Modeling Glioblastoma Multiforme

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2004-2005 Major Qualifying Project

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The 2005 Provost MQP Honorable Mention

Abstract –

Glioblastoma multiforme (GBM), a highly lethal brain cancer, accounts for over 30% of brain tumors in adult patients. Patients typically survive only 12-18 months after diagnosis. Our model describes the dynamics of GBM via a system of partial differential equations for tumor cells, nutrients, toxins, and mechanical resistance of brain matter. Using a 2D conservative Alternating Direction Implicit scheme, we numerically approximate the solution to our model and implement it in C for simulation on a parallel computer.

Mathematical Model

Our continuum model for the growth of Glioblastoma multiforme describes the dynamic changes in four quantities: tumor cell concentration, nutrient concentration, toxin concentration, and mechanical resistance. Each quantity has its own governing equation together forming a coupled system of four non-linear partial differential equations.

$$\frac{\partial \rho}{\partial t} = \nabla \cdot \left(D_\rho(r)\nabla \rho\right) + \beta_\rho \rho - \gamma \nabla \cdot (\rho \nabla \phi)$$

$$\frac{\partial \phi}{\partial t} = \nabla \cdot \left(D_\phi(r)\nabla \phi\right) - \beta_\phi \rho + q_\phi$$

$$\frac{\partial \tau}{\partial t} = \nabla \cdot \left(D_\tau(r)\nabla \tau\right) + \beta_\tau \rho$$

$$\frac{\partial r}{\partial t} = -\kappa \max\left(\frac{\partial \rho}{\partial t}, 0\right)$$

ρ	tumor cell concentration
ϕ	nutrient concentration
τ	toxin concentration
r	mechanical resistance

Coefficients

Diffusion Coefficient

$$D_*(r) = \frac{\sigma_*}{1+\eta_* r}$$

$$\sigma_*, \eta_* > 0$$

$$* = \rho, \phi, \text{or } \tau$$

Fractional Rate of Nutrient Consumption

$$\beta_\phi(\phi) = \begin{cases} \frac{\omega_0}{b_0}\phi, & \phi < b_0 \\ b_0, & \phi \ge b_0 \end{cases}$$

Fractional Rate of Net Proliferation

$$\beta_\rho\left(\frac{\phi}{\rho}\right) = \frac{A\frac{\phi}{\rho}}{B+\frac{\phi}{\rho}} - C\tau$$

Fractional Rate of Toxin Production

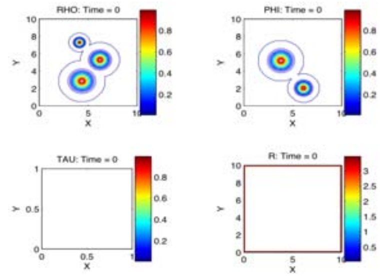
$$\beta_\tau \propto \beta_\rho$$

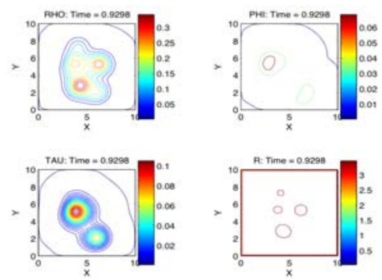
Biological Assumptions

- **Tumor cells, nutrients, and toxins *diffuse* through brain matter.**
- **Tumor cells *consume* nutrients and *produce* toxins.**
- **Toxins *kill* tumor cells.**
- **Migrating tumor cells *erode* mechanical resistance.**

Simulation Results

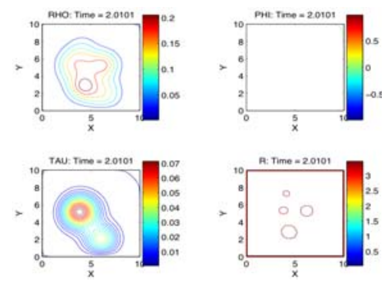
The following figures show results from an example computer simulation of the model. The figure to the right shows the initial conditions of the system. Tumor cells and nutrients are distributed as illustrated and no toxins exist. The resistance is a constant throughout.





The figure to the left shows how the tumor cells have diffused and begun migrating towards nutrient concentrations. Toxins have been produced as a result of tumor proliferation. Resistance has decayed as the tumor cells move.

The figure to the right shows the system after much time has elapsed. Nutrients have been completely consumed, thus the tumor cells only diffuse now. The locations of decayed resistance show where the tumor cells have migrated through towards the now consumed nutrients.



Future Work

- **Obtain empirical data to develop parameter values.**
- **Measure the tumor velocity, *I.e. the speed at which the tumor mass grows.***
- **Emulate and compare results with the simulation developed in [1].**

References:

[1] Y. Mansury and T. Deisboeck, The impact of search precision in an agent-based tumor model, *J. of Theo. Bio.*, 24, 325-337 (2003).

[2] L. Sander and T. Deisboeck, Growth patters of microscopic brain tumors, *Phys. Rev.*, 66, 051901 (2002).

Acknowledgements

Special thanks to:

- **Dr. Kirk Jordan (IBM), Dr. Thomas Deisboeck (Harvard/MIT) for <…>**
- **CIMS for <…>**

Advisor: **Prof. Suzanne Weekes**

Sponsor: **IBM, <…>**