Mathematical model of brain tumour with chemotherapy
treatment

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Abstract In recent years, it became clear that a better understanding of the interactions among the main elements involved in the cancer network is necessary for the treatment of cancer and the suppression of tumour growth. In this work we propose a system of coupled differential equations that model brain tumour under treatment by chemotherapy, which considers interactions among the glial cells, the cancer cells, the neurons, and the chemotherapeutic agents. We study the conditions for the tumour growth to be eliminated, and identify values of the parameters for which the inhibition of the tumour growth is obtained with a minimal loss of healthy cells.

Keywords chemotherapy · tumour · brain

1 Introduction

Cells growth is a phenomenon that has been studied in the fields of mathematics, biology, physics, etc (Adam et al., 1996). Unregulated cells growth may be associated with a wide group of diseases, where cells become a lump or cause illness. As a result, several growth models related to tumours have appeared in the literature (Mechón & Condat, 2008; Aroesty et al., 1973), such as models.
for the metastasis (Pinho et al., 2002), the lack of nutrients (Scaleranpdi et al., 1999), the competition for resources, and the cytotoxic activity produced by the immune response (Cattani et al., 1988; Wheldon, 1988).

The most common malignant intrinsic primary tumours of the adult human brain are the gliomas (Inaba et al., 2011). This name is coined due to the fact that the cancer attacks the glial cells, leaving the neurons intact. However, the death of glial cells affects the neurons, because they are responsible for delivering nutrients, to provide structural support to them (Glees, 1955), and to control the biochemical compositions of the fluid surrounding the neurons. Chemotherapeutic agents affect all the cells (Schuette, 2004). The neurons are the main responsible for the information processing from external and internal environments (Otis & Sofronie, 2008; Fieldes, 2006; Shaham, 2005). However, glial cells are also responsible for the processing of information by mediating the neural signal. Neurons and their synapses fail to function without glial cells.

In this paper, we propose a mathematical model for the growth of brain cancer, where the cancer only attacks the glial cells, causing a glioma (Bulstrode, 2012; Stupp et al., 2009). The cancer cells arise from normal cells. The transformation is permanent. A cancerous cell never returns to be normal again, resulting in invasion and destruction of surrounding healthy tissue by cancer cells (Alberts et al., 1994; Hahn & Weinberg, 2002). In our model, we consider interactions among glial cells, neurons, cancer cells, and the chemotherapeutic agent. The novelty of our model was to introduce the interaction between glial cells and neurons. With this in mind, the main features of our model are: (i) treatment will likely preserve glial cells, (ii) cancer can be eliminated, but not without also destroying neurons. If the treatment is ceased without the complete elimination of cancer cells, concentration of cancer cells increases, (iii) there is an optimal duration for the treatment that reduces significantly the number of cancer cells by preserving the levels of glial cells and minimising the impact on the neural populations.

This paper is organized as follows: in Section 2 we introduce the coupled differential equations modelling the suppression of glioma by a chemotherapeutic agent. In Section 3, we discuss about equilibria and local stabilities of our model. An equilibrium point for example is a solution of the model that describes a successful chemotherapy, that is a complete elimination of cancer cells. In section 4, we study what are the optimal parameters in the model that lead to a drastic reduction of cancer cells, but still preserving glial and neural cells at normal levels. In the last section, we present the conclusions.

### 2 Brain tumour model

Figure 1 shows a diagram illustrating the many agents, and their interactions being considered in our model. The cancer cells only attack the glial cells. Neurons are not attacked by cancer cells, and they interact with glial cells. The chemotherapeutic agent behaves as a predator acting on all cells.
Our model is described by
\[
\begin{align*}
\frac{dG(t)}{dt} &= \Omega_1 G(t) \left(1 - \frac{G(t)}{K}\right) - \Psi_1 G(t)C(t) - \frac{P_1 G(t)Q(t)}{A_1 + G(t)}, \\
\frac{dC(t)}{dt} &= \Omega_2 C(t) \left(1 - \frac{C(t)}{K}\right) - \Psi_2 G(t)C(t) - \frac{P_2 C(t)Q(t)}{A_2 + C(t)}, \\
\frac{dN(t)}{dt} &= \psi \dot{G}(t)H(-\dot{G})N(t) - \frac{P_3 N(t)Q(t)}{A_3 + N(t)}, \\
\frac{dQ(t)}{dt} &= \Phi - \zeta Q(t),
\end{align*}
\]
where \(G\) represents the glial cells concentration (in \(\text{kg/m}^3\)), \(C\) represents the cancerous cells concentration (in \(\text{kg/m}^3\)), \(N\) the neurons cells concentration (in \(\text{kg/m}^3\)), \(Q\) is the concentration of the chemotherapeutic agent (in \(\text{mg/m}^2\)), and \(H(x)\) is the Heaviside function, defined as
\[
H(x) = \begin{cases} 
0, & x < 0, \\
\frac{1}{2}, & x = 0, \\
1, & x > 0.
\end{cases}
\] (5)

