

# A COMPLEX MODEL OF CELL EVOLUTION IN LEUKEMIA INCLUDING COMPETITION AND THE ACTION OF THE IMMUNE SYSTEM\*

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Dedicated to Dr. Vasile Drăgan on the occasion of his 70<sup>th</sup> anniversary

## Abstract

The model studied in this paper describes the competitive interaction between healthy and malignant cells in leukemia with the involvement of the immune system. The model consists of 9 delay-differential equations with 9 delays. Local stability is investigated for the equilibrium points of the system. Lyapunov-Krasovskii functionals related

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to some of these points are constructed. The evolution of the disease is studied numerically within different scenarios that show that some particular circumstances can lead to recovery. This can be an important support for combined therapies that trigger the leukemia and at the same time stimulate the action of the immune system.

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## 1 Introduction

Leukemia is a cancer of the blood and bone marrow distinguished by a large number of white blood cells. Chronic myelogenous leukemia (CML), or chronic granulocytic leukemia, is a clonal stem cells disorder. It is characterized by the proliferation of granulocytes and their precursors in the bone marrow and the accumulation of these cells in the blood stream. The trigger of CML is a chromosomal abnormality, called the Philadelphia chromosome (denoted Ph) that causes the formation of the Bcr-Abl fusion gene. This gene is thought to be the one responsible for the abnormal myelocyte proliferation (see [16], [31]).

Although CML is one of the most studied types of leukemia (see [13], [3], [25], [12], [19]), only relatively recently has the immune system been included in models (see [8], [21], [22], [23],[26], [27]). This is mainly due to the fact that the immune system is very complex and its mechanism is not completely understood.

A description of the activation of the immune system and the effect of the immune system on the population of malignant cells can be found in [8]. The model presented in this paper is an extension of the model from [8]. In order to obtain a more accurate representation of the biological interactions that occur during CML, we included the competition between the healthy and the malignant cells. It is a novelty for cell competition to be considered. It is also the first time that a feedback action of the immune system is studied while taking into consideration the appropriate time delays. The paper [26] studies a model of ordinary differential equations (ODE) where only the dynamics of the mature leukemic cells related to the response of the immune system is considered. The approach in [21],[22],[23], [27], that partly inspired the present paper, consider another set of ODE equations for the leukemic cells and are different also in other aspects from the present