

NUMERICAL SOLUTIONS FOR PDES PROJECT PROPOSAL:

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INTRODUCTION

The development of mathematical models to describe the dynamics of tumor growth has made the analysis of the disease easier and less expensive. There are many ordinary differential equations that describe the dynamics of tumor growth [9, 10, 5, 11]. A major modeling deficit of such models, however, is that they fail to capture the spatial dependence of tumor growth. As stated in [4], it is not merely the cell count of tumors that makes them deadly; rather, how the tumor spatially occupies surrounding organs and tissues is what makes them so deadly. Thus various partial differential equation models of tumor growth have been developed [1, 7, 8]. In my final project I will use the model developed in [2] to (i) study and understand the physical interpretation of the states and parameters, (ii) study and implement appropriate PDE integrators to test convergence, (iii) model the growth of tumors in 2D space over time, (iv) use the numerical solution of the system in time to compute dynamic active subspaces and analyse parameter dependence for one state of the system.

THE NON-DIMENSIONALIZED MATHEMATICAL MODEL

$$\frac{\partial n}{\partial t} = D_n \nabla^2 n - \gamma \nabla \cdot (n \nabla f) \quad (1)$$

$$\frac{\partial f}{\partial t} = -\eta m f \quad (2)$$

$$\frac{\partial m}{\partial t} = d_m \nabla^2 m + \alpha n - \beta m \quad (3)$$

STATES AND PARAMETERS

State	Description
n	<i>tumor cell density</i>
f	<i>ECM concentration</i>
m	<i>MDE concentration</i>

Table 1: Description of states in mathematical model

For the purposes of this project proposal I have assumed that the parameters are distributed uniformly from 10% below and above the nominal values provided in [2].

Parameter	Description	Lower Bound	Nominal Value	Upper Bound
d_n	<i>tumor random motility coefficient</i>	0.0009	0.001	0.0011
γ	<i>cancer cell proliferation rate</i>	0.0045	0.005	0.0055
η	<i>degradation rate</i>	9	10	11
d_m	<i>MDE diffusion coefficient</i>	0.0009	0.001	0.0011
α	<i>MDE production rate</i>	0.09	0.1	0.11
β	<i>natural MDE decay rate</i>	-0.01	0	0.01

Table 2: Description of non-dimensionalized parameters in mathematical model

WHAT IS AN ACTIVE SUBSPACE AND WHY IS IT INTERESTING?

Imagine you are visiting Colorado for the first time and your friend has asked you to write a letter describing the beautiful Rocky Mountains. If you get off the plane and face East, you will be disappointed to see no mountains whatsoever. Facing West, however, there is a perfect view. You just need to look in the right direction.

Consider a function $f(\mathbf{x})$ that maps the relationship between input parameters, $\mathbf{x} \in \mathbb{R}^n$ and an output (e.g., cell count, drug concentration, temperature). Let $\mathbb{E}_{\mathbf{x}}[\cdot]$ be the expectation over the parameters. *Active subspaces* [3] are eigenspaces of the matrix,

$$\mathbf{C} = \mathbb{E}_{\mathbf{x}}[\nabla f(\mathbf{x})\nabla f(\mathbf{x})^T] = \mathbf{W}\mathbf{\Lambda}\mathbf{W}^T.$$

The eigenvalue λ_i is equal to the mean-squared directional derivative of $f(\mathbf{x})$ in the direction of the corresponding eigenvector \mathbf{w}_i . The largest eigenvalue λ_1 indicates \mathbf{w}_1 is the direction in the parameter space along which $f(\mathbf{x})$, changes the *most* on average. Let \mathbf{W}_1 contain the eigenvectors associated with the $k < n$ largest eigenvalues. The linear combinations $\mathbf{W}_1^T \mathbf{x}$ are the *most important* parameters. Although active subspaces give model insight and computational tractability for scalar-valued functions, it is not enough. This analysis does not extend to time-dependent systems.

WHY SHOULD WE CARE ABOUT TIME DEPENDENCE?

For the scope of this project I will mirror the recent attempt at computing independent subspaces at each point in time [6]. This analysis will enable uncertainty quantification, sensitivity analysis, and parameter estimation for a state of the PDE.

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