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MATHEMATICAL MODELLING OF TUMOUR CHEMOTHERAPY BY CONTINUOUS INFUSION DRUG

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Abstract: We present a theoretical framework based on logistic growth and Michaelis-Menten kinetics for describing the interaction between tumour density and drug concentration, through an infusion pump. According to the logistics growth and Michaelis-Menten kinetics, the growth rate of tumours increases with the availability of drugs only up to a certain point. Cancer chemotherapy by continuous infusion pump has the advantage of achieving large concentrations of the drug at the tumour site while minimising adverse effects on the rest of the body, in contrast to conventional methods. The model in this work has aspects of logistic growth, which cover a method for determining tumour density and drug concentrations that will eliminate the tumour. Stability analysis is done by solving nonlinear equations and finding stable and unstable points, where the coordinates of the stable points represent the tumour density and the amount of drug. The stability of the equilibrium point for the model and illustrative numerical examples are provided to show the accuracy of the model.

Keywords: infusion drug delivery; michaelis-menten kinetics; logistic growth; chemotherapy; stability.

2020 AMS Subject Classification: 92C50.

1. INTRODUCTION

Tumours cause mortality globally, and their therapies are diverse and inconsistently effective. The four primary modalities of cancer treatment are surgery, chemotherapy, radiation, and

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immunotherapy [1]. This research examines cancer therapy by chemotherapy using an infusion pump. Chemotherapy is a cancer treatment that employs pharmaceuticals to eradicate cancer cells [2]. Numerous varieties of chemotherapeutic agents exist, although they all function in the same manner, namely they inhibit the proliferation of cancer cells, hence obstructing their growth and dissemination inside the body [2]. An infusion pump is a medical apparatus that administers fluids, including nutrients and drugs, to a patient's body in regulated quantities. It may provide nutrition or pharmaceuticals, including insulin, other hormones, antibiotics, chemotherapeutic agents, and analgesics [3]. Recent researchers have presented mathematical model studies on tumour chemotherapy [4],[5], [6],[7],[8],[9],[10],[11],[12]. The following articles studied infusion pump therapy [13],[14],[15],[16], [17]. In our research, we will control the amount of doses that enter the patient's body through the device via Michaelis-Menten kinetics. In this model, the flat circular infusion device has been surgically implanted in patients requiring prolonged drug therapy. This intervention effectively reduces inflammation in external infusion devices and improves mobility. The use of insulin infusion for diabetes management and cancer treatment is considered an experimental approach. The developers of this device propose the use of heparin for the management of thromboembolic disorders, dopamine for the treatment of Parkinson's disease, and hormones for the treatment of other neurological disorders, delivered directly to the body [1]. The internal infusion pump can be reconstructed without surgical intervention; however, there are drawbacks associated with its construction. Apart from these medical considerations, we will analyse how mathematical models, such as the one described earlier, help to clarify the process of setting up and controlling the infusion pump. According to our assumptions, it is now possible to describe the course of chemotherapy as a system of equations involving the drug C and the tumour cells w.

This paper is laid out as follows: in the second section, we formulate the equations and draw the schematic diagram, and then correct the equations according to the units of each term to balance the equations and reduce the number of variables in the equations by doing the nondimensionalisation of the model equations. In the third section, we find the equilibrium points and test them in terms of whether they are stable or unstable. In the fourth section, we take

numerical examples according to certain conditions discussed in each case and draw them in the MATHEMATICA program and numerically in the MATLAB program, noting the agreement of the solution with the numerical solution. Finally, in section five, we present our conclusions.

2. FORMULATING THE MODEL

We begin with a schematic illustration of the application of cancer chemotherapy between tumour volume and drug concentration by an infusion pump as shown in Fig. 1. F refers to the flow rate of the pump and u to the rate of blood flow away from the tumour site. In many situations, drugs that sustain the health of a patient cannot be administered orally but must be injected directly into the circulation. This can be done with serial injections, or in particular instances, using continuous infusion, which delivers some constant level of medication over an extended time interval.

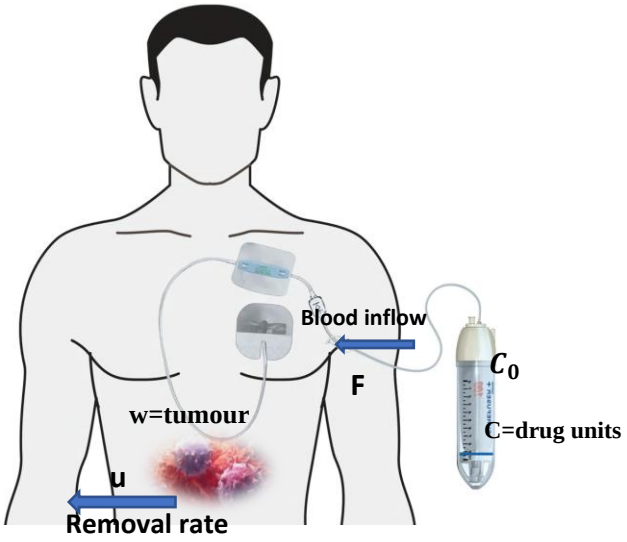

Figure 1. Logistic modeling device for continuous infusion chemotherapy, a tumour (w) is considered to be a group of identical cells, all of which are uniformly exposed to C units of the drug.

The appropriate word equations are, now, the system of equations involving the tumour cell *w* and the drug C equation which might contain terms as follows

$$\left\{\begin{matrix}\text{rate change of}\\ \text{tumour for time}\end{matrix}\right\} = \left\{\begin{matrix}\text{growth rate of}\\ \text{cells}\end{matrix}\right\} - \left\{\begin{matrix}\text{drug induced}\\ \text{death rate}\end{matrix}\right\}, \quad (1)$$

$$\begin{Bmatrix}\text{rate change of}\\ \text{drug for time}\end{Bmatrix} = \begin{Bmatrix}\text{rate drug}\\ \text{infused}\end{Bmatrix} - \begin{Bmatrix}\text{rate of}\\ \text{uptake}\\ \text{by cells}\end{Bmatrix} - \begin{Bmatrix}\text{rate of}\\ \text{removal by}\\ \text{the circulation}\end{Bmatrix}, \tag{2}$$

we assume that w is the number of tumour cells per unit of blood volume.

C is the number of drug units in circulation per unit of blood volume.

Now, we will write what each term in Eqs. ((1)-(2)) represents

$$\begin{Bmatrix}\text{rate change of}\\ \text{tumour for time}\end{Bmatrix} = \frac{\mathrm{dw}}{\mathrm{dt}}, \tag{3}$$

the tumour grows logistically, where M is the caring capacity

$$\begin{Bmatrix}\text{growth rate of}\\ \text{cells}\end{Bmatrix} = \mathrm{A}(C)\mathrm{w}(1-\frac{w}{M}), \tag{4}$$

and

$$\begin{Bmatrix}\text{drug induced}\\ \text{death rate}\end{Bmatrix} = \mathrm{Fw}\left(1-\frac{w}{M}\right). \tag{5}$$

On the other hand, the rate change of drug is defined as

$$\begin{Bmatrix}\text{rate change of}\\ \text{drug for time}\end{Bmatrix} = \frac{\mathrm{dC}}{\mathrm{dt}}, \tag{6}$$

where the three terms in Eq . (2) are,

$$\begin{Bmatrix}\text{rate drug}\\ \text{infused}\end{Bmatrix} = \mathrm{F}C_0, \tag{7}$$

$$\begin{Bmatrix}\text{rate of}\\ \text{uptake}\\ \text{by cells}\end{Bmatrix} = -\alpha\,\mathrm{A}(C)\mathrm{w}(1-\frac{w}{M}), \tag{8}$$

and

$$\begin{Bmatrix}\text{rate of}\\ \text{removal by}\\ \text{the circulation}\end{Bmatrix} = -\mathrm{uC}. \tag{9}$$

We are combining the assumptions of a rate change of tumour for time t with a rate change of drug for the time of differential equations.

Putting together the assumptions of Eqs. (3),(4), and (5) in Eq. (1), we get

$$\frac{dw}{dt} = \mathrm{A}(C)w(1 - \frac{w}{M}) - Fw(1 - \frac{w}{M}). \quad (10)$$

By substituting Eqs. (6),(7),(8), and (9) in Eq. (2), we get

$$\frac{dC}{dt} = FC_0 - \alpha\, A(C)w\left(1 - \frac{w}{M}\right) - uC. \quad (11)$$

The parameters in the above system and their descriptions are summarised in Table 1.

