(x,y)=g_1(y). \quad (3.34)$$

After substitution Eq (3.27), in Eq (3.25), we get

$$\left(\left(-\frac{r_2}{\kappa}-\beta\right)xy-\frac{r_2y^2}{\kappa}+(r_2-d_2)y\right)\left(\frac{\partial}{\partial y}g_1(y)\right)-\alpha\left(\frac{\partial}{\partial x}g_0(x,y)\right)-\gamma g_1(y)-\lambda_3=0. \quad (3.35)$$

From equation (3.28) results

$$g_0(x,y)=-\frac{\left(\frac{\beta\kappa x^2y}{2}+d_2\kappa xy-r_2\kappa xy+\frac{r_2x^2y}{2}+r_2xy^2\right)\left(\frac{d}{dy}g_1(y)\right)}{\alpha\kappa}-\frac{\gamma\kappa xg_1(y)+\lambda_3\kappa x}{\alpha\kappa}+g_2(y). \quad (3.36)$$

Now substitution Eq (3.27) , (3.29), in Eq (3.26), we get

$$\frac{1}{2\alpha\kappa^2}\Bigg(2\left((-\beta\kappa-r_2)x+(r_2-d_2)\kappa-r_2y\right)\left(\left(-\frac{\kappa\beta+r_2}{2}\right)x+(r_2-d_2)\kappa-r_2y\right)xy^2\left(\frac{d^2}{dy^2}g_1(y)\right)+2\left((-\beta\kappa-r_2)x+(r_2-d_2)\kappa-r_2y\right)y\left(\left(-\frac{\kappa\beta+2r_1-r_2}{2}\right)x+(-\beta y-\gamma-d_1-d_2+r_1+r_2)\kappa-(r_1+2r_2)y\right)x\left(\frac{d}{dy}g_1(y)\right)+2\kappa\left((-\beta\kappa-r_2)x+(r_2-d_2)\kappa-r_2y)\alpha y\left(\frac{d}{dy}g_2(y)\right)+\left(r_1\gamma x^2-\left((-\beta y-d_1+r_1)\kappa-r_1y\right)\gamma x+\alpha\kappa\nu\right)g_1(y)+r_1\lambda_3x^2+(\beta\lambda_3y-\alpha\lambda_1+d_1\lambda_3-r_1\lambda_3)\kappa+r_1\lambda_3y\right)x-\alpha\kappa(\lambda_2y+\lambda_0)\Bigg)=0. \quad (3.37)$$

Now collect the Eq (3.30), with respect to x and compute the coefficients of $x^i, i=0,1,2,3$.

For $i=3$:

$$\frac{1}{2\alpha\kappa^2}\left(2(-\beta\kappa-r_2)\left(-\frac{\beta\kappa+r_2}{2}\right)y\left(\frac{d^2}{dy^2}g_1(y)\right)+2(-\beta\kappa-r_2)y\left(-\frac{\beta\kappa+2r_1+r_2}{2}\right)\left(\frac{d}{dy}g_1(y)\right)\right)=0. \quad (3.38)$$

After solving the above ordinary differential equation, we get

$$g_1(y)=c_1+c_2y^{-\frac{2r_1}{\beta\kappa+r_2}}. \quad (3.39)$$

We must the power of y is integer then we must $c_2=0$, then

$$g_1(y)=c_1. \quad (3.40)$$

For $i = 2$:

$$\frac{1}{2\alpha\kappa^2}\Bigg(2\Big(\big((r_2-d_2)\kappa-r_2y\big)\Big(-\frac{\beta\kappa+r_2}{2}\Big)+(-\beta\kappa-r_2)\big((r_2-d_2)\kappa-r_2y\big)\Big)y^2\left(\frac{d^2}{dy^2}g_1(y)\right)+2\Big(\big((r_2-d_2)\kappa-r_2y\big)y\Big(-\frac{\beta\kappa+2r_1+r_2}{2}\Big)+(\beta\kappa-r_2)y\big((-\beta y-\gamma-d_1-d_2+r_1+r_2)\kappa-(r_1+2r_2)y\big)\Big)\left(\frac{d}{dy}g_1(y)\right)+2\kappa(r_1\gamma g_1(y)+r_1\lambda_3)\Bigg)=0. \quad (3.41)$$

Now substitution the Eq (3.33), in the Eq (3.34), we get

$$2\kappa(r_1\gamma g_1(y)+r_1\lambda_3)=0. \quad (3.42)$$

Since $\kappa \neq 0$, then $\lambda_3 = -c_1\gamma$.

