ABSTRACT

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Title of the Thesis: Mathematical modeling, analysis of tumor-immune competitive systems and its control strategies

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Cancer remains one of the most significant global health challenges, necessitating innovative approaches to better understand its dynamics and devise effective control strategies. In this thesis, we study tumor-immune competitive systems and incorporate the effect of discrete and distributed time delays, along with the theory of optimal control. Discrete and distributed time delays have been added because the interaction in the cell populations is not an instantaneous process and is followed by some time lag(s). We also investigate the effect of drugs through optimal control theory. Initially, we study a three-dimensional model of tumor cells, immune effector cells, and immuno-stimulatory cytokine IL-2. Subsequently, we incorporate a discrete time lag τ into our mathematical model. We explore the complex dynamics of tumor-immune interactions, which arise through Hopf bifurcation by varying the time lag τ and other system parameters. Next, our study incorporates a continuously distributed time delay through the introduction of a kernel function as an additional compartment. This compartment can be interpreted as the distributed immune activation delay, further enriching the model and capturing the complexity of biological scenarios. Next, we have constructed a mathematical model for a tumor-immune competitive system using a biologically inspired approach. The model is based on a coupled system of ordinary differential equations, incorporating various components such as tumor cells, CD8+T cells, macrophages, antigen-presenting dendritic cells, regulatory T-cells (Tregs) and various cytokines, including IL-10, TGF-β, IL-12 and IFN-γ. Our immune system requires additional time to generate a suitable response after recognizing tumor cells. Therefore, it is crucial to incorporate time delays into our mathematical model to accurately depict the interplay between tumors and the immune system. To gain deeper insights into this interaction, we introduce multiple time delays into our model. Across biologically relevant parameter values, we found that the influence of multiple time delays on model dynamics was negligible. This observation implies that delays can be regarded as supplementary components with limited impact on the overall dynamics of the tumor-immune interaction system. Next, We utilized the theory of optimal control to investigate the dynamic behavior of the proposed tumor-immune interaction model. Our analysis focused on a mathematical model that describes the interaction between tumors and the immune system, with a specific emphasis on treatment strategies. Our primary objective was to propose an improved treatment approach for eliminating tumor cells by combining chemotherapeutic and immunotherapeutic drugs. To minimize the population of tumor cells and maximize the presence of immune cells, we introduced four control strategies. By implementing these controls, we observed a notable phenomenon: the tumor cell population reached an equilibrium point quickly, while the immune components were maximized. This finding suggests that the application of control parameters effectively controlled tumor cell growth and enhanced the immune response. This thesis concludes with a discussion of potential future directions.

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