Singularity of control in a model of acquired chemotherapy resistance

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This study investigates how optimal control theory may be used to delay the onset of chemotherapy resistance in tumours. We study a two-compartment model of drug-resistant tumour growth under angiogenic signalling. An optimal control problem with simple tumour dynamics and an objective functional explicitly penalising drug resistant tumour phenotype is formulated. Global existence and positivity of solutions, bifurcations (including bistability and hysteresis) with respect to the chemotherapy dose are studied. Two optimisation problems are then considered. In the first problem a constant, indefinite chemotherapy dose is optimised to maximise the time needed for the tumour to reach a critical (fatal) volume. In the second problem, an optimal dosage over a short, 30-day time period, is found. It is concluded that, after an initial full dose interval, an administration of intermediate dose is optimal over a broad range of parameters.

References

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