For $i = 1$:

$$\frac{1}{2\alpha\kappa^2}\Bigg(2\big((r_2-d_2)\kappa-r_2y\big)^2y^2\left(\frac{d^2}{dy^2}g_1(y)\right)+2\big((r_2-d_2)\kappa-r_2y\big)y\big((-\beta y-\gamma-d_1-d_2+r_1+r_2)\kappa-(r_1+2r_2)y\big)\left(\frac{d}{dy}g_1(y)\right)+2\kappa\Bigg(\big(\alpha(-\beta\kappa-r_2)y\big)\left(\frac{d}{dy}g_2(y)\right)-\big((-\beta y-d_1+r_1)\kappa-r_1y\big)\gamma g_1(y)+(\beta\lambda_3y-\alpha\lambda_1+d_1\lambda_3-r_1\lambda_3)\kappa+r_1\lambda_3y\Bigg)\Bigg)=0. \quad (3.43)$$

After substitution $g_1(y) = c_1$ and $\lambda_3 = -c_1\gamma$ in Eq (3.36), we get

$$\frac{1}{\alpha\kappa}(-(-\beta\kappa-r_1)\gamma c_1-\beta c_1\gamma\kappa-c_1\gamma r_1)y-(r_1-d_1)\kappa\gamma c_1+(-\gamma c_1d_1+\gamma c_1r_1-\alpha\lambda_1)\kappa=0. \quad (3.44)$$

Then $\lambda_1 = 0$.

For $i = 0$:

$$\frac{1}{\alpha\kappa}\left(\big((r_2-d_2)\kappa-r_2y\big)\alpha\left(\frac{d}{dy}g_2(y)\right)y+\alpha\kappa\nu g_1(y)-\alpha\kappa(\lambda_2y+\lambda_0)\right)=0. \quad (3.45)$$

After substitution the $g_1(y) = c_1$, in Eq (3.38), we get

$$\frac{1}{\alpha\kappa}\left(\big((r_2-d_2)\kappa-r_2y\big)\alpha\left(\frac{d}{dy}g_2(y)\right)y+\alpha\kappa\nu c_1-\alpha\kappa(\lambda_2y+\lambda_0)\right)=0. \quad (3.46)$$

Now solving the above ordinary differential equation, we get

$$g_2(y)=\int\frac{\kappa(\nu c_1-\lambda_2y-\lambda_0)}{y(\kappa d_2-\kappa r_2+r_2y)}dy+c_2. \quad (3.47)$$

After solving the above integration, we get

$$g_2(y)=\frac{\big((-\nu c_1+\kappa\lambda_2+\lambda_0)r_2-\kappa d_2\lambda_2\big)\ln\big((-\kappa+y)r_2+\kappa d_2\big)+r_2\ln(y)(\nu c_1-\lambda_0)}{r_2(d_2-r_2)}. \quad (3.48)$$

Since $g_2(y)$ is a polynomial function depends on variable y, then we must $(-\nu c_1+\kappa\lambda_2+\lambda_0)r_2-\kappa d_2\lambda_2 = 0$ and $\nu c_1 - \lambda_0 = 0$, then $\lambda_0 = \nu c_1$ and $\lambda_2 = 0$, Hence $g(x,y,z) = c_1 z$ with cofactor $L = \nu c_1 - \gamma c_1 z$.

Case (ii) Similarly we can prove that, the exponential factor of polynomial differential system (3.1), is e^{xy+z}, with the cofactor $\nu - \gamma z$.

