Development of Glioblastoma growth model

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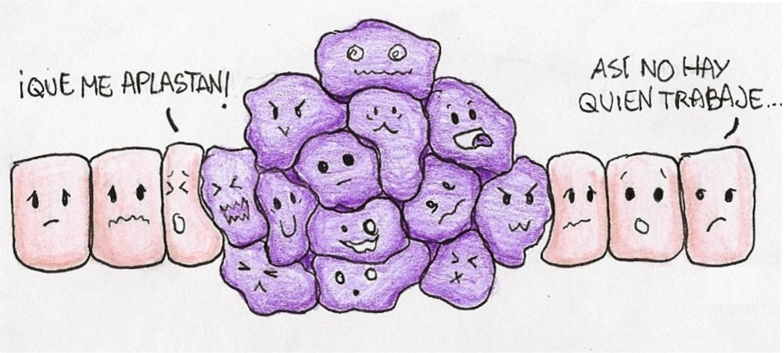
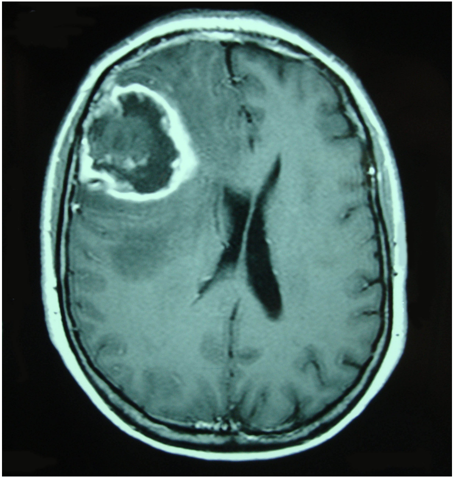
Index

1. Introduction

Motivation



Motivation



Purpose

Our goal is to understand and reproduce this developmet in different situations. For it,

- We are going to create a PDE-ODEs model with which we will work.
- Later, we will start studying theoretical properties of it.
- Finally, we are going to show some simulations about this model.

Index

Formulation

$$\frac{\partial T}{\partial t} = \nabla \cdot \left(D\left(\Phi, T\right) \nabla T \right) + \rho\left(\Phi, T\right)\ T \left(1 - \frac{T + N + \Phi}{K} \right) - \alpha\ f\left(\Phi, T\right)\ T - \beta\ N\ T$$

2. Glioblastoma Model

Formulation

$$\frac{\partial T}{\partial t} = \nabla \cdot (D(\Phi, T)\nabla T) + \rho(\Phi, T)\ T\left(1 - \frac{T + N + \Phi}{K}\right) - \alpha\ f(\Phi, T)\ T - \beta\ N\ T$$

$$\frac{\partial \Phi}{\partial t} = \gamma\ f(\Phi, T)\ \frac{T}{K}\Phi\left(1 - \frac{T + N + \Phi}{K}\right) - \delta\ T\ \Phi - \beta\ N\ \Phi$$

2. Glioblastoma Model

Formulation

$$\frac{\partial T}{\partial t} = \nabla \cdot \left(D\left(\Phi, T\right) \nabla T\right) + \rho\left(\Phi, T\right)\; T \left(1 - \frac{T + N + \Phi}{K}\right) - \alpha\; f\left(\Phi, T\right)\; T - \beta\; N\; T$$

$$\frac{\partial N}{\partial t} = \alpha\; f\left(\Phi, T\right)\; T + \beta\; N\; T + \delta\; T\; \Phi + \beta\; N\; \Phi$$

$$\frac{\partial \Phi}{\partial t} = \gamma\; f\left(\Phi, T\right) \frac{T}{K} \Phi \left(1 - \frac{T + N + \Phi}{K}\right) - \delta\; T\; \Phi - \beta\; N\; \Phi$$

2. Glioblastoma Model

Parameters

$$f(\Phi, T) = \sqrt{1 - \left(\frac{\Phi}{\Phi + T}\right)^2}, \quad D(\Phi, T) = \bar{D}\,\frac{\Phi}{\Phi + T}, \quad \rho(\Phi, T) = \bar{\rho}\,\frac{\Phi}{\Phi + T}$$

Variable	**Description**	**Value**
$D(\phi)$	Diffusion Speed	cm^2/day
$\rho(\phi)$	Proliferation rate	day^{-1}
β	Change rate to necrosis influence	day^{-1}
α	Hypoxic death rate by persistent anoxia	day^{-1}
γ	Vasculature proliferation rate	day^{-1}
δ	Vasculature death by tumor action	day^{-1}
K	Carriying capacity	cel/cm^3

