Optimal control of combined chemotherapies in phenotype-structured cancer cell populations evolving towards drug resistance

Camille Pouchol, Jacques-Louis Lions Laboratory, INRIA Mamba Team & UPMC, Paris, France

We investigate optimal therapeutical strategies combining cytotoxic and cytostatic drugs for the treatment of a solid tumour. The difficulty comes from the usual pitfalls of such treatments: emergence of drug-resistance and toxicity to healthy cells.

We consider an integro-differential model for which the structuring variable is a continuous phenotype. Such models come from theoretical ecology and have been developed to understand how selection occurs in a given population of individuals. Two populations of healthy and cancer cells, both structured by a phenotype representing resistance to the drugs, are thus considered. The optimal control problem consists of minimising the number of cancer cells after some fixed time T.

We first analyse the effect of constant doses on the long-time asymptotics through a Lyapunov functional. The optimal control problem is solved numerically, and for large T, we also theoretically determine the optimal strategy in a restricted class of controls.