Table 1. Summary of the quantities and model parameters and dimensions of the model Eqs. (10) and (11)

Quantity	Description	Dimensions
C_0	The concentration of drug solution in the infusion pump	(Mass/Volume)
C	The concentration of drug solution in a patient body	(Mass/Volume)
F	The pump flow rate	(Volume/unit time)
V	The volume of the blood in direct contact with the tumour area	Volume
u	Rate of blood flow away from the tumour site	(Volume/unit time)
α	Drug exhaustion rate	(Mass/Number)
w	The number of tumour cells per unit of blood volume (tumour density)	(Number/Volume)
A_{max}	The maximal tumour reproduction rate	(1/unit time)
A_n	The amount of medication at which the growth rate is in the middle of the upper limit	(Mass/Volume)
A(C)	The tumour growth rate and drug consumption	(1/unit time)
M	The carrying capacity of the tumour volume	(Number/Volume)

2.1 Corrected Version

By writing the exact dimension of Eqs. (10) and (11) we find they are not quite correct, so we now have to discover the mistakes made in writing them.

$$\frac{\mathrm{dw}}{\mathrm{dt}} = \mathrm{A(C)}w(1 - \frac{w}{M}) - Fw(1 - \frac{w}{M}),$$

$$\frac{\text{number}}{\text{volume}*\text{time}} = \frac{1}{\text{time}} * \frac{\text{number}}{\text{volume}}\left(1 - \frac{\frac{\text{number}}{\text{volume}}}{\frac{\text{number}}{\text{volume}}}\right) - \frac{\text{volume}}{\text{time}} * \frac{\text{number}}{\text{volume}}\left(1 - \frac{\frac{\text{number}}{\text{volume}}}{\frac{\text{number}}{\text{volume}}}\right),$$

We discovered an inconsistency in the second term for Eq. (10) by looking at the dimensions; one way to correct this problem is to divide Fw by the quantity that holds the size dimensions. Since the only parameter available is V, we can regard $\frac{\text{Fw}}{\text{V}}$, as the appropriate correction. Note that Fw is the number of tumour cells leaving per unit of time, so $\frac{Fw}{V}$, is the effective density of tumour cells leaving per unit of time, thus we find the following corrected version of Eq. (10).

$$\frac{dw}{dt} = \text{A}(C)w\left(1 - \frac{w}{M}\right) - \frac{Fw}{V}\left(1 - \frac{w}{M}\right), \tag{12}$$

Now, we write a corrected version of Eq. (11).

$$\frac{\text{dC}}{\text{dt}} = FC_0 - \alpha\, A(C)w\left(1 - \frac{w}{M}\right) - \text{uC},$$

$$\frac{\text{mass}}{\text{volume}*\text{time}} = \frac{\text{volume}}{\text{time}} * \frac{\text{mass}}{\text{volume}} - \frac{\text{mass}}{\text{number}} * \frac{1}{\text{time}} * \frac{\text{number}}{\text{volume}}\left(1 - \frac{\frac{\text{number}}{\text{volume}}}{\frac{\text{number}}{\text{volume}}}\right) - \frac{\text{volume}}{\text{time}} * \frac{\text{mass}}{\text{volume}}.$$

A similar analysis applied to Eq.(11), and reveals that the terms FC_0 and uc should be divided by V after correcting by the same procedure, thus we arrive at the following corrected version of Eq. (13),

$$\frac{dC}{dt} = \frac{FC_0}{V} - \alpha\, A(C)w\left(1 - \frac{w}{M}\right) - \frac{uC}{V}. \tag{13}$$

2.2 Michaelis-Menten Kinetics

The growth rate increases with drug availability only to a certain threshold. The individual tumour cells can only absorb drugs and proliferate at a restricted pace. A mechanism that exemplifies this phenomenon is the Michaelis-Menten kinetics,

$$A(C) = \frac{A_{max}C}{A_n + C}\,. \tag{14}$$

As shown in Fig.2, the interaction of tumours with drugs is based on the drug catalysis of cell tumours, which is based on a similar model of enzyme catalysis by Michaelis and Menten, developed in [19]. Kinetics are characterised by a maximal rate of drug growth rate (denoted. A_{max})

and sensitivity to concentration (denoted A_n, referred to as the Michaelis–Menten constant) this latter term is the concentration of the drug that causes the growth rate to function at ½ A_{max} [20] . The reaction exhibits a slow rise in percentage when the concentrations are low. When concentrations are elevated, the drug's growth rate does not show a percentage change but reaches its maximum rate [21].

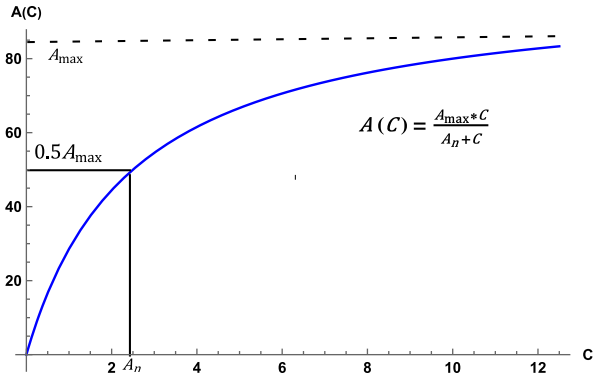

Figure 2. Michaelis-Menten kinetics: tumour growth rate and drug consumption A(C) is assumed to be a saturating function of drug concentration.

Substitute Eq. (14) in Eq. (12) and Eq.(13).

$$\frac{dw}{dt} = \left(\frac{A_{max}C}{A_n+C}\right) w(1-\frac{w}{M}) - \frac{Fw}{V}(1-\frac{w}{M}), \tag{15}$$

$$\frac{dC}{dt} = \frac{FC_0}{V} - \alpha\left(\frac{A_{max}C}{A_n+C}\right) w(1-\frac{w}{M}) - \frac{uC}{V}. \tag{16}$$

2.3 Nondimensionalisation of the Model

Rescaling, or nondimensionlising, is the process of transforming a collection of equations (often ordinary differential equations or partial differential equations) into dimensionless forms by modifying the scale of the variables in the model. For the selection of the optimal rescaling technique, we first analyse the situation in which the tumour and medications are uniformly distributed throughout space, thus spatially uniform.

We make a dimensional analysis of Eqs. (15) and (16). We then substitute $\mathrm{w} = \mathrm{w}^*\hat{\mathrm{w}}$, $\mathrm{C} = \mathrm{C}^*\hat{\mathrm{C}}$, $\mathrm{t} = \mathrm{t}^*\tau$. into Eq. (15), where w^*, C^* and t^* are those which have no dimensions and $\hat{\mathrm{w}}$, $\hat{\mathrm{C}}$, τ are those which represent the units of measurement.

$$\frac{dw^*\widehat{w}}{dt^*\tau} = \left(\frac{A_{max}\mathrm{C}^*\hat{C}}{A_n+\mathrm{C}^*\hat{C}}\right) w^*\widehat{w}(1-\frac{w^*\widehat{w}}{M}) - \frac{Fw^*\widehat{w}}{V}(1-\frac{w^*\widehat{w}}{M}). \quad (17)$$

Now we multiply both sides by τ, divided by $\widehat{w}$, and the result is

$$\frac{dw^*}{dt^*} = \tau\left(\frac{A_{max}\mathrm{C}^*\hat{C}}{A_n+\mathrm{C}^*\hat{C}}\right) w^*(1-\frac{w^*\widehat{w}}{M}) - \tau\frac{Fw^*}{V}(1-\frac{w^*\widehat{w}}{M}), \quad (18)$$

We take a common factor ($\hat{C}$) from the denominator of the first term.

$$\frac{dw^*}{dt^*} = \tau A_{max}\left(\frac{\mathrm{C}^*}{\frac{A_n}{\hat{C}}+\mathrm{C}^*}\right) w^*(1-\frac{w^*\widehat{w}}{M}) - \frac{\tau F}{V}w^*(1-\frac{w^*\widehat{w}}{M}). \quad (19)$$

We choose,

$$\tau = \frac{V}{F}, \hat{C} = A_n, \text{ and } \widehat{w} = M, \quad (20)$$

substitute Eq. (20) in Eq. (19),

$$\frac{dw^*}{dt^*} = \frac{V}{F}A_{max}\left(\frac{C^*}{1+C^*}\right) w^*(1-w^*) - w^*(1-w^*). \quad (21)$$

Let $\alpha_1 = \frac{V}{F}A_{max}$, (22)

$$\frac{dw^*}{dt^*} = \alpha_1(1-w^*)\left(\frac{\mathrm{C}^*}{1+\mathrm{C}^*}\right) w^* - w^*(1-w^*), \quad (23)$$

remove the stars from the equation, so that the final version of Eq.(15) is,

$$\frac{dw}{dt} = \alpha_1(1-w)\left(\frac{C}{1+C}\right) w - w(1-w). \quad (24)$$