Index

Estimates

1. L^∞ bounds
   - $0 \leq T, \Phi \leq K$
   - $0 \leq N \leq \bar{N}$
   - $T, N, \Phi \in L^\infty\left([0, T_f]; L^\infty(\Omega)\right)$
2. L^2 bounds
   - $T \in L^\infty\left([0, T_f]; L^2(\Omega)\right) \cap L^2\left([0, T_f]; H^1(\Omega)\right)$

Existence and uniqueness for linear diffusion model

Theorem

Given $T_0, N_0, \Phi_0 \in \Omega$ *such that* $0 < T_0 + N_0 + \Phi_0 \leq K$, *exits a unique solution* (T, N, Φ) *for the problem with linear diffusion that satisfies*

- $N, \Phi \in C^1\left([0, T_f]\,; \mathcal{C}^0\left(\bar{\Omega}\right)\right)$
- $T \in \mathcal{C}^0\left([0, T_f]\,; \mathcal{C}^0\left(\bar{\Omega}\right)\right)$

Way: *Leray-Schauder fixed-point therorem* with

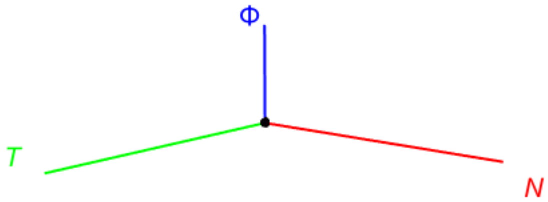
$$\begin{array}{ccccccc} \mathcal{R}: & \mathcal{C}^0\left([0,T_f]\,;\mathcal{C}^0\left(\bar{\Omega}\right)\right) & \stackrel{R_1}{\rightarrow} & \left(\mathcal{C}^1\left([0,T_f]\,;\mathcal{C}^0\left(\bar{\Omega}\right)\right)\right)^2 & \stackrel{R_2}{\rightarrow} & \mathcal{C}^0\left([0,T_f]\,;\mathcal{C}^0\left(\bar{\Omega}\right)\right) \\ & \tilde{T} & & (N,\Phi) & & T \end{array}$$

Stability

- Model without diffusion has 3 types of equilibrium solutions

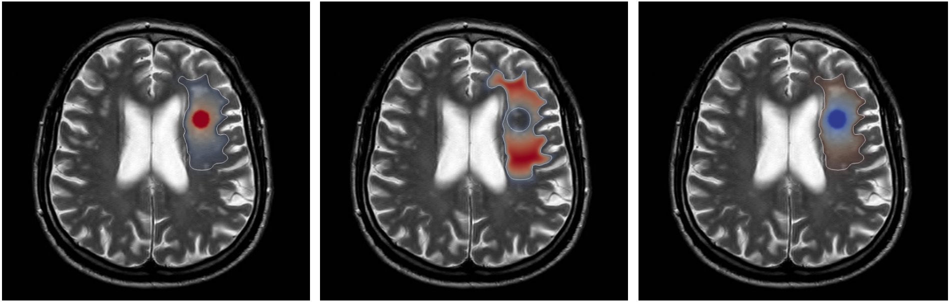
  1. $(0, 0, 0)$
  2. $(0, (N_0)_*, 0)$, $(N_0)_* > 0$
  3. $(0, 0, (\Phi_0)_*)$, $(\Phi_0)_* > 0$