Proposition 3.3. when $\alpha \neq 0$, a set of all exponential factors for the biological system (3.1), consists of the following three:

i. The exponential factor $\frac{\big((d_2-r_2)+\gamma z\big)\kappa+r_2(z+1)y}{(d_2-r_2)\kappa+r_2y}$ with cofactor γz and with parameters $\gamma = r_2 - d_2$, $\nu = 0$.

ii. The exponential factor $\frac{\Big(6(\gamma^3-\gamma^3z+\nu^3)\kappa^2+2\Big(\big((-z^3-1)y-x\big)\gamma^2+z\big((3\nu z+\gamma)y+\alpha\big)\gamma-3\nu^2yz+\frac{\alpha\nu}{6}\Big)r_2\kappa-\alpha r_2^2yz\Big)}{6\gamma^2\left(\gamma\kappa-\frac{r_2y}{3}\right)\kappa}$ with cofactor $\frac{2r_2x}{\kappa}+\gamma z+\frac{\nu(\alpha r_2-3\gamma^2\kappa)}{3\kappa\gamma^2}$ and with parameters $r_1 = 0, d_1 = 6\gamma, d_2 = r_2 - 3\gamma$.

iii. The exponential factor $\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2y}$ With cofactor γz and with parameters $\nu = 0$, $d_2 = r_2 - 6\gamma$.

Theorem 3.4. The biological system (3.1), has a Darboux first integral of the form

$$H(x,y,z)=\left(e^{z+\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2y}}\right)^{\alpha_1} \text{ if } \lambda = 0,$$

$\nu = 0, \xi_1 = 0, \xi_2 = \alpha_1$ where $\lambda, \alpha_1, \xi_1, \xi_2 \in \mathbb{R}$.

Proof. By Proposition 3.1, Theorem 3.2, and Proposition 3.3, the system (3.1), has an invariant algebraic surface of the form $y + \frac{(d_2-r_2)\kappa}{r_2}$ with cofactors $\frac{-r_2y}{\kappa}$ and has an exponential factor of the form e^z, $e^{\frac{\Big(6(\gamma^3-\gamma^3z+\nu^3)\kappa^2+2\Big(\big((-z^3-1)y-x\big)\gamma^2+z\big((3\nu z+\gamma)y+\alpha\big)\gamma-3\nu^2yz+\frac{\alpha\nu}{6}\Big)r_2\kappa-\alpha r_2^2yz\Big)}{6\gamma^2\left(\gamma\kappa-\frac{r_2y}{3}\right)\kappa}}$ and $e^{\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2y}}$ with cofactors $\nu-\gamma z, \frac{2r_2x}{\kappa}+\gamma z+\frac{\nu(\alpha r_2-3\gamma^2\kappa)}{3\kappa\gamma^2}$ and γz respectively,

By Darboux Theorem there exist $\lambda, \alpha_1, \xi_1, \xi_2 \in \mathbb{R}$, such that

$$\lambda\left(-\frac{r_2y}{\kappa}\right)+\alpha_1(\nu-\gamma z)+\xi_1\left(\frac{2r_2x}{\kappa}+\gamma z+\frac{\nu(\alpha r_2-3\gamma^2\kappa)}{3\kappa\gamma^2}\right)+\xi_2(\gamma z)=0. \quad (3.49)$$

Then by theorem (2.8),

$$H(x,y,z) = \left(y + \frac{(d_2-r_2)\kappa}{r_2}\right)^{\lambda} (e^{z}) \left(e^{\frac{\left(6(\gamma^3-\gamma^3 z+\nu^3)\kappa^2+2\left(\left(((-z^3-1)y-x\right)\gamma^2+z((3\nu z+\gamma)y+\alpha)\gamma-3\nu^2 yz+\frac{\alpha\nu}{6}\right)r_2\kappa-\alpha r_2^2 yz\right)}{6\gamma^2\left(\gamma\kappa-\frac{r_2 y}{3}\right)\kappa}}\right) \left(e^{\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2 y}}\right)^{\xi_2}. \quad (3.50)$$

Is a Darboux first integral of the system (3.1), after solving the Eq (3.42),
we get then $\lambda = 0, \nu = 0, \xi_1 = 0, \xi_2 = \alpha_1$ and by proposition 3.2 $\beta = \frac{-r_2}{\kappa}$, after substitutions the $\lambda = 0, \nu = 0, \xi_1 = 0$,
$\xi_2 = \alpha_1,\ \beta = \frac{-r_2}{\kappa}$ in the Eq (3.43), then

Table 1. The system (2) exhibits with 3D projection.

