

DRUG-INDUCED DRUG RESISTANCE EVOLUTION IN CANCER CELL POPULATION DYNAMICS

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Abstract

Considering cancer as an evolutionary disease, we aim at understanding, and overcoming by drug delivery strategies [1, 2], the means by which cancer cell populations develop resistance mechanisms towards drug therapies. Rather than focusing on molecular mechanisms that are responsible for resistance at the individual cell level, we introduce phenotypes of resistance structuring cancer cell populations. Cell population densities are dependent upon a continuous phenotype [3], and optionally upon their position in space [4], thus structuring the whole cell population in a manner relevant to the problem at stake.

Drug-induced drug resistance, the question we are tackling from a theoretical and experimental point of view, may be due to biological mechanisms of different natures, mere local regulation, epigenetic modifications (reversible or not) or genetic mutations (irreversible), according to the extent to which the genome of the cells in the population is affected. In this respect, the models we develop are more likely to be biologically corresponding to epigenetic modifications, although induction of emergent resistant cell clones due to mutations under drug pressure are not to be excluded. From the biologist’s point of view, we study phenotypically heterogeneous, but genetically homogeneous, cancer cell populations in cell cultures under drug pressure. According to the cell populations at stake and the exerted drug pressure, is drug resistance a permanently acquired phenotypic trait or is it reversible? Can it be avoided or overcome by rationally designed combinations of drugs (to be optimised [6])? These are some of the questions we try to answer in

a collaboration between a team of mathematicians and another one of biologists, both dealing with cancer and Darwinian evolution of cell populations[5].

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