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Hopf bifurcation analysis and optimal control of Treatment in a delayed oncolytic virus dynamics

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Abstract

During cancer viral therapy, there is a time delay from the initial virus infection of the tumor cells up to the time those infected cells reach the stage of being able to infect other cells. Because the duration of this “time delay” varies with each virus, it is important to understand how the delay affects the cancer viral therapy. Herein, we have introduced a mathematical model to explain this time delay. The existence of equilibrium (i.e., whether the treatment was unsuccessful or partially successful) was determined in this model by using a basic reproduction ratio of viral infection (R_0) to immune response (R_1). By using the bifurcation parameter as a delay τ , we proved a sufficient condition for the local asymptotic stability of two equilibrium points and the existence of Hopf bifurcation. In addition, we observed that the time delay caused the partial success equilibrium to be unstable and worked together with Hopf bifurcation to create a stable periodic oscillation. Therefore, we investigated the effects of viral cytotoxicity or infection rate, which are characteristics of viruses, on the Hopf bifurcation point. In order to support the analytical findings and to further analyze the effects of delay during cancer viral therapy, we reconstructed the model to include two controls: cancer viral therapy and immunotherapy. In addition, using numerical simulation, we suggested an optimal control problem to examine the effects of delay on oncolytic immunotherapy.

Key words: delay , Cancer-viral therapy, Hopf bifurcation, Optimal treatment strategy, Oncolyticimmunotherapy, infection rate, viral cytotoxicity

Mathematics Subject Classification (2010) : 92D25, 49J15, 93D20

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