539e A Multi-Layer, Multi-Dimensional Framework for Modeling Tumor Growth

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Cancer modeling is a developing branch of applied mathematics, and clearly any method that provides insight into cancer is of significant value. In cancer research, mathematical modeling may be used to study the cancer phenomena, predict the tumor growth dynamically, and guide the chemotherapy strategies. As cancer phenomena are dominated by stochastic, non-linear, and multiscale processes, for which there is no clear mechanism of understanding, cancer modeling is a highly challenging frontier.

In this work, a generalizable multi-layer, multi-dimensional modeling framework is introduced for description and prediction of tumor growth dynamics. The framework introduced involves multiple model layers, with each layer representing a key object in the system, such as tumor cells, normal cells, immune system, nutrient supply, and chemotherapy administration. The system is considered in a multi-dimensional dynamic model where the spatially varying factors taken into consideration include the shape of tumor block, blood vessel density, and transport phenomena of nutrient supply and drug delivery. The correlations among these layers are presented by the interlayer mathematical formations including partial differential equations for spatial changes, dynamic coefficients for time responses of cells to chemotherapy, stochastic models for events such as somatic evolution, and piecewise-continuous parameterization for modeling the discrete changes in drug concentrations.

The major advantage of the framework introduced is its flexibility for continual improvement. Each layer can include a model of desired level of sophistication. The number of layers is also flexible based on the modeling interest, available information, and model complexity requirements. It is convenient to introduce additional layers to model additional important characteristics including different cell types, sub-cellular factors such as mutation rates, cell-cell signaling, signal transduction mechanisms, as well as multi-drug chemotherapy modes without significant modifications in the other layers. The multi-layer framework is capable of simulating the system dynamics, including spatial changes.

Based on the framework described above, a novel tumor-growth model will be introduced for use in clinical tumor growth predictions. The model introduced is a simplified tumor model (two spatial dimensions plus time variations) with a necrotic inner core surrounded by a thin active growth layer. The particular model developed includes five layers as the tumor cells, normal cells, immune system, angiogenesis, and drug treatment. The 2-D modeling enables including the transport phenomena related considerations in the model, such as oxygen and nutrient supply into the tumor core, necrosis cell generation due to nutrient deprivation, and consequent angiogenesis. In addition to this tissue-level characteristics, the cell-level somatic adaptation and evolution of the cancer cells, as well as a few sub-cellular level factors such as nutrient and blood vessel growth factor concentrations in the tissue and tumor, are also included to create a multi-scale model. It is demonstrated that the model is capable of predicting tumor growth based on data available in literature. The development of the modeling framework into a general tool for tumor growth simulation is also discussed.