Table 1 shows the parameters that we consider. In Eqs. (1) and (2), the first term is the logistic growth, the second term is the interaction between glial and cancer cells, and the last term is the effect of the chemotherapeutic agent. The first term of Eq. (3) is related with the decrease in the neural population due to glial cells death, and the second term is the interaction with the chemotherapeutic agent. Equation (4) describes the dynamics of the chemotherapeutic agent, presenting an exponential decay in concentration. Our main contribution in this work is to model the dependence of neurons on the glial cells, described by the term \(\psi \dot{G}(t)H(-\dot{G})N(t)\), in Eq. (3). When the glial concentration decreases, \(\dot{G}\) becomes negative, making this term to contribute negatively to \(N(t)\), leading to a decrease in the neuron concentration. Whereas, the term is null if the rate of glial concentration, \(\dot{G}\), is null or positive. Therefore, a decrease in the glial concentration causes death of neurons, whereas an increase does not contribute to a change in the neural population.
Table 1 Description of the parameters according to literature.

<table>
<thead>
<tr>
<th>Description</th>
<th>Parameter</th>
<th>Values</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferation rate</td>
<td>Ω1 for GCs</td>
<td>0.0068 day⁻¹</td>
<td>$\Omega_1 \leq \Omega_2$ (Pinho et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>Ω2 for CCs</td>
<td>0.012 day⁻¹</td>
<td>Reference (Spratt &amp; Spratt, 1964)</td>
</tr>
<tr>
<td>Loss influences ψ for N due GCs</td>
<td></td>
<td>0 – 0.02</td>
<td>Reference (Pinho et al., 2013)</td>
</tr>
<tr>
<td>Predation coefficients P1 for GCs</td>
<td></td>
<td>2.4 $\times$ 10⁻⁵ m²(mg.day)⁻¹</td>
<td>Reference (Pinho et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>P2 for CCs</td>
<td>2.4 $\times$ 10⁻² m²(mg.day)⁻¹</td>
<td>$P_2 &gt; P_1$ (Rzeski et al., 2004)</td>
</tr>
<tr>
<td></td>
<td>P3 for N</td>
<td>2.4 $\times$ 10⁻⁵ m²(mg.day)⁻¹</td>
<td>$P_3 = P_1$</td>
</tr>
<tr>
<td>Chemotherapy agent rate Φ for infusion</td>
<td></td>
<td>0 – 150 mg (m².day)⁻¹</td>
<td>Daily doses (Stupp et al., 2005)</td>
</tr>
<tr>
<td></td>
<td>ζ for washout</td>
<td>0.2 day⁻¹</td>
<td>Reference (Borges et al., 2014; Said et al., 2007)</td>
</tr>
<tr>
<td>Holling type 2 A1, A2, A3</td>
<td></td>
<td>510</td>
<td>$A_1 = A_2 = A_3 = K$</td>
</tr>
<tr>
<td>Competition coefficients Ψ1 between GCs and CCs</td>
<td></td>
<td>3.6 $\times$ 10⁻⁵ day⁻¹</td>
<td>Cancer hypothesis (Pinho et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>Ψ2 between CCs and GCs</td>
<td>3.6 $\times$ 10⁻⁶ day⁻¹</td>
<td>$\Psi_2 &lt; \Psi_1$</td>
</tr>
<tr>
<td>Carrying capacity K = K₁, K₂, K₃</td>
<td></td>
<td>510 kg/m³</td>
<td>Reference (Azevedo et al., 2009)</td>
</tr>
</tbody>
</table>

