OPTIMAL CONTROL OF SOME MATHEMATICAL MODELS FOR THE GROWTH OF SPHERICAL TUMORS ORIENTED TO THERAPY

Abstract. In this work we study several systems of partial differential equations that describe the growth of a spherical tumour under the influence of a therapeutic treatment. A variety of PDE models for tumor growth have been developed in the last three decades; see for instance (1), (4). First, we present some existence, regularity and asymptotic stability results. Then, we analyse some related optimal control problem, as make in (2), (3). After, we study is primarily based on achieving an optimal control, where we choose an appropriate cost functional. We prove existence results, deduce the associated optimality systems and we present iterative algorithms for the computation of the solution. We focus on the evolution of a MCS (Multicellular Spheroids System) growing in response to a single, externally-supplied nutrient, such as oxygen or glucose, and a growth inhibitor. Below we present our model studied,

$$
\begin{align*}
\epsilon \frac{\partial \sigma}{\partial t} - \nabla^2 \sigma + f_1(\sigma) &= 0 \quad (1) \\
\epsilon \frac{\partial v}{\partial t} - \nabla^2 v + f_2(v) &= w
\end{align*}
$$

where $\sigma = \sigma(x,t), v = v(x,t)$ and $w = w(t)$ are respectively the nutrient concentration, the density of antibodies and the amount of processed drug. Here $\epsilon$ is a small positive coefficient given by the quotient

$$
\epsilon = \frac{T_{\text{diffusion}}}{T_{\text{growth}}},
$$

where $T_{\text{diffusion}}$ is the diffusion time scale and $T_{\text{growth}}$ is the tumor-doubling time scale. Typically, $\epsilon$ is 1 minute over 1 day, so that $\epsilon \ll 1$.

Model I, nonecrotic core with $\varepsilon = 0$

Considering a spherical shape $\Omega(t) = \{x ; |x| < R(t)\}$ at each time $t$, the boundary $\Gamma_t$ of the tumor is given by $r = R(t)$, where $R$ is the radius of the tumor. In this case we study the optimal control problem for the following free boundary problem

$$
\begin{align*}
\dot{R} &= H(t, R; u), \quad t \in (0, T) \\
R(0) &= R_0,
\end{align*}
$$

for an appropriate $H$ given by

$$
H(t, R; u) = \frac{1}{R^2(t)} \int_0^{R(t)} G(\sigma, v)r^2 dr
$$

where $G(\sigma, v) = \mu(\sigma - \sigma^*) - k(v - v^*)_+$.  

Model II, with necrotic core and $\varepsilon = 0$

Now we have two free boundaries, given by the unknown functions $\rho = \rho(t)$ and $R = R(t)$. Let us introduce the sets $\Omega_N(t) = \{x ; r < \rho(t)\}$ (the necrotic core) and $\Omega_P(t) = \{x ; \rho(t) < r < R(t)\}$ (the proliferating region), where $|x| = r$. We solve the same problem (4) where, here, $H$ given by
\[ H(t, R; u) = \frac{A\rho^3(t)}{3R^2(t)} + \frac{\mu}{R^2(t)} \int_{\rho(t)}^{R(t)} (\sigma - \sigma^*) r^2 dr - \frac{k}{R^2(t)} \int_{\rho(t)}^{R(t)} (\nu - \nu^*) r^2 dr, \quad (6) \]

**Some numerical simulations**

We make some numerical simulations with the considered systems. In a first moment, let’s consider the system without control and then we will see what happens when we introduced a control.

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**References.**


