MS5033
Mesoscale Microstructure Modeling
Project Formulation

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Problem Statement

In mathematical cancer modeling, the development of solid tumors involves various mechanisms, including cell-cell adhesion, growth dynamics, and angiogenesis, among others. This project models the progression of solid tumors using a coupled system of Cahn–Hilliard-type convection-reaction-diffusion equations. The model represents the tumor with a two-cellular structure, consisting of viable (proliferating) cells and dead cells forming the necrotic core.

Model Parameters

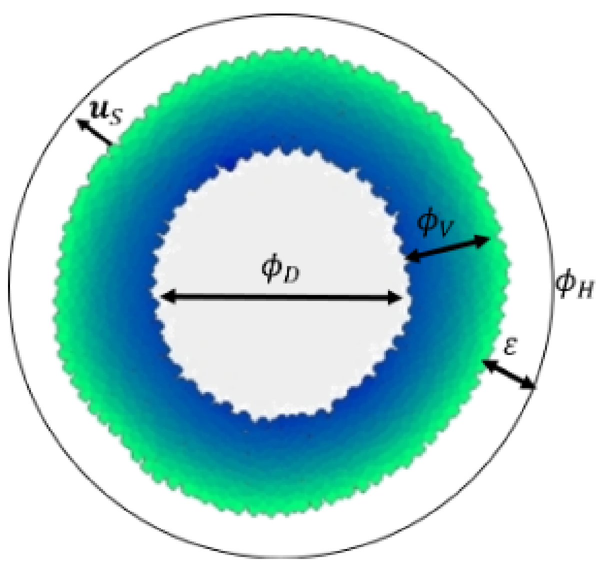

Figure 1: Model Parameters on a tumor cell

- ϕ_V: volume fraction of viable tissue
- ϕ_D: volume fraction of dead tissue
- ϕ_H: volume fraction of healthy tissue
- u_S: tissue velocity
- ε: thickness of interface between healthy and tumoral tissue
- p: cell-to-cell (solid) pressure
- n: nutrient concentration

Equations

$$\phi_V + \phi_D + \phi_H = 1 \tag{1}$$

$$\phi_T = \phi_V + \phi_D, \text{ where } \phi_T \text{ is the total volume fraction of tumor tissue} \tag{2}$$

$$\frac{\partial \phi_T}{\partial t} = M\nabla \cdot (\phi_T \nabla \mu) + S_T - \nabla \cdot (\phi_T u_S) \tag{3}$$

$$\frac{\partial \phi_D}{\partial t} = M\nabla \cdot (\phi_D \nabla p) + S_D - \nabla \cdot (\phi_D u_S) \tag{4}$$

$$\nabla \cdot (D(\phi_T)\nabla n) + T_c(\phi_T, n) - n(\phi_T - \phi_D) = 0 \tag{5}$$

where,

$$\mu = f'(\phi_T) - \epsilon^2 \nabla^2 \phi_T \tag{6}$$

$$f(\phi) = \phi^2 (1-\phi)^2 / 2 \tag{7}$$

$$\nabla \cdot u_S = S_T \tag{8}$$

$$u_S = -\kappa(\phi_T, \phi_D)(\nabla p - \frac{\gamma}{\epsilon}\nabla \phi_T) \tag{9}$$

$$S_T = nG(\phi_T)\phi_V - \lambda_L \phi_D \tag{10}$$

$$S_D = (\lambda_A + \lambda_N \mathscr{H}(n_N - n))(\phi_T - \phi_D) - \lambda_L \phi_D \tag{11}$$

Discretization

- Spatial discretization: Finite Difference method
- Temporal discretization: Implicit Crank-Nicolson scheme
- Advection terms: Discretized using third-order upwind WENO approximation
- Laplacians and operators: Approximated to second order with averaging operators
- Implemented using a multigrid algorithm on a uniform mesh

The discretized equations used in the implementation are:

$$\begin{aligned}\phi^k_{T,i,j} - \phi^{k-1}_{T,i,j} = \frac{sM}{2} &\left[\nabla_d(\phi^k_T \nabla_d \mu^k)_{i,j} + \nabla_d(\phi^{k-1}_T \nabla_d \mu^{k-1})_{i,j}\right] \\ &- \frac{s}{2}\left[\nabla_d \cdot (\mathbf{u}^k_S \phi^k_T)_{i,j} + \nabla_d \cdot (\mathbf{u}^{k-1}_S \phi^{k-1}_T)_{i,j}\right] \\ &+ \frac{s}{2}\left[S^k_T + S^{k-1}_T\right]_{i,j}\end{aligned} \tag{12}$$

$$\mu^k_{i,j} = f'(\phi^k_{T,i,j}) - \varepsilon^2 \Delta_d \phi^k_{T,i,j} \tag{13}$$

$$\begin{aligned}\phi^k_{D,i,j} - \phi^{k-1}_{D,i,j} = \frac{sM}{2} &\left[\nabla_d(\phi^k_T \nabla_d \mu^k)_{i,j} + \nabla_d(\phi^{k-1}_T \nabla_d \mu^{k-1})_{i,j}\right] \\ &- \frac{s}{2}\left[\nabla_d \cdot (\mathbf{u}^k_S \phi^k_D)_{i,j} + \nabla_d \cdot (\mathbf{u}^{k-1}_S \phi^{k-1}_D)_{i,j}\right] \\ &+ \frac{s}{2}\left[S^k_D + S^{k-1}_D\right]_{i,j}\end{aligned} \tag{14}$$

$$\begin{aligned}0 = &\nabla_d \cdot \big(\kappa(\phi^k_T, \phi^k_D)_{i,j} \nabla_d p\big) + S^k_{T,i,j} \\ &- \frac{\gamma}{\varepsilon} \nabla_d \cdot \big(\kappa(\phi^k_T, \phi^k_D)_{i,j} \nabla_d \phi^{k-1}_T\big)\end{aligned} \tag{15}$$

$$0 = \nabla_d \cdot \big(D(\phi^k_T) \nabla_d n\big)_{i,j} + n\eta_{i,j}\left[(\phi_{T,i,j} - \phi_{D,i,j}) + S^k_{C,i,j}\right] - ncS^k_{C,i,j} \tag{16}$$

where

$$S^k_{C,i,j} := v^H_p (1 - Q(\phi_{T,i,j})) + v^T_p Q(\phi_{T,i,j}) \tag{17}$$

Initial Conditions

The initial condition is a slightly elliptical initial tumor.

Boundary Conditions

The model equations are valid throughout Ω, and no internal boundary conditions are required for ϕT, ϕD, or any other variables. For outer-boundary conditions, we choose $\mu = p = 0$, $n = 1$, $\zeta * \Delta \phi_T = \zeta * \Delta \phi_D = 0$ on $\partial\Omega$,

where ζ is the outward-pointing unit normal on the outer boundary $\partial\Omega$. Conditions $\mu = p = 0$ allow for the free flow of cells and water across the outer boundary to accommodate growth.

References

1. Wise, S. M., Lowengrub, J. S., & Cristini, V. (2011). An adaptive multigrid algorithm for simulating solid tumor growth using mixture models. *Mathematical and Computer Modelling*, 53, 1–20.

2. Cristini, V. & Lowengrub, J. S. (2010). *Multiscale Modeling of Cancer: An Integrated Experimental and Mathematical Approach*. Cambridge University Press.

3. University of Oxford (2014). *Cell-based Chaste: A Multiscale Computational Framework for Modelling Cell Populations*.