Introducing the normalized variables

$$ g = \frac{G}{K_1}, \quad c = \frac{C}{K_2}, \quad n = \frac{N}{K_3}, $$

(6)

where $K_i$ is the carrying capacity of the glial, cancer, and neural cells, respectively, we obtain the normalized mathematical model

$$\begin{align*}
\frac{dg(t)}{dt} &= \Omega_1 g(t)(1 - g(t)) - \beta_1 g(t)c(t) - \frac{p_1 g(t)Q(t)}{a_1 + g(t)}, \\
\frac{dc(t)}{dt} &= \Omega_2 c(t)(1 - c(t)) - \beta_2 g(t)c(t) - \frac{p_2 c(t)Q(t)}{a_2 + c(t)}, \\
\frac{dn(t)}{dt} &= \alpha g(t)H(-\dot{g})n(t) - \frac{p_3 n(t)Q(t)}{a_3 + n(t)}, \\
\frac{dQ(t)}{dt} &= \phi - \zeta Q(T),
\end{align*}$$

(7)

with

$$\begin{align*}
\beta_1 &= \Psi_1 K_2, \quad \beta_2 = \Psi_2 K_1, \quad \alpha = \psi K_1, \\
a_1 &= \frac{A_1}{K_1}, \quad a_2 = \frac{A_2}{K_2}, \quad a_3 = \frac{A_3}{K_3}, \\
p_1 &= \frac{P_1}{K_1}, \quad p_2 = \frac{P_2}{K_2}, \quad p_3 = \frac{P_3}{K_3},
\end{align*}$$

(8)
where Table 2 exhibits the values of the normalized parameters. The normalized model provides variables that reflect the relative density of a population of cells with respect to the mass density of the brain approximately $K = 510$ kg/m$^3$. For example, $n = 0.3$ would mean 30% of total number of neurons that an individual could have. This normalized model allows to make comparative analysis when the model is used to simulate cancer grown in different individuals. A healthy individual, in this normalized model, would be described by the state variables $g = 1$, $c = 0$, and $n = 1$.

Table 2 Values of the normalized parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$</td>
<td>$1.8 \times 10^{-2}$ day$^{-1}$</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>$1.8 \times 10^{-3}$ day$^{-1}$</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>$0.0 - 10.0$</td>
</tr>
<tr>
<td>$a_1 = a_2 = a_3$</td>
<td>1.0</td>
</tr>
<tr>
<td>$p_1 = p_3$</td>
<td>$4.7 \times 10^{-8}$ m$^2$(mg.day)$^{-1}$</td>
</tr>
<tr>
<td>$p_2$</td>
<td>$4.7 \times 10^{-5}$ m$^2$(mg.day)$^{-1}$</td>
</tr>
</tbody>
</table>

Firstly, we check the behaviour of the cancer without the infusion of a chemotherapeutic agent. Since there is no treatment the cancer cells kill the glial cells (Fig. 2a), while the cancer cells grow (Fig. 2b). Without the glial support, the neurons die (Fig. 2c). For $t = 500$ there are around 34% of glial cells, and approximately 27% of neurons. Due to the logistic growth of the glial cells, they resist longer than the neurons from the attack of cancer. As a result, without chemotherapy (Fig. 2d) the cancer cells are going to kill all the cells (Figs. 2a, and c).

Then, we use the infusion of a chemotherapeutic agent in order to suppress the cancer growth. Figure 3 shows a case where our model exhibits a suppressed state. In the interval $0 < t < 50$ the glial cells concentration decreases (Fig. 3a) due to the attack of cancer and the presence of the chemotherapeutic agent, as well as, for $t > 50$ we have $c < 0.005$ (Fig. 3b). Figure 3(c) exhibits a fast decay of the neurons due to the effect of the chemotherapeutic agent on the neuron population and the decay of glial cells. Glial cells recover their normal concentration level which slows down the decay of neuron cells. If the chemotherapeutic agent is not suspended it will eventually kill all neurons, since in our model we are not considering the neurogenesis. The chemotherapeutics induce neurons death is a side effect known as neurotoxicity. Lomustine, cisplatin, topotecan, and vincristine are antitumor agents that induce cell death. Antje Wick and collaborators (Wick et al., 2004) analysed the effect of these drugs on the neurons. They verified which drugs lead to cell death in cerebellar granule neurons in a concentration dependent manner.
Fig. 2 Temporal evolution of the concentration of (a) glial cells, (b) cancer cells, (c) neurons and (d) chemotherapeutic agent ($\Phi = 0$). We consider $g(0) = 0.99$, $c(0) = 0.01$, $n(0) = 0.99$, $Q(0) = 0.0$, and parameters according to Table 2.

3 Local stability

The study of the local stability is important to verify if the suppression of cancer is stable or unstable, or to understand whether a non desired state is stable. The model has some equilibria points $E(g, c, n, Q)$. They are solution of the system $\dot{g}(t) = 0$, $\dot{c}(t) = 0$, $\dot{n}(t) = 0$, $\dot{Q}(t) = 0$. We consider the equilibria points physiologically feasible.