Now, in a similar method, we substitute the definitions of the parameters w, C, and t into Eq. (16). We then get

$$\frac{d\mathrm{C}^*\hat{C}}{dt^*\tau} = \frac{FC_0}{V} - \alpha\left(\frac{A_{max}\mathrm{C}^*\hat{C}}{A_n+\mathrm{C}^*\hat{C}}\right) w^*\widehat{w}\left(1-\frac{w^*\widehat{w}}{M}\right) - \frac{u\mathrm{C}^*\hat{C}}{V}, \quad (25)$$

If we multiply both sides by τ, divided by $\hat{c}$, the result is,

$$\frac{dC^*}{dt^*} = \frac{\tau}{\hat{C}}\frac{FC_0}{v} - \alpha\tau\left(\frac{A_{max}C^*}{\frac{A_n}{\hat{C}}+C^*}\right) w^*\frac{\widehat{w}}{\hat{C}}(1-\frac{w^*\widehat{w}}{M}) - \frac{u}{V}*C^*\tau, \quad (26)$$

we substitute Eq. (20) in Eq. (26),

$$\frac{dC^*}{dt^*} = \frac{\frac{V}{F}}{A_n}\frac{F}{V}\, C_\circ - \alpha\, \frac{V}{F}\left(\frac{A_{max}C^*}{1+C^*}\right) w^* \frac{\hat{w}}{\hat{C}}(1 - w^*\frac{M}{M}) - \frac{u}{V}c^*\frac{V}{F}, \tag{27}$$

$$\frac{dC^*}{dt^*} = \frac{C_\circ}{A_n} - \alpha\frac{V}{F}\ \left(\frac{A_{max}C^*}{1+C^*}\right)\ w^*\frac{\hat{w}}{\hat{C}}(1 - w^*) - \frac{u}{F}C^*. \tag{28}$$

$$\frac{dC^*}{dt^*} = \alpha_2 - \frac{\alpha V A_{max}\hat{w}}{F\hat{C}} \cdot \frac{C^*}{1+C^*}\ w^*(1 - w^*) - \frac{u}{F}C. \tag{29}$$

Let $\alpha_2 = \frac{c_\circ}{A_n}, \alpha_3 = \frac{\alpha V A_{max} M}{F A_n}$ and $\alpha_4 = \frac{u}{F}$. (30)

And substitute Eq. (30) in Eq. (29).

$$\frac{dC^*}{dt^*} = \ \alpha_2 - \alpha_3\ (\frac{C^*}{1+C^*})\ w^*(1 - w^*) - \alpha_4 C. \tag{31}$$

We then remove the stars from the equation,

$$\frac{dC}{dt} = \ \alpha_2 - \alpha_3 w(1 - \mathrm{w})\left(\frac{C}{1+C}\right) - \alpha_4 C. \tag{32}$$

The system of Eq. (15) and (16) with eight parameters is transformed to the dimensionless system with four parameters after the nondimensionalisation process as

$$\dot{w} = \alpha_1(1 - w)\left(\frac{C}{1+C}\right) w - w(1 - w). \tag{33}$$

$$\dot{C} = \alpha_2 - \alpha_3 w(1 - \mathrm{w})\left(\frac{C}{1+C}\right) - \alpha_4 C. \tag{34}$$

Where hypotheses $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ in Eqs. (22) and (30) are dimensionless values.

3. LINEAR STABILITY ANALYSIS

In this section, we will discuss steady-state solutions for the model and, linear stability analysis for the continuous infusion model.

3.1 Steady-State Solutions for Model

The equilibrium points $(\bar{w}, \bar{C})$, for the dynamical system can be found by making the right-hand of Eqs. (33) and (34) equal to zero as a first step [22], $\dot{w} = 0$, $\dot{C} = 0$.

$$\alpha_1\bar{w}(1 - \bar{w})\left(\frac{\bar{C}}{1+\bar{C}}\right) - \bar{w}(1 - \bar{w}) = 0. \tag{35}$$

$$\alpha_2 - \alpha_3\bar{w}(1-\bar{w})\left(\frac{\bar{C}}{1+\bar{C}}\right) - \alpha_4\bar{C} = 0. \quad (36)$$

From Eq. (35),

$$\bar{w}(1-\bar{w})\left(\alpha_1\left(\frac{\bar{C}}{1+\bar{C}}\right) - 1\right) = 0,$$

either $\bar{w}(1-\bar{w}) = 0$, which leads to $\bar{w} = 0$ or $\bar{w} = 1$, $\alpha_1\left(\frac{\bar{C}}{1+\bar{C}}\right) = 1$, which leads to

$$\frac{\bar{C}}{1+\bar{C}} = \frac{1}{\alpha_1} \text{ leads to, } \bar{C}\,\alpha_1 = 1 + \bar{C}, \quad (37)$$

$$\bar{C} = \frac{1}{\alpha_1 - 1}. \quad (38)$$

Substituting $\bar{w} = 0$, and $\bar{w} = 1$ in Eq. (36), $\alpha_2 - 0 - \alpha_4\bar{C} = 0$, leads to, $\bar{C} = \frac{\alpha_2}{\alpha_4}$.

The first steady-state point is $S_1 = (\bar{w}_1, \bar{C}_1) = \left(0, \frac{\alpha_2}{\alpha_4}\right)$, and the second steady-state point is $S_2 = (\bar{w}_2, \bar{C}_2) = \left(1, \frac{\alpha_2}{\alpha_4}\right)$. (39)

Substituting Eq. (38) in Eq. (36) gives

$$\alpha_2 - \alpha_3\bar{w}(1-\bar{w})\left(\frac{\frac{1}{\alpha_1-1}}{1+\frac{1}{\alpha_1-1}}\right) - \alpha_4\,\frac{1}{\alpha_1-1} = 0,$$

$$\alpha_2 - \alpha_3\bar{w}(1-\bar{w})\left(\frac{1}{\alpha_1}\right) - \frac{\alpha_4}{\alpha_1-1} = 0,$$

$$\bar{w} = \frac{(-1+\alpha_1)\alpha_3 \mp \sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}.$$

The third steady state-point is (40)

$$S_3 = (\bar{w}_3, \bar{C}_3) = \left(\frac{(-1+\alpha_1)\alpha_3 + \sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right).$$

and the fourth steady-state point is

$$S_4 = (\bar{w}_4, \bar{C}_4) = \left(\frac{(-1+\alpha_1)\alpha_3 - \sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right).$$

To summarise this section, the steady-state of the model is

$$S_1 = (\bar{w}_1, \bar{C}_1) = \left(0, \frac{\alpha_2}{\alpha_4}\right). \quad (41)$$

$$S_2 = (\bar{w}_2, \bar{C}_2) = \left(1, \frac{\alpha_2}{\alpha_4}\right). \quad (42)$$

$$S_3 = (\bar{w}_3, \bar{C}_3) = \left(\frac{(-1+\alpha_1)\alpha_3+\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right), \tag{43}$$

$$S_4 = (\bar{w}_4, \bar{C}_4) = \left(\frac{(-1+\alpha_1)\alpha_3-\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right). \tag{44}$$

In the next section, we shall try to determine whether S_1, S_2, S_3 and S_4 are stable steady-states.

3.2 Linear Stability Analysis for Continuous Infusion Model

Linearisation is the use of analytical techniques specifically developed for studying linear systems to analyse the properties of a nonlinear function close to a precise point. The linearisation of a function is the identification of the first-order term of its Taylor expansion in the vicinity of the end of interest inside a system defined by the described equation [23]. The Jacobian matrix eigenvalues calculated at a hyperbolic equilibrium point may be used in the stability analysis of autonomous systems to determine the properties of that equilibrium. Presented below is a comprehensive explanation of the linearisation theorem. Further clarification is required for linearisation in time-varying systems [24], where the stability criteria are $Tr(J) < 0$ and $det(J) > 0$.

