Optimal Control Problems for Mathematical Models of Cancer Treatments

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Abstract

In any cancer treatment, the question arises how therapeutic agents (various drugs, radiation dosages, antiangiogenic agents, cancer vaccines, ...) should be given in order to be at the same time reasonably safe and effective. Mathematically, the scheduling of therapeutic agents over time in order to minimize some objective related to tumor burden (e.g., tumor volume) and quality of life of the patient (e.g., some penalty on the toxic side effects of treatment) while the underlying system follows some dynamics (in this case determined by the processes of tumor development and treatment interactions) is an optimal control problem. In this talk, we highlight some results about the structure of treatment protocols that can be inferred from mathematical models with the methods and tools of optimal control.

A systematic study of cancer treatments requires that one takes into account not only the tumor and its growth, but also its microenvironment which comprises the cancerous cells, (sensitive and resistant to the treatment), healthy cells, tumor vasculature, immune system and more. As more aspects of the tumor microenvironment are taken into account, optimal solutions change from bang-bang solutions (which correlate with the standard medical practice of giving maximum tolerated doses with rest periods) to administration schedules that favor singular controls (which administer agents at specific time varying reduced dose rates). This raises the possibility of metronomic administrations of agents (at low concentrations over prolonged periods without any major interruptions), an alternative scheduling approach that has shown some success in pediatric cancers.

The use of direct geometric constructions as a means of realizing sufficient conditions for optimality [6] will be illustrated in the construction of both local and global fields of optimal controlled trajectories (regular syntheses) for increasingly more complex models. This leads from optimal syntheses of bang-bang controls [2] to highly nontrivial structures that include singular arcs [1, 3, 5], saturation phenomena [3], and even chattering concatenations [4] as pharmacokinetic models for the drugs are included.

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