Now, we analyse the local stability for an undesirable equilibrium, where this equilibrium is given by $E_0(0, 0, 0, \Phi_\zeta^{-1})$. The eigenvalues of the Jacobian matrix are

$$
\lambda_1^{(0)} = \Omega_1 - \frac{p_1\Phi}{\zeta a_1},
$$

$$
\lambda_2^{(0)} = \Omega_2 - \frac{p_2\Phi}{\zeta a_2},
$$

$$
\lambda_3^{(0)} = -\frac{p_3\Phi}{\zeta a_3},
$$

$$
\lambda_4^{(0)} = -\zeta.
$$

Through the sign of the real part of each eigenvalue we can check the stability of the equilibrium. In a hyperbolic equilibrium, if the real part of each eigenvalue is strictly negative, then the equilibrium is locally asymptotically stable. If
Fig. 3 Temporal evolution of the concentration of (a) glial cells, (b) cancer cells, (c) neurons and (d) chemotherapy, continuous treatment $\Phi = 100$. We consider $g(0) = 0.99$, $c(0) = 0.01$, $n(0) = 0.99$, $Q(0) = 0.0$ and parameters according to Table 2.

positive, then the equilibrium is unstable. In order to ensure the stability of $E_0(0, 0, 0, \Phi \zeta^{-1})$ it is necessary that

$$\Phi > \frac{\Omega_1 a_1 \zeta}{p_1},$$

(13)

and

$$\Phi > \frac{\Omega_2 a_2 \zeta}{p_2},$$

(14)

where these results are obtained through $\lambda_1^{(0)} < 0$, and $\lambda_2^{(0)} < 0$. The values of the normalized parameters are positive, then the eigenvalues $\lambda_3^{(0)}$, and $\lambda_4^{(0)}$ are negative. We consider $a_1 = a_2 = 1$, $\Omega_1 = 0.0068$, $\Omega_2 = 0.012$, $p_1 = 4.7 \times 10^{-8}$, $p_2 = 4.7 \times 10^{-5}$, and $\zeta = 0.2$ (table 1). With these values we obtain that $E_0$ is linearly asymptotically stable for $\Phi > 28936.17$. In other words, if $\Phi > 28936.17$ the chemotherapeutic agent kills all cells, they will never recover. Stability of the non-cells state is however granted for a very large atypical value of the infusion rate $\Phi$.

We also consider the equilibrium $E_1(\overline{g}, 0, \overline{n}, \overline{Q})$, representing the complete elimination of cancer cells in the normalized model, but preserving glial and
neuron cells. This equilibrium is obtained by the solution of

$$\Omega_1 \Phi (1 - \Phi) - \frac{p_1 \Phi \Phi}{a_1 + \Phi} = 0, \quad \Phi = \zeta \Phi$$

$$- \frac{p_2 \Phi \Phi}{a_3 + \Phi} = 0, \quad \Phi = \zeta \Phi$$

where we obtain $\pi = 0$ and $\Phi = \Phi^{-1}$. Thus, the equilibrium $E_1(\Phi, 0, \pi, \Phi)$ is
given by $E_1(\Phi, 0, 0, \Phi^{-1})$, meaning that all neurons are also eliminated.

The first equation of (15) can be rewritten as

$$\Phi^2 + (a_1 - 1)\Phi - a_1 + \frac{p_1 \Phi}{\Theta} = 0,$$

with solution $\Phi = \left\{ 1 - a_1 \pm \left[ (a_1 - 1)^2 + 4(a_1 - p_1 \Phi / \Theta) \right]^{1/2} \right\} / 2$. In this way,
we verify that $\Phi$ has a null solution when $p_1 \Phi / \Theta < a_1$, and a real, positive
and not null solution when $p_1 \Phi / \Theta < a_1$. Using the parameters of Table 2, $\Phi$
has a real, positive and non null solution when $\Phi < 28936.17$.

