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Optimal schedules for therapies in metastatic cancers.

An actual important challenge in oncology is to determine the best temporal administration protocols for either a given drug or the combination of various treatments, in order to reduce the cancer disease or at least stabilize it. In this talk, we present a model for the evolution of the density of the metastatic population structured by size and "angiogenic capacity" (= vasculature) modified by the action of both an anti-angiogenic treatment which affects the vasculature of the tumors and a cytotoxic treatment attacking the cancerous cells. The model is a non-autonomous transport equation in dimension 2 with a nonlocal boundary condition

$$(1)\begin{cases} \partial_t \rho + \mathrm{div}(G\rho) = 0 &]0,\infty[\times\Omega \\ -G\cdot\overrightarrow{\nu}\,\rho(t,\sigma) = N(\sigma)\int_\Omega \beta(x,\theta)\rho(t,x,\theta)dxd\theta + f(t,\sigma) &]0,\infty[\times\partial\Omega \\ \rho(0,\cdot) = \rho^0(\cdot) & \Omega \end{cases} .$$

First, we will show the well-posedness of this problem : existence and uniqueness of solutions. The existence is proved by convergence of a numerical scheme consisting in straightening the characteristics and discretize them. We also present the numerical analysis of this scheme. We use then the model to investigate *in silico* the effect of various schedules of anticancerous drugs both on the primary tumor and the metastases, for example in the problem of the combination of a cytotoxic drug (chemotherapy) and an anti-angiogenic one. These considerations lead us to define and investigate an optimal control problem for determining the best schedule of the drug integrating both the metastases and primary tumor dynamics.

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