# Self-organization of cancerous cell populations in leukemia progression under targeted therapy

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Leukemia is a form of cancer of the blood cells. Healthy white blood cells grow and divide in an orderly and controlled way, but in leukemia the process gets out of control and the cells divide too quickly. In Chronic Myeloid Leukemia (CML), too many myeloid cells (one of the main types of white blood cells) are produced and released into the blood when they are immature and unable to work properly, leading to an increased risk of infection and strongly limiting the production of healthy red cells and platelets. Front line therapy for the treatment of patients affected by CML is based on the administration of Tyrosine Kinase Inhibitors (TKIs), such as imatinib, dasatinib, nilotinib or axitinib [Faber et al. 2006]. Despite the fact that they represent the first example of a successful molecular targeted therapy, the development of resistance to these drugs is observed in a proportion of patients, especially those in advanced stages.

In this work, effects of environmental randomness and fluctuations on the occurrence of self-organization phenomena in the evolutionary dynamics of cancerous cell populations are investigated. Complexity features in cancer development and progression are modeled by using a Monte Carlo method to simulate the stochastic evolution of initially healthy cells which can experience genetic mutations, modifying their reproductive behavior and becoming leukemic clones [Pizzolato et al. 2011]. In particular, we simulate a TKIs-like treatment of patients affected by CML by modifying the fitness and the death rate of cancerous cells and we study the fluctuations on cancer growth dynamics and the developing of resistance to the standard therapy [Pizzolato et al. 2016]. We also consider the possibility of varying the drug administration dosage within specific temporal windows. Several scenarios in the evolutionary dynamics of white blood cells, as a consequence of the efficacy of the different modelled therapies, periodic or continuous, are described. The best results, in terms of a permanent disappearance of the leukemic phenotype, are achieved with a continuous therapy and higher dosage. However, our findings demonstrate that an intermittent therapy could represent a valid choice in patients with high risk of toxicity, when a long-term therapy is considered. Moreover, a suitably tuned therapy can enhance the treatment efficacy and reduce the probability of developing resistance.

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