Calculating a lower band for the value of $\Phi$ for which the equilibrium
$E_1(\Phi, 0, 0, \Phi^{-1})$ is stable, we determine the stability of this equilibrium. The
eigenvalues of the Jacobian matrix are

$$\lambda_1^{(1)} = \Omega_1 (1 - 2\Phi) - \frac{p_1 \Phi}{\zeta (a_1 + \Phi)^2},$$

$$\lambda_2^{(1)} = \Omega_2 - \beta_2 \Phi - \frac{p_2 \Phi}{\zeta a_2},$$

$$\lambda_3^{(1)} = -\frac{p_1 \Phi}{\zeta a_3},$$

$$\lambda_4^{(1)} = -\zeta.$$

In order to ensure the stability of $E_1(\Phi, 0, 0, \Phi^{-1})$ it is necessary

$$p_1 \Phi < \Omega_1 (1 - 2\Phi)(a_1 - \Phi)^2,$$

and

$$p_2 \Phi < a_2 (\Omega_2 - \beta_2 \Phi),$$

where these results are obtained through $\lambda_1^{(1)} < 0$, and $\lambda_2^{(1)} < 0$. The values
of the dimensionless parameters are positives, then the eigenvalues $\lambda_3^{(1)}$, and
$\lambda_4^{(1)}$ are negatives.

For $a_1 = 1.0$ (Table 2) Eq. (21) is satisfied for all $\Phi \geq 0.5$. Considering $a_2 =
1.0, \Omega_2 = 0.012, p_2 = 4.7 \times 10^{-5}, \zeta = 0.2$, and $\beta_2 = 1.8 \times 10^{-3}$ (Table 2) in Eq.
(22) we have $\Phi > 51.064 - 7.660 \Phi$. As a result, for $E_1(\Phi, 0, 0, \Phi^{-1})$ the system
presents an asymptotically stable equilibrium for $\Phi > 43.189$. Therefore, for
realistic values of the infusion rate $43.189 < \Phi < 28979.255$, we should expect
that cancer can be eliminated, i. e., \( c \leq 10^{-11} \). In our normalized model, \( c \leq 10^{-11} \) corresponds to a real quantity of cancerous cells concentration equal to zero, \( C = 0 \). Doing similar analyses in the non-normalized system, we observe that the equilibrium \( E(\bar{g}, 0, \bar{n}, \bar{Q}) \) is also stable for \( 43.189 < \Phi < 28979.255 \).

We construct the parameter space shown in Fig. 4 to obtain a picture of the stability according to parameters related with the chemotherapy. We can observe three regions. Region I represent parameter which the cancer cells kill the glial cells and neurons, region II represents parameters for which the equilibrium \( E_1(\bar{G}, 0, 0, \Phi\zeta^{-1}) \) is locally stable, and in region III represents parameters for which the equilibrium \( E_0(0, 0, 0, \Phi\zeta^{-1}) \) is locally stable. The region II shows that cancer can be eliminated without the elimination of the glial cells. However, the longer the duration of treatment, the larger the decrease in the neural population. It is therefore vital to understand what are the optimal parameters for which \( c \leq 10^{-11} \) is achieved in the shortest time.

![Fig. 4](Colour online) Parameter space \( \eta \) versus \( \Phi \): in the region I the cancer cells kill the glial cells and neurons, the region II shows which the equilibrium \( E_1(\bar{G}, 0, 0, \Phi\zeta^{-1}) \) is locally stable, and in the region III the equilibrium \( E_0(0, 0, 0, \Phi\zeta^{-1}) \) is locally stable.

A strongly desired equilibrium is \( E_2(\bar{G}, 0, \bar{\pi}, 0) \). In this case we have \( \bar{G} = 1 \) and \( \pi \) has a constant value. The eigenvalues are \( \lambda_1 = -\Omega_1 \), \( \lambda_2 = \Omega_2 - \beta_2 \), \( \lambda_3 = 0 \), and \( \lambda_4 = -\zeta \). Using the parameters given in Table 2 we obtain negative values for \( \lambda_1 \) and \( \lambda_4 \), \( \lambda_2 \) has a positive value, and \( \lambda_3 \) presents a null value. This equilibrium is an unstable saddle point. Then, if treatment is ceased without the complete elimination of the cancer cells (\( c = 0 \)), the cancer concentration in our model increases.
4 Cancer elimination

Here, we study the performance of our model to understand what are the conditions such that cancer concentration in the normalized model reaches levels related to no cancer \((c \leq 10^{-11})\), while glial and neuron cells concentration are kept high.

