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Abstract

Numerical method for ε-optimal approximation of tumor growth inhibition by GM-CSF treatment

In this thesis we construct a computational method for ε-optimized approximation inhibition of tumor growth using GM-CSF treatment.

First of all, we formulate and solve the system of partial differential equations. Each of equations describes one of the biological elements: live and dead tumor cells, macrophages, endothelial cells, and the cytokines, such as M-CSF, GM-CSF, VEGF, sVEGFR-1, MCP-1/CCL2 and oxygen. We use a two-phase free boundary model where the tumor is modeled as a growing continuum $\Omega(t)$ with boundary $\Gamma_1(t) = \partial\Omega(t)$, both of which evolve in time. As live and dead tumor cells can be found only in tumor, functions representing them are assumed to be in $\Omega(t)$. Other functions representing biological elements are assumed to be in both tumor and healthy so the whole domain D. Tumor shape and size is controlled by a macroscopic velocity field v, where v in $\Omega(t)$ is not zero, while $v = 0$ in $D\backslash\Omega(t)$. All these equations contain nonlinear components as well as first, second and even third order partial derivatives.

In order to solve such a complicated system of equations, we create our own numerical method to find optimal control of inhibiting tumor growth by GM-CSF using the finite element method implemented in the FreeFem ++ package.

Due to the level of system complexing, it is not enough to use FreeFem ++ build in schemes, it is necessary to create computational algorithm. Particular attention should be paid to the functions' non-linearity, derivatives of higher orders, and especially the method of building a new boundary at each subsequent time step. Furthermore, we construct dual dynamic programming approach to formulate sufficient ε-optimality condition of the treatment and next we calculate numerically ε-optimal treatment.

Finally we are able to verify the dissertation thesis positively, i.e. confirmation that it is possible to calculate the ε-optimal dosage of GM-CSF, resulting in inhibition of tumor growth.