Parameters	Unit	Description	Parameter value
r_1	day^{-1}	The growth rate of non-infected tumor cells	10^{-2}
κ	$cell$	The maximum capacity that tumor cells can occupy	30
d_1	$cell\ day^{-1}$	Uninfected tumor cells death rate	3×10^{-3}
β	day^{-1}	The rate of spread of the virus	147×10^{-3}
α	day^{-1}	Parts of tumor cells killed by chemotherapy	10^{-8}
r_2	day^{-1}	The growth rate of infected tumor cells	2
d_2	$cell\ day^{-1}$	The rate of death of infected tumor cells	2
γ	day^{-1}	The rate of decline in the concentration of chemotherapy	9×10^{-1}

$$H(x,y,z) = \left(e^{z+\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2 y}}\right)^{\alpha_1}. \quad (3.51)$$

Now, by definition of first integral (2.2), $H(x,y,z)$ satisfies

$$\left(r_1 x\left(1-\frac{x+y}{\kappa}\right) - d_1 x + \frac{r_2 xy}{\kappa} - \alpha z\right)\left(\frac{\partial H}{\partial x}\right) + \left(r_2 x\left(1-\frac{x+y}{\kappa}\right) + \frac{r_2 xy}{\kappa} - d_2 x\right)\left(\frac{\partial H}{\partial y}\right) + (-\gamma z)\left(\frac{\partial H}{\partial z}\right) = 0. \quad (3.52)$$

Then the system (3.1), has a Darboux first integral of the form

$$H(x,y,z) = \left(e^{z+\frac{6\kappa\gamma^2+(-r_2(z^6+1)y-6\kappa\gamma z)\gamma+r_2\gamma yz}{6\gamma^2\kappa-\gamma r_2 y}}\right)^{\alpha_1}.$$

Remark 3.5. The following statements true for the biological system (3.1), has a polynomial first integral of the form.

i. $H(x,y,z) = xy^2 - x^2y + xy + 1$ if and only if $\alpha = 0,\ \beta = -\frac{3r_2}{\kappa},\ d_1 = \frac{r_2(\kappa-1)}{\kappa}$ and $d_2 = \frac{r_2(\kappa+1)}{\kappa}$.

ii. $H(x,y,z) = xy + 1$ if and only if $\alpha = 0,\ \beta = -\frac{r_1+r_2}{\kappa},\ d_1 = r_1 + r_2 - d_2$.

The **Table 2.** shows the system (2) exhibits with 3D projection and by choosing a different value for each of the parameter's $r_1, \kappa, d_1, \beta, \alpha, r_2, d_2$ and γ, for a particular set of beginning conditions, 3D projection of the system (2) was plotted.

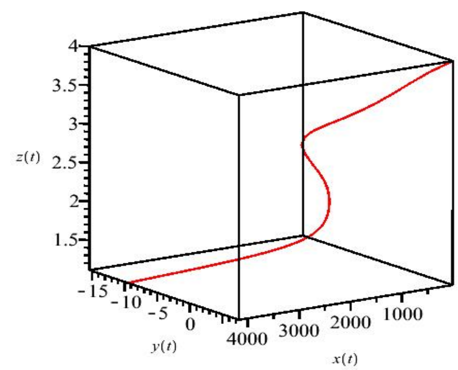

Figure 1. Local phase portraits of system (2) for initial conditions $x(0) = 15$, $y(0) = 7.5$, and $z(0) = 4$, $r_1 = 10^{-2}$, $\kappa = 30$, $d_1 = 3 \times 10^{-3}$, $\beta = 147 \times 10^{-3}$, $\alpha = 10^{-8}$, $r_2 = 2$, $d_2 = 2$and $\gamma = 10^{-1}$: On the x, y, and z planes, there is a 3D projection.

Conclusion

The results of this study lead to the following conclusions. First, system (3.1) has exactly one invariant algebraic surface $y + \frac{(d_2-r_2)\kappa}{r_2}$, where $\beta = -\frac{r_2}{\kappa}$ (see Theorem 3.1), secondly, the biological system (3.1) includes just one initial integral and a few exponential elements (see Theorem 3.2 and Proposition 3.3). Finally, the system (1.1) has a Darboux first integral (see Theorem 3.4).

Conflict of interest

None.

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