Figure 3 shows a case for eliminated cancer. However, the neurons concentration is decreased by 1.5\% when the tumour has significantly decreased. In this case, cancer is eliminated, but a significant population of neurons are damaged. For this reason we optimize the values of the chemotherapeutic agents in order not only to minimise the impact on neurons but also to maximize the effect of the drug on cancer cells. Our aim is to understand how the neuron population is when \(c \leq 10^{-11}\). The therapeutic implication for neurons is shown in Figure 5, the neuron concentration (colour bar) when \(c \leq 10^{-11}\), as a function of the parameters \(\alpha\) and \(\Phi\). The region of \(\alpha\) and \(\Phi\) values responsible for the reduction of approximately 2\% in the neuron concentration (yellow online) is \(0.96 \leq n \leq 0.98\), while the region \(0.80 \leq n \leq 0.84\) (dark blue online) presents approximately a reduction of 17\%. This region of parameters causes a large rate of death of the glias (large \(\dot{g}\)). The chemotherapy rate \(\Phi\) also contributes to this low level of \(n\).

\[
\text{Fig. 5 (Colour online) Neuron concentration as a function of } \alpha \text{ versus } \Phi, \text{ where } g(0) = 0.99, c(0) = 0.01, n(0) = 0.99, \text{ and } Q(0) = 0.0. \text{ The colour bar represents the value of the neuron concentration, } n, \text{ after a successful chemotherapy.}
\]

Since that glial cells provide support functions for the neurons, we also analyse the concentration of the glial cells with the chemotherapy treatment. For the parameter values showed in Fig. 5, the percentage of glial cells remains larger than 95\%. Equations (7) show that the glial cells equation does not depend on the parameter \(\alpha\), but it depends on the parameter \(\Phi\) due to \(Q\). When \(\Phi\) increases, we verify that \(c\) decreases. However, there is not a significant
variation in g due to the lifetime cancer \( \tau \) according to the chemotherapy agent rate. In other words, increasing the value of \( \Phi \) the lifetime of cancer quickly decreases, and in this time interval the glial cells concentration does not have a significant alteration, due to the fact that the glial cells are able to recover to their initial state.

Figure 6 shows the time \( \tau \) to achieve suppression of cancer as a function of \( \Phi \). There is a power-law relation of the type \( \tau \propto \Phi^\sigma \), with \( \sigma = -1.36 \) for \( \Phi \leq 60 \) and \( \sigma = -1.41 \) for \( \Phi \geq 60 \). This power-law shows that a significant decrease in \( \tau \) happens if \( \Phi \leq 60 \), whereas little modification in \( \tau \) happens if \( \Phi > 60 \). Therefore, the optimal way of reducing the time of treatment by using the minimal amount of \( \Phi \) is obtained if \( \Phi \approx 60 \). Looking at Fig. 5, neurons will also be significantly preserved if \( \alpha \leq 2 \). The same scalings are obtained if another \( \alpha \) if considered. The chemotherapeutic agent which provides the quickest is \( \Phi \leq 60 \). Treatment will cause less impact on neural population if the individual being treated (characterizes by a particular \( \alpha \)) is provided with an infusion rate \( \Phi \) such that the point \((\Phi, \alpha)\) falls in the yellow region in Fig. 5.

![Graph of \( \tau \) versus \( \Phi \)](image)

**Fig. 6** \( \tau \) versus \( \Phi \), and the same values as Figure 5. The slope for \( \Phi \leq 60 \) is about \(-12.36\), and for \( \Phi \geq 60 \) the slope is about \(-1.41\).

5 Conclusions

We proposed a mathematical model for the evolution of a brain tumour under the attack of chemotherapeutic agents. Our model describes the interactions among glial cells, neurons, and cancer, with a chemotherapy to suppress the brain tumour. The novelty in this model is the glial effect on the neurons.

We studied some aspects of the dynamics of cancerous growth, as well as, we analysed its suppression and elimination varying parameters of the
The main target of treatment is the decrease in the number of cancer cells. A successful chemotherapy eliminates all the cancer cells minimising the neurons and glial cells injury. Through local stability we found a range of values for the infusion rate ($43.189 < \Phi < 28979.255$) that allows for the elimination of cancer, as well as, the cancer will not return. As a matter of fact the Temozolomide is a chemotherapeutic drug used for brain tumour, where the infusion rate is $75 < \Phi < 200$ (mg/m$^2$) (Wick et al., 2009). According to our model, this rate is likely to preserve high levels of the neural population, despite not being the rate that decreases cancer the most rapidly.

We realised numerical simulations and obtained values of the infusion of chemotherapeutic agents in that the cancer growth is eliminated within the shortest time. Our main result was to show that chemotherapy can be applied mitigating the side effects of drugs on the neurons death, if the appropriated rate is used.

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