Influence of the age structure on the stability in a tumor-immune model for chronic myeloid leukemia

Kyriaki Dariva

kyriaki.dariva@univ-st-etienne.fr

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Abstract

The Chronic Myeloid leukemia (CML) is a blood and bone marrow cancer. It is characterized by mutations in the white blood cells which tend to proliferate rapidly and to have better survival capacities than healthy cells. The immune system plays an important role in the long term response.

We propose and analyze a system of partial differential equations (PDEs) for chronic myeloid leukemia (CML), generalizing the ordinary differential equations' system (ODE) proposed in [2, 3]. This model describes the proliferation and differentiation of leukemic cells in the bone marrow and the interactions of leukemic and immune cells. We consider that the differentiation of cells can be described by a continuous variable which we use to structure our system. The model is based on a non-monotonic immune response. At low levels, immune response increases with the tumor load whereas for high levels, tumor is suppressing the effect of immune system (immunosuppression). In particular, under certain hypothesis, immune response grows fast at intermediate levels (in the 'immune window').

With this model we find an unstable disease free-equilibrium point and alternated stability of high equilibria (high tumor load), the highest one being stable. Stability of the steady state describing remission induced by a control due to the immune system depends on the shape of the distribution of maturity of differentiated cells.

The stability of the remission steady state is fully characterized by the roots of the characteristic equation:

$$P(\lambda) = Q(\lambda) \int_0^{+\infty} e^{-\lambda x} \bar{p}(x) dx$$

where $\bar{p}$ is a probability measure on $\mathbb{R}^+$ corresponding to the normalized distribution of maturity of differentiated cells and $\text{degP} = 3$, $\text{degQ} = 1$. The steady

state can lose stability due to the shape of $\bar{p}$. In contrast to the linear case (P of degree 1 and Q constant) where there is a minimal mean value of the distribution for stability loss given by a Dirac mass [1], in our case the Dirac is not optimal. We give a concrete counterexample of a distribution that is less stable than the Dirac (in a sense to be precised).

References

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