If we assume that the right-hand sides of Eqs. (33) and (34) as,

$$f(w, C) = \alpha_1 w(1-w)\left(\frac{C}{1+C}\right) - w(1-w). \tag{45}$$

$$g(w, C) = \alpha_2 - \alpha_3 w(1-w)\left(\frac{C}{1+C}\right) - \alpha_4 C. \tag{46}$$

then the nonlinear functions f and g are assumed to have steady-state solutions, denoted by $\bar{w}$ and $\bar{C}$,

The Jacobin matrix for the nonlinear system Eqs. (45)(46) is

$$J(w, C) = \begin{bmatrix} \frac{\partial f}{\partial w} & \frac{\partial f}{\partial c} \\ \frac{\partial g}{\partial w} & \frac{\partial g}{\partial c} \end{bmatrix}, \tag{47}$$

where,

$$\frac{\partial f}{\partial w} = -1 + 2w + \frac{C(1-2w)\alpha_1}{1+C}, \frac{\partial f}{\partial c} = -\frac{(-1+w)w\alpha_1}{(1+C)^2}, \tag{48}$$

$$\frac{\partial g}{\partial w} = \frac{C(-1+2w)\alpha_3}{1+C},\ \frac{\partial g}{\partial c} = \frac{(-1+w)w\alpha_3}{(1+C)^2} - \alpha_4. \tag{49}$$

We then substitute Eqs (48) and (49) in Eq (47).

$$J(w,C) = \begin{bmatrix} -1+2w+\frac{C(1-2w)\alpha_1}{1+C} & -\frac{(-1+w)w\alpha_1}{(1+C)^2} \\ \frac{C(-1+2w)\alpha_3}{1+C} & \frac{(-1+w)w\alpha_3}{(1+C)^2} - \alpha_4 \end{bmatrix}. \tag{50}$$

For the first equilibrium point $s_1 = \left(0, \frac{\alpha_2}{\alpha_4}\right)$,

$$J_{S_1} = J\left(0, \frac{\alpha_2}{\alpha_4}\right) = \begin{bmatrix} -\frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha_2+\alpha_4} & 0 \\ -\frac{\alpha_2\alpha_3}{\alpha_2+\alpha_4} & -\alpha_4 \end{bmatrix}. \tag{51}$$

$$Tr(J_{S_1}) = TrJ\left(0, \frac{\alpha_2}{\alpha_4}\right) = -\frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha 2+\alpha 4} - \alpha_4, \tag{52}$$

$$det\,(J_{S_1}) = detJ\left(0, \frac{\alpha_2}{\alpha_4}\right) = -\alpha_4\left(-\frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha 2+\alpha 4}\right) = \alpha_4\left(\frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha_2+\alpha_4}\right). \tag{53}$$

For the second equilibrium point $s_2 = \left(1, \frac{\alpha_2}{\alpha_4}\right)$,

$$J_{S_2} = J\left(1, \frac{\alpha_2}{\alpha_4}\right) = \begin{bmatrix} \frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha_2+\alpha_4} & 0 \\ \frac{\alpha_2\alpha_3}{\alpha_2+\alpha_4} & -\alpha_4 \end{bmatrix}. \tag{54}$$

$$Tr(J_{S_2}) = TrJ\left(1, \frac{\alpha_2}{\alpha_4}\right) = \frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha_2+\alpha_4} - \alpha_4, \tag{55}$$

$$det\,(J_{S_2}) = detJ\left(1, \frac{\alpha_2}{\alpha_4}\right) = -\alpha_4\left(\frac{\alpha_2-\alpha_1\alpha_2+\alpha_4}{\alpha 2+\alpha 4}\right). \tag{56}$$

For the third equilibrium point

$$s_3 = \left(\frac{(-1+\alpha_1)\alpha_3+\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right),$$

$$J_{S_3} = J\left(\frac{(-1+\alpha_1)\alpha_3+\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right) = \tag{57}$$

$$\begin{bmatrix} 0 & \frac{(-1+\alpha_1)((-1+\alpha_1)\alpha_2-\alpha_4)}{\alpha_3} \\ \frac{\sqrt{(-1+\alpha_1)\alpha_3[(-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4]}}{(-1+\alpha_1)\alpha_1} & -\frac{(-1+\alpha_1)^2\alpha_2+\alpha_4}{\alpha_1} \end{bmatrix},$$

$$Tr(J_{S_3}) = -\left(\frac{(-1+\alpha_1)^2\alpha_2+\alpha_4}{\alpha_1}\right). \tag{58}$$

$$det(J_{S_3}) = \frac{((-1+\alpha_1)\alpha_2-\alpha_4)\sqrt{(-1+\alpha_1)\alpha_3[-4\alpha_1^2\alpha_2-\alpha_3+\alpha_1(4\alpha_2+\alpha_3+4\alpha_4)]}}{\alpha_1\alpha_3}, \quad (59)$$

For the fourth equilibrium point $s_4 =$

$$\left(\frac{(-1+\alpha_1)\alpha_3+\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right) =,$$

$$J_{S_4} = J\left(\frac{(-1+\alpha_1)\alpha_3+\sqrt{(-1+\alpha_1)\alpha_3((-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4))}}{2(-1+\alpha_1)\,\alpha_3}, \frac{1}{\alpha_1-1}\right) = \quad (60)$$

$$\begin{bmatrix} 0 & \frac{(-1+\alpha_1)((-1+\alpha_1)\alpha_2-\alpha_4)}{\alpha_3} \\ -\frac{\sqrt{(-1+\alpha_1)\alpha_3[(-1+\alpha_1)(-4\alpha_1\alpha_2+\alpha_3)+4\alpha_1\alpha_4]}}{(-1+\alpha_1)\alpha_1} & -\frac{(-1+\alpha_1)^2\alpha_2+\alpha_4}{\alpha_1} \end{bmatrix}.$$

$Tr(J_{S_4}) = -\frac{(-1+\alpha_1)^2\alpha_2+\alpha_4}{\alpha_1}$, it is clear that $Tr(J_{S_4}) < 0$. (61)

$$det(J_{S_4}) = \frac{(-((-1+\alpha_1)\alpha_2)+\alpha_4)\sqrt{(-1+\alpha_1)\alpha_3[-4\alpha_1^2\alpha_2-\alpha_3+\alpha_1[4\alpha_2+\alpha_3+4\alpha_4]]}}{\alpha_1\alpha_3}, \quad (62)$$

The trace and determent values change depending on the values of the α_1, α_2, α_3, α_4, and according to the determination and tracking values we determine whether the point is stable or unstable.

In conclusion to the delivery of drugs by continuous infusion system, we will interpret the various results to extract helpful information from the mathematical analysis. To summarise our findings, we have determined that a sensibly operating delivery of drugs will always have a stable steady-state solution with the tumour. Remember that this equilibrium can be biologically meaningful provided that, α_1,α_2, α_3 and α_4 satisfy the inequalities

$\alpha_1 > 1$. From Eq. (38), $\alpha_1 - 1 > 0$, leads to $\alpha_1 > 1$, (63)

The steady-state points appear in five cases according to the conditions which are summarised in Table 2.

Table 2. Cases and conditions under which points appear.

Cases	Conditions	Point 1	Point 1	Point 3	Point 4
Case 1	$0 < \alpha_1 \leq 1$	Yes	Yes	No	No
Case 2	$1 < \alpha_1 < 1 + \frac{\alpha_4}{\alpha_2}$	Yes	Yes	No	Yes
Case 3	$\alpha_1 = 1 + \frac{\alpha_4}{\alpha_2}$	Yes	Yes	No	No
Case 4	$\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 > 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$	Yes	Yes	Yes	Yes
Case 5	$\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 < 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$	Yes	Yes	No	No

Note that in the table above.

- Yes, mean $w \geq 0$ and $c \geq 0$.
- No, mean $w < 0$ and $c < 0$.

4. Numerical Results and Discussion

In this section, the interaction between tumour volume and drug concentration by the infusion pump is studied. We apply a numerical case for the five substitute values in Table 3 and Table 4. MATHEMATICA codes are used to find the equilibrium points of the model in Eqs. (45) and (46) and draw phase-plane diagrams; phase diagrams can depict each of these situations graphically. MATLAB R2023a is used to find out the numerical solution of the system of Eqs. (45) and (46), where the blue curve indicates the tumour density and the red curve indicates the drug concentration.

4.1 Standard Parameters Set

To apply numerical examples to Eqs. (35) and (36), we must choose values that satisfy the conditions in Table 2 and take different cases to show what happens in each case; therefore, we choose the set of parameters mentioned in Table 3. For the parameter V, according to a 2020 article, [25], there are around 10.5 pints (5 litres) mean (V=5000 ml) of blood in the average human adult body, although this will vary depending on various factors. The parameter F is theoretically known since they are calibrated by the manufacturer of the pump; atypical value of F is in the range of (1-6 ml/day) [26]. A_{max} is the maximal tumour reproduction rate I and is equal to the amount of the dose given. If we take the value of the dose given in the logistic model [7], r =0.022828 this leads

to $A_{max} = 0.022828$. A_n is defined as the amount of medication at which the growth rate is in the middle of the upper limit $A_n = 0.022828$.

Table 3. The value of model parameters and their units.