- PDE-ODE system has the same equilibriums



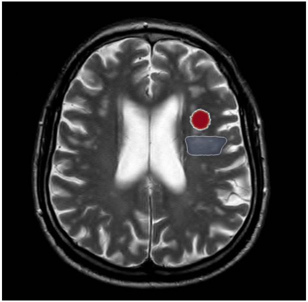
Index

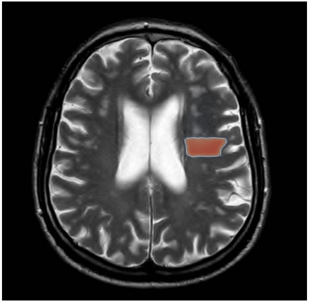
Vasculature fixed. Results

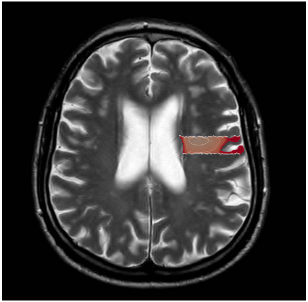


(a) Necrosis (b) Tumor (c) Vasculature

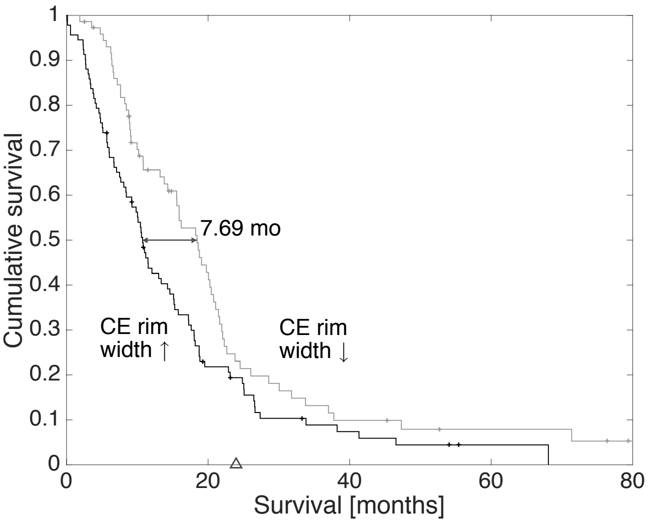
Variable vasculature. Results


(a) Necrosis


(b) Tumor


(c) Vasculature

Survival by Rim width groups



Model

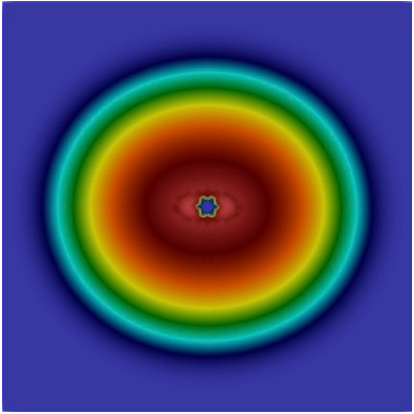
$$\frac{\partial T}{\partial t} = \nabla \cdot \left(D\left(\Phi, T\right) \nabla T\right) + \rho\left(\Phi, T\right)\, T \left(1 - \frac{T + N + \Phi}{K}\right) - \boldsymbol{\alpha}\, f\left(\Phi, T\right)\, T - \beta\, N\, T$$

$$\frac{\partial N}{\partial t} = \boldsymbol{\alpha}\, f\left(\Phi, T\right)\, T + \beta\, N\, T + \delta\, T\, \Phi + \beta\, N\, \Phi$$

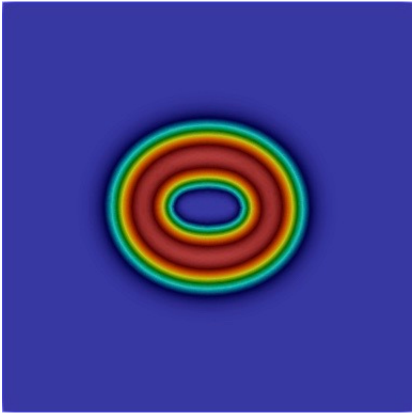
$$\frac{\partial \Phi}{\partial t} = \gamma\, f\left(\Phi, T\right) \frac{T}{K} \Phi \left(1 - \frac{T + N + \Phi}{K}\right) - \delta\, T\, \Phi - \beta\, N\, \Phi$$

4. Simulations

Rim width-Volume

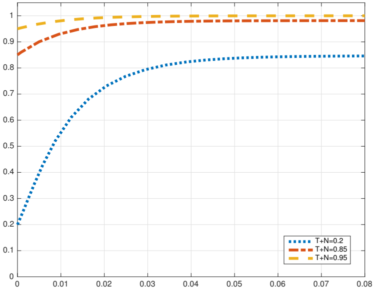


(a) $\alpha = 1$

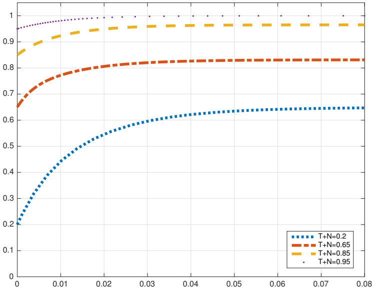


(b) $\alpha = 500$

Tumor and Necrosis growth



(a) $\alpha = 1$



(b) $\alpha = 500$

Thanks !