Singular controls and chattering arcs in syntheses of optimal solutions for mathematical models in biomedicine

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Abstract

In the talk we will show how the tools of geometric optimal control can be applied to analyze mathematical models in biomedicine. We will focus on models for tumor anti-angiogenesis, a novel medical approach to cancer treatment that aims at preventing the development of the blood vessel network a tumor needs for growth. Mathematical models originally introduced by a group of researchers from Harvard School of Medicine and National Cancer Institute of NIH will be analyzed as optimal control problems with a Mayer type objective of minimizing the size of the tumor at the end of therapy. The nonlinear dynamics in the problem describes the growth of the tumor volume and its vascularization under the effects of control functions representing the dosage of the angiogenic inhibitors with a constraint on the total amount. Using Lie bracket calculations and the Legendre-Clebsch condition a complete solution to the problem in terms of a synthesis of optimal controls and trajectories, with explicit formulas of singular controls and corresponding singular arc will be given. For most models this synthesis consists of an optimal singular arc of order one which concatenates with the bang-bang trajectories. However, the rules for concatenations require a detailed analysis and taking into account the saturation of the singular control gives rise to various types of the syntheses. On the other hand, extending the model by adding the pharmacokinetics of the drugs as an integrator type equation changes the dimensionality of the problem and the singular arc becomes of order two which gives rise to chattering arcs. Also, extending the model by adding a second control representing the dosage of a chemotherapy drug, so-called model for combination therapy, increases the dimension of the state and the multi-control aspect makes the analysis more challenging. The singular control now generates a flow of corresponding singular extremals and the lack of uniqueness complicates the construction of the synthesis. Partial results for this case will be presented and open problems stated.