Symbol	Description	Typical value	Unite	Source
V	The volume of the blood in direct contact with the tumour area	131.41755, 394.25267, 525.67022, 657.08778, 657.08778.	Ml	[25]
F	The pump flow rate	6	*(Ml/day)*	[26]
A_{max}	The maximal tumour reproduction rate	0.022828	*(1/day)*	[7]
$C_\circ$	The concentration of the drug in the infusion pump	0.022828	*(Mass/ml)*	[7]
A_n	The amount of medication at which the growth rate is in the middle of the upper limit	0.022828	*(Mass/ ml)*	estimated
M	Carrying capacity	15.21866, 15.21866, 15.21866, 58.33771, 58.33771.	*(Number/volume)*	estimated
α	The drug exhaustion rate	0.0005.	*(Mass/number)*	estimated
U	Rate of blood flow away from the tumour site.	4.39.	*(Ml/day)*	estimated

We will substitute the values in Table 3. into Eqs. (22) and (31) we will get the values of α_1, α_2, α_3 and α_4 as in the following Table 4.

Table 4. Dimensionless parameter values of the model.

Nondimensional parameter	Dimension form	value	Unite
α_1	$\frac{V}{F} A_{max}$	0.5, 1.5, 2, 2.5, 2.5.	dimensionless
α_2	$\frac{C_\circ}{A_n}$	1, 1, 1, 1, 1.	dimensionless
α_3	$\frac{\alpha v A_{max} M}{A_n}$	1, 1, 1, 3.8333, 3.333.	dimensionless
α_4	$\frac{u}{F}$	1, 1, 1, 1, 1.	dimensionless

Finally, the interpretation of these equilibrium points is as follows: Using several examples as shown in Table 4, we solve the equations to find the points and identify the stable and unstable points. We take different cases as in Table 2 and observe how the solution behaves. A numerical

simulation of the system of Eqs. (45) and (46) is performed to illustrate the analytical behaviour to provide a picture of the level. As a result, the model can be predicted in terms of how it will behave under a variety of initial conditions but for a pre-defined set of parameter values. The curve (path) of the initial values is shown in Fig.3. Using MATHEMATICA(13.2) and seeing the agreement of the qualitative analysis with the numerical solution later, we take the stable points to denote the tumour density and the drug dose.

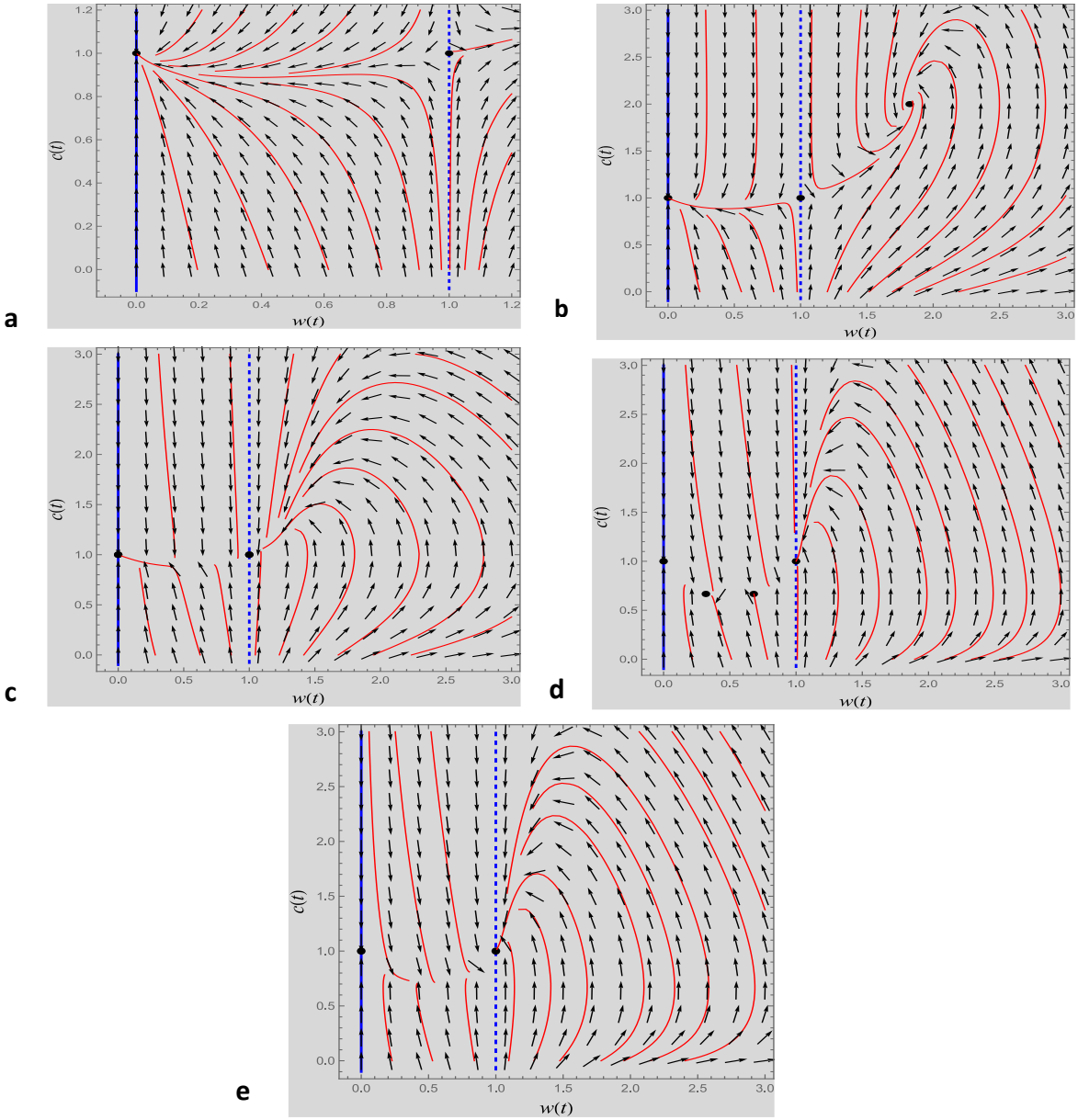

Figure 3. MATHEMATICA generated a phase-plane diagram (the delivery of drugs by continuous infusion of a two-species system) with

a) Case one If $0 < \alpha_1 \leq 1$ when $\alpha_1 = 0.5, \alpha_2 = 1, \alpha_3 = 1,\ \alpha_4 = 1.$

b) Case two If $1 < \alpha_1 < 1 + \frac{\alpha_4}{\alpha_2}$ when $\alpha_1 = 1.5, \alpha_2 = 1, \alpha_3 = 1,\ \alpha_4 = 1.$

c) Case three If $\alpha_1 = 1 + \frac{\alpha_4}{\alpha_2}$ when $\alpha_1 = 2, \alpha_2 = 1, \alpha_3 = 1,\ \alpha_4 = 1.$

d) Case four If$\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 > 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$, $\alpha_1 = 2.5, \alpha_2 = 1, \alpha_3 = 3.8333, \alpha_4 = 1.$

e) Case five If$\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 < 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$, $\alpha_1 = 2.5, \alpha_2 = 1, \alpha_3 = 2.8333,\ \alpha_4 = 1.$

Case Study One,

It is seen from the numerical results of the first case that meet the condition $0 < \alpha_1 \leq 1$, that it has two points, one is stable $(0,1)$ and the other is unstable $(1,1)$ where $\alpha_1 = 0.5, \alpha_2 = 1, \alpha_3 = 1,$ and $\alpha_4 = 1.$ in Fig. 4 (a), and (b) that the tumour goes to the stable point $(0,1)$. We took different initial conditions greater than the stable point when the initial condition was w_0=0.5, C=1.5 and noticed that the curve was heading towards the stable value as in Fig.4(a) and we took different initial conditions close to the stable point when the initial condition was w_0=0.5, C=0.5 and noticed that the curve was heading towards the stable value as in Fig.4(b) This is consistent with the analytical aspect of the problem, which is the linear stability analysis in Fig.3(a). We notice that there is one stable point $(0,1)$, so to find the real values with dimension units of tumours and drugs, we use $w = w^*\hat{w} = 0 * 15.21866 = 0$ (Number/Volume), $C = C^*\hat{C} = 1 * 0.022828 = 0.022828$ (Mass/Volume).

