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OPTIMAL STRATEGIES OF CAR T-CELL THERAPY IN THE TREATMENT OF LEUKEMIA WITHIN THE LOTKA–VOLTERRA PREDATOR–PREY MODEL

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A controlled mathematical model of leukemia treatment is considered. The model is based on the three-dimensional Lotka–Volterra predator–prey model, which describes a recently developed leukemia treatment technology called Chimeric Antigen Receptor (CAR) T-cell therapy, and is given on a fixed time interval by a system of four differential equations. The equations describe the interaction between populations of healthy and cancer cells, CAR T-cells, and cytokines. The CAR T-cells act as predators, while healthy and cancer cells act as prey. The CAR T-cell therapy leads to serious side-effects associated with the rapid growth of cytokines, and therefore their dynamics is also included in the model. The model also contains two bounded control functions reflecting the intensity of the therapy (the first control) and the intensity of administration of drugs that suppress the activity of the immune system (the second control). We study the problem of minimizing the objective function related to the number of cancer and healthy cells, as well as cytokines, both at the final moment of a given time interval and during this entire interval. The Pontryagin maximum principle is applied for the analysis of the problem; it is used to establish the bang-bang nature of an optimal first control and to estimate the number of its switchings. It is shown that an optimal second control is a constant function on the entire time interval. The BOCOP-2.2.1 environment is used for the numerical analysis of the problem. The results of numerical calculations are presented, demonstrating various types of optimal protocols for CAR-T therapy.

Keywords: leukemia, nonlinear control system, optimal control, Pontryagin maximum principle, bang-bang control, switching function, generalized Rolle theorem.

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