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GLOBAL ANALYSIS OF A CANCER MODEL WITH DRUG RESISTANCE DUE TO LAMARCKIAN INDUCTION AND MICROVESICLE TRANSFER

Attila Dénes* and Gergely Röst

Bolyai Institute, University of Szeged,
Aradi vértanúk tere 1., H-6720 Szeged, Hungary

denesa@math.u-szeged.hu (*corresponding author),
rost@math.u-szeged.hu

Development of resistance to chemotherapy in patients with cancer strongly effects the patients' outcome. Due to chemotherapeutic agents, Darwinian selection induces intrinsic resistance. Besides this, Lamarckian induction resulting in drug resistance may take place, when resistance emerges upon changes taking place inside the cells as a result of the therapeutic drug. A recent discovery in cancer research uncovered a third possibility, indicating that this phenotype conversion can occur via the transfer of microvesicles from resistant to sensitive cells, mimicking the spread of an infectious agent. We present a model describing the evolution of sensitive and resistant tumour cells considering Darwinian selection, Lamarckian induction and microvesicle transfer. We identify three threshold parameters which determine the existence and stability of the three possible equilibria. Using a simple Dulac function, we give a complete description of the dynamics of the model depending on the three threshold parameters. Numerical simulations are shown to demonstrate the possible effects of increasing drug concentration, and we characterize the possible bifurcation sequences.

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