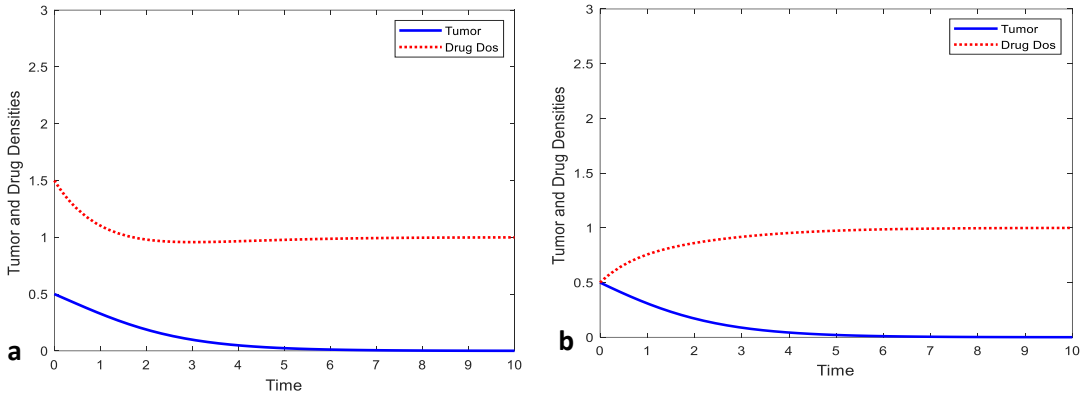

Figure 4. MATLAB numerical results of the delivery of drugs by continuous infusion of a two-species system, $\alpha_1 = 0.5, \alpha_2 = 1, \alpha_3 = 1, \alpha_4 = 1.$

a) When the initial condition w_0=0.5, C=1.5. **b)** When the initial condition w_0=0.5, C=0.5.

Case Study Two

From the numerical results of the second case that meets the condition, $1 < \alpha_1 < 1 + \frac{\alpha_4}{\alpha_2}$, it is seen that it has three points, two are stable $(0,1)$, $(1.82288,2)$ and the other is unstable $(1,1)$ where $\alpha_1 = 1.5, \alpha_2 = 1, \alpha_3 = 1, \alpha_4 = 1$, in Fig. 5 (a),(b),(c), and (d) the tumour goes to the point where the tumour is stable when the point is stable $(0,1)$. We took different initial conditions greater than the stable point when the initial condition was w_0=0.5, C=1.5 and noticed that the curve is heading towards the stable value as in Fig.5(a) and we took different initial conditions close to the stable point when the initial condition was w_0=0.5, C=0.5, and noticed that the curve is heading towards the stable value as in Fig.5(b). When the point was stable $(1.82288,2)$ we took different initial conditions greater than the stable point when the initial condition was w_0=1.9, C=2.2 and we noticed that the curve was heading towards the stable value as in Fig.5(c). We took different initial conditions smaller than the stable point when the initial condition was w_0=1.3, C=1.8, and noticed the curve heading towards the stable value as in Fig.5(d). This is consistent with the analytical aspect of the problem, which is the linear stability analysis in Fig.3(b). Noting that there are two stable points $(0,1)$ and $(1.82288,2)$, to find the real values with dimension units of tumours and drugs, we use $w = w^*\hat{w} = 0 * 15.21866 = 0$, $C = C^*\hat{C} = 1 * 0.022828 = 0.022828$, $w = w^*\hat{w} = 1.822880 * 15.21866 = 27.74179$ (Number/Volume), $C = C^*\hat{C} = 2 * 0.022828 = 0.045656$ (Mass/Volume).

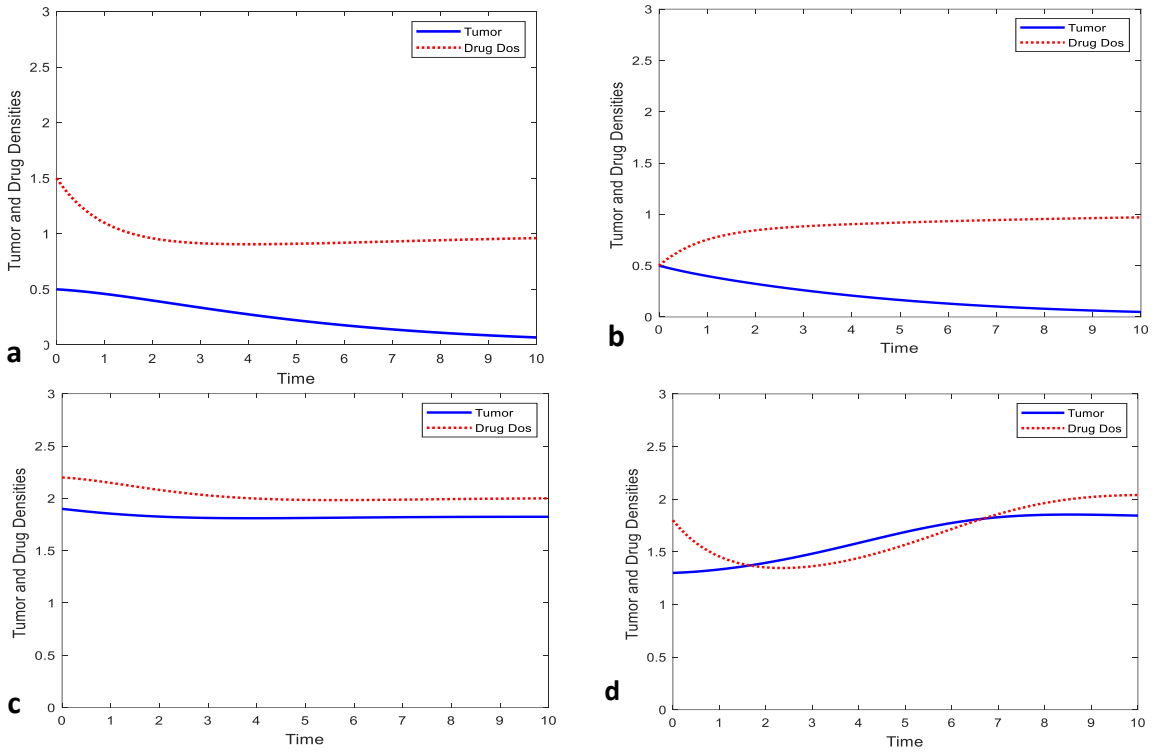

Figure 5. MATLAB numerical results of the delivery of drugs by continuous infusion of a two-species system, $\alpha_1 = 1.5, \alpha_2 = 1, \alpha_3 = 1,\ \alpha_4 = 1$

a) When the initial condition w_0=0.5, C=1.5.**b)** When the initial condition w_0=0.5, C=0.5.

c) When the initial condition w_0=1.9, C=2.2.**d)** When the initial condition w_0=1.3, C=1.8.

Case Study Three

It is seen from the numerical results of the third case that meets the condition. $\alpha_1 = 1 + \frac{\alpha_4}{\alpha_2}$, that it has two points, two are stable $(0,1), (1,1)$ where $\alpha_1 = 2, \alpha_2 = 1, \alpha_3 = 1$, and $\alpha_4 = 1$, in Fig. 6 (a),(b),(c), and (d) the tumour goes to the point where the tumour is stable $(0,1)$. We took different initial conditions greater than the stable point when the initial condition was w_0=0.5, C=1.5 and noticed the curve heading towards the stable value as in Fig.5(a). We took different initial conditions close to the stable point when the initial condition was w_0=0.5, C=0.5, and noticed that the curve was heading towards the stable value as in Fig.5(b). When the point was stable $(1,1)$ we took different initial conditions greater than the stable point when the initial

condition was w_0=1.8, C=1.8, and noticed that the curve was heading towards the stable value as in Fig.6(c). We took different initial conditions smaller than the stable point when the initial condition was w_0=0.9, C=0.9, and noticed that the curve was heading towards the stable value as in Fig.6(d). This is consistent with the analytical aspect of the problem, which is the linear stability analysis in Fig.3(c). We notice that there are two stable points (0,1) and (1,1), $w = w^*\hat{w} = 0 * 15.21866 = 0$, $C = C^*\hat{C} = 1 * 0.022828 = 0.022828$. To find the real values with dimension units of tumours and drugs, we use $w = w^*\hat{w} = 1 * 15.21866 = 15.21866$ (Number/Volume), $C = C^*\hat{C} = 1 * 0.022828 = 0.022828$ (Mass/Volume).

