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

Camille Pouchol*[1]

[1]Laboratoire Jacques-Louis Lions (LJLL) – INRIA, Université Paris VII - Paris Diderot, CNRS : UMR7598, Université Pierre et Marie Curie (UPMC) - Paris VI – B.C. 187 75252 Paris Cedex 05, France

Résumé

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.

*Intervenant