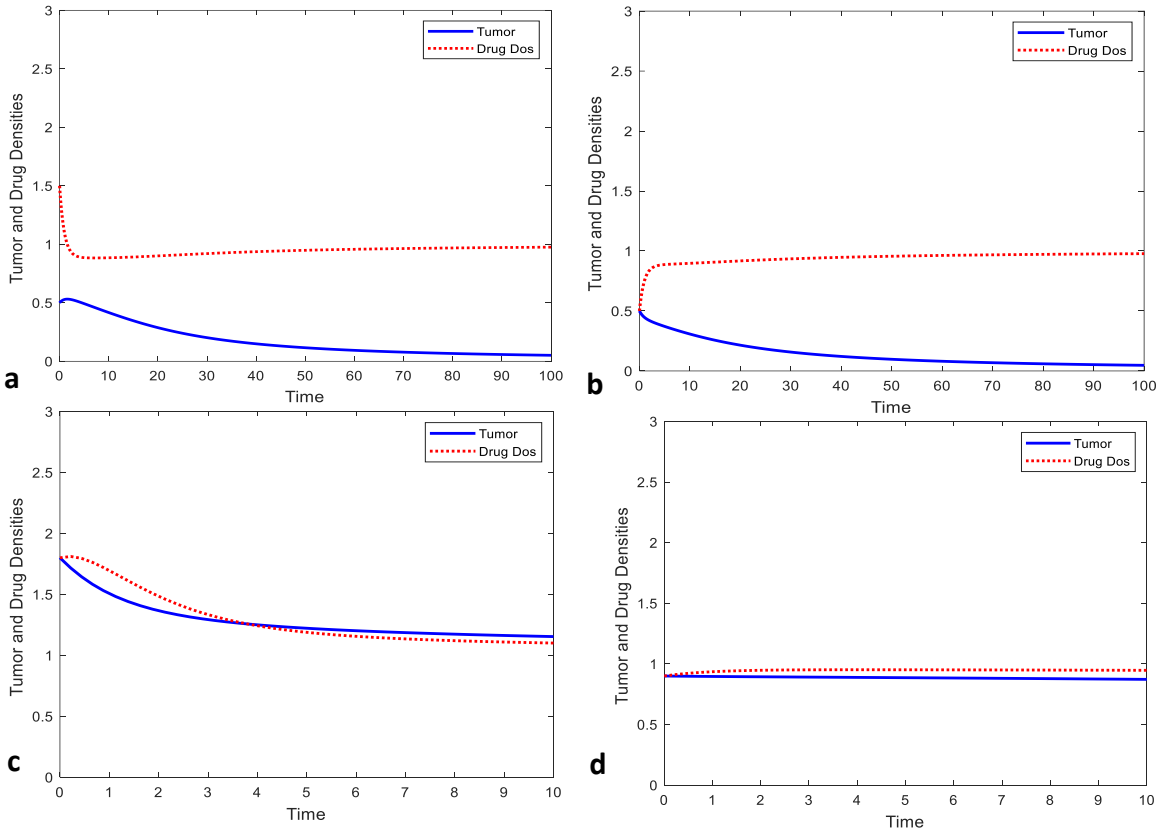

Figure 6. MATLAB numerical results of the delivery of drugs by continuous infusion of a two-species system, $\alpha_1 = 2, \alpha_2 = 1, \alpha_3 = 1, \alpha_4 = 1$.

a) When the initial condition w_0=0.5, C=1.5. **b)** When the initial condition w_0=0.5, C=0.5.

b) When the initial condition w_0=1.8, C=1.8. **c)** When the initial condition w_0=0.9, C=0.9.

Case Study Four

It is seen from the numerical results of the fourth case that meets the condition, $\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 > 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$, that it has four points, two are stable $(1,1)$, $(0.319421, 0.666667)$, and two are unstable $(0,1)$, $(0.680579, 0.666667)$ where $\alpha_1 = 2.5$, $\alpha_2 = 1$, $\alpha_3 = 3.8333$, $\alpha_4 = 1$, in Fig. 7(a),(b),(c), and (d) the tumour goes to the point where the tumour is stable. We took different initial conditions greater than the stable point when the initial condition was w_0=1.5, C=1.5 and noticed that the curve was heading towards the stable value as in Fig.7(a) and we took different initial conditions smaller than the stable point when the initial condition was w_0=0.9, C=0.9, and noticed that the curve was heading towards the stable value as in Fig.7(b). When the point was stable, $(0.319421, 0.666667)$, we took different initial conditions greater than the stable point when the initial condition was w_0=0.4, C=0.8, and noticed the curve heading towards the stable value as in Fig.7(c). We then took different initial conditions smaller than the stable point when the initial condition was w_0=0.2, C=0.4, and noticed that the curve was heading towards the stable value as in Fig.7(d). This is consistent with the analytical aspect of the problem, which is the linear stability analysis in Fig.3(d). We notice that there are two stable points $(1,1)$ and $(0.319421, 0.666667)$, and to find the real values with dimension units of tumours and drugs, we use $w = w^* \hat{w} = 1 * 58.33771 = 58.33771$, $C = C^* \hat{C} = 1 * 0.022828 = 0.022828$, $w = w^* \hat{w} = 0.319421 * 58.33771 = 18.63428$, where the tumour (w) (Number/Volume), $C = C^* \hat{C} = 0.666667 * 0.022828 = 0.01521$, (Mass/Volume).

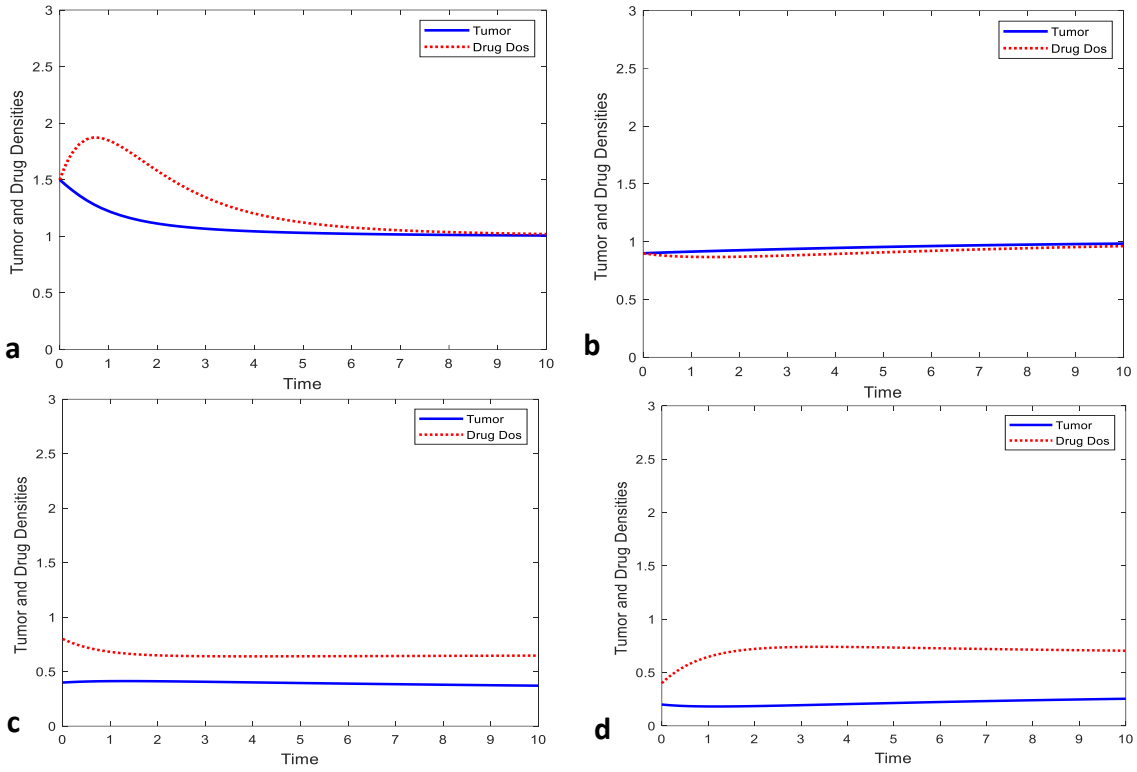

Figure 7. MATLAB numerical results of the delivery of drugs by continuous infusion of a two-species system, $\alpha_1 = 2.5, \alpha_2 = 1, \alpha_3 = 3.8333,\ \alpha_4 = 1.$

a) When the initial condition w_0=1.5, C=1.5. **b)** When the initial condition w_0=0.9, C=0.9.

c) When the initial condition w_0=0.4, C=0.8. **d)** When the initial condition w_0=0.2, C=0.4.

Case Study Five

It is seen from the numerical results of the fifth case that meets the condition, $\alpha_1 > 1 + \frac{\alpha_4}{\alpha_2}$ and $\alpha_3 < 4\alpha_1\left(\alpha_2 - \frac{\alpha_4}{\alpha_1 - 1}\right)$, that it has two points, one is stable $(1,1)$, and one is unstable $(0,1)$ where $\alpha_1 = 2.5, \alpha_2 = 1, \alpha_3 = 2.8333,\ \alpha_4 = 1$, in Fig. 8(a) and (b) the tumour goes to the point where the tumour is stable $(1,1)$. We took different initial conditions greater than the stable point when the initial condition was w_0=2, C=2, and noticed that the curve was heading towards the stable value as in Fig.8(a). We took different initial conditions smaller than the stable point when the initial condition was w_0=0.8, C=0.9, and noticed that the curve was heading towards the stable value as in Fig.8(b). This is consistent with the analytical aspect of the

problem, which is the linear stability analysis in Fig.3(e). We notice that there is one stable point (1,1), so to find the real values with dimension units of tumours and drugs, we use

$w = w^{*}\hat{w} = 1 * 58.33771 = 58.33771$, $C = C^{*}\hat{C} = 1 * 0.022828 = 0.022828$,

$w = w^{*}\hat{w} = 1 * 58.33771 = 58.33771$, (Number/Volume)

$C = C^{*}\hat{C} = 1 * 0.022828 = 0.022828$, (Mass/Volume).

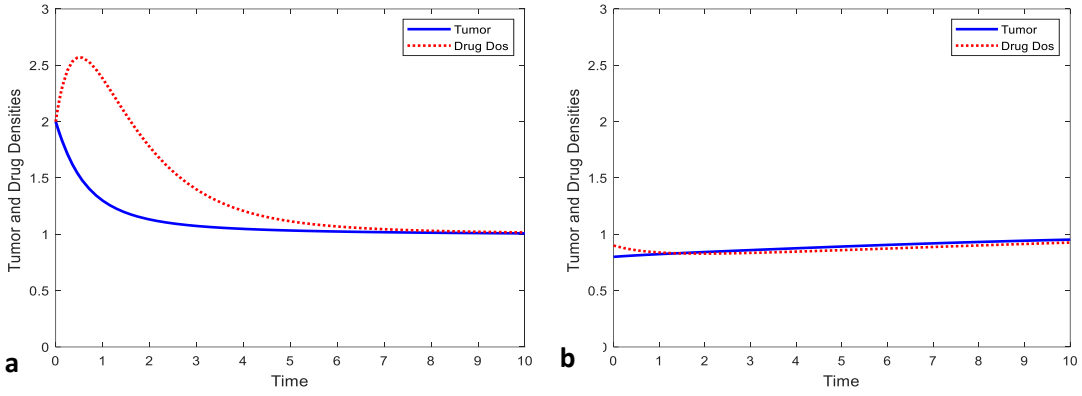

Figure 8. MATLAB numerical results of the delivery of drugs by continuous infusion of a two-species system, $\alpha_1 = 2.5$, $\alpha_2 = 1$, $\alpha_3 = 2.8333$, $\alpha_4 = 1$.

a) When the initial condition w_0=2, C=2. **b)** When the initial condition w_0=0.8, C=0.9.

5. CONCLUSION

In this paper, we have incorporated logistic growth with Michaelis-Menten kinetics to describe the interaction between tumour growth and chemotherapy drug concentration. The formulation of the model was corrected and rescaled by a nondimensionalisation process .The resulting model consists of coupled ordinary differential equations with nonlinear source terms describing tumour growth and drug exhaustion rate. One of the main advantages of this approach is that the model is amenable to mathematical analysis, providing greater insights into the nature of the numerical results. For instance, the linear stability analysis and identify parameter regimes for which stable points arise. In the simulations of numerical results and discussion section, the parameter values of the kinetics for all five cases guarantee that the tumour cells will decline with using chemotherapy drugs via a continuous infusion pump.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

REFERENCES

[1] Z. Liu, C. Yang, A mathematical model of cancer treatment by radiotherapy, Comput. Math. Methods Med. 2014 (2014), 172923. https://doi.org/10.1155/2014/172923.

[2] NHS, Overview: Chemotherapy, https://www.nhs.uk/conditions/chemotherapy, Accessed: Oct. 09, 2024.

[3] FDA, Infusion pumps, https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/infusion-pumps. Accessed: Sep. 22, 2024.

[4] ParagonCare, What is an infusion pump and how does it work? https://paragoncare.com.au/news/what-infusion-pump-and-how-does-it-work. Accessed: Sep. 22, 2024.

[5] S. Jawad, M. Winter, Z.A.S.A. Rahman, et al. Dynamical behavior of a cancer growth model with chemotherapy and boosting of the immune system, Mathematics 11 (2023), 406. https://doi.org/10.3390/math11020406.

[6] S.N. Al- Azzawi, F.A. Shihab, Modified mathematical model of tumor treatment by radiotherapy, Baghdad Sci. J. 17 (2020), 0841. https://doi.org/10.21123/bsj.2020.17.3.0841.

[7] S. Sabah Hassan, H.M. Al-Saedi, Comparative study of tumor growth based on single species models, BIO Web Conf. 97 (2024), 00118. https://doi.org/10.1051/bioconf/20249700118.

[8] U. Ledzewicz, H. Schättler, Combination of antiangiogenic treatment with chemotherapy as a multi‐input optimal control problem, Math. Methods Appl. Sci. 45 (2022), 3058–3082. https://doi.org/10.1002/mma.7977.

[9] S. Sharpe, H.M. Dobrovolny, Predicting the effectiveness of chemotherapy using stochastic ODE models of tumor growth, Commun. Nonlinear Sci. Numer. Simul. 101 (2021), 105883. https://doi.org/10.1016/j.cnsns.2021.105883.

[10] P. Schlicke, C. Kuttler, C. Schumann, How mathematical modeling could contribute to the quantification of metastatic tumor burden under therapy: insights in immunotherapeutic treatment of non-small cell lung cancer, Theor. Biol. Med. Model. 18 (2021), 11. https://doi.org/10.1186/s12976-021-00142-1.

[11] H.Y. Liu, H.L. Yang, L.G. Yang, Dynamics analysis in a tumor-immune system with chemotherapy, Chin. Phys. B 30 (2021), 058201. https://doi.org/10.1088/1674-1056/abcf49.

[12] R. Padmanabhan, N. Meskin, A.E.A. Moustafa, Chemotherapy models, in: Mathematical Models of Cancer and Different Therapies, Springer, Singapore, 2021: pp. 55–75. https://doi.org/10.1007/978-981-15-8640-8_3.

[13] R.W. Jones, Application of optimal control theory in biomedicine, Automatica 23 (1987), 130–131. https://doi.org/10.1016/0005-1098(87)90126-9.

[14] B.F. Dibrov, A.M. Zhabotinsky, Y.A. Neyfakh, et al. Mathematical model of cancer chemotherapy. periodic schedules of phase-specific cytotoxic-agent administration increasing the selectivty of therapy, Math. Biosci. 73 (1985), 1–31. https://doi.org/10.1016/0025-5564(85)90073-2.

[15] C.M. Newton, Biomathematics in oncology: modeling of cellular systems, Annu. Rev. Biophys. Bioeng. 9 (1980), 541–579. https://doi.org/10.1146/annurev.bb.09.060180.002545.

[16] P.J. Blackshear, T.D. Rohde, F. Prosl, et al. The implantable infusion pump: a new concept in drug delivery, Med. Prog. Technol. 6 (1979), 149–161.

[17] J. Aroesty, T. Lincoln, N. Shapiro, et al. Tumor growth and chemotherapy: mathematical methods, computer simulations, and experimental foundations, Math. Biosci. 17 (1973), 243–300. https://doi.org/10.1016/0025-5564(73)90072-2.

[18] J. Malinzi, K.B. Basita, S. Padidar, et al. Prospect for application of mathematical models in combination cancer treatments, Inf. Med. Unlocked 23 (2021), 100534. https://doi.org/10.1016/j.imu.2021.100534.

[19] Wikipedia, Leonor Michaelis, https://en.wikipedia.org/w/index.php?title=Leonor_Michaelis, Accessed: Mar. 30, 2024.

[20] T.P. Kenakin, Predicting agonist effect, in: Pharmacology in Drug Discovery, Elsevier, 2012: pp. 37–50. https://doi.org/10.1016/B978-0-12-384856-7.00003-3.

[21] V. Leskovac, Comprehensive enzyme kinetics, Kluwer Academic/Plenum Pub., New York, 2003.

[22] N.W. Tschoegl, Fundamentals of equilibrium and steady-state thermodynamics, Elsevier, 2000.

[23] Wikipedia, Linearization, https://en.wikipedia.org/w/index.php?title=Linearization, Accessed: Mar. 19, 2024.

[24] P. Hartman, A lemma in the theory of structural stability of differential equations, Proc. Amer. Math. Soc. 11 (1960), 610–620. https://doi.org/10.1090/S0002-9939-1960-0121542-7.

[25] R. Sharma, S. Sharma, Physiology, blood volume, StatPearls Publishing, 2024.

[26] L. Edelstein-Keshet, Mathematical models in biology, SIAM, 2005. https://doi.org/10.1137/1.9780898719147.