Second semester report

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Thesis title: Physics of cancer

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1 Introduction

In the previous semester, we studied the proper parameters to reproduce the behaviour of the hematopoietic system using the hierarchical differentiation model. We began to implement the necessary modifications to reproduce the progression of Chronic Myeloid Leukemia (CML). The first observation was that CML blast phase arises from a blast cell, in our model, this type of cells are represented by the cells from levels in between the hierarchy. This trait can be explained by an increase of the parameter γ for all the levels below (less differentiated) the progenitor level.

2 Research work

In this semester we focused on other relevant characteristics about the development of the disease. The presence of blast cells in blood is crucial for a correct diagnostic and evaluation of the prognostic tools from each patient. The role of the bone marrow cell density is also important. The rapid increase of cancerous cells in the bone marrow affect the interaction of the cells with the extracellular environment, possibly promoting the migration of immature cells from the bone marrow to the bloodstream.

At this point, we realized a two-compartment model is necessary to mimic the behaviour of the cell migration from bone marrow to blood. In healthy individuals, the migration of cells is only allowed for the terminally differentiated level, this ensures that only mature cells are found in the blood. When the number of cells in the bone marrow increases the cells are forced to migrate from the bone marrow, due to the physical space restriction of the bone marrow.

The migration of the cells is controlled by a monotone increasing function $\rho(N)$ that depends only on the current total number of cells N in the bone marrow at time t. We have tried with several types of functions of the exponential, linear and logarithmic types, achieving the desired behaviour for the chronic phase. The development of the chronic phase is driven by the leukemic stem cells at the bottom of the hierarchy. The growth of these cells, promotes the migration of cells from the bone marrow to blood, leading to the appearance of blast cells in the blood, showing the characteristic behaviour of the disease at the chronic phase.

The leaking from cells from different levels is determined by an exponential function that depends on the level position into the hierarchy and a free parameter. Cells from the more mature levels will tend to migrate more than immature levels. The appearance of the blast and the last phase of the disease is driven by somatic evolution and the presence of cells with more mutations. The point where the uncontrolled growth of cells starts is the onset of the blast phase. We have been experimenting with different functions for the leaking dynamics of different levels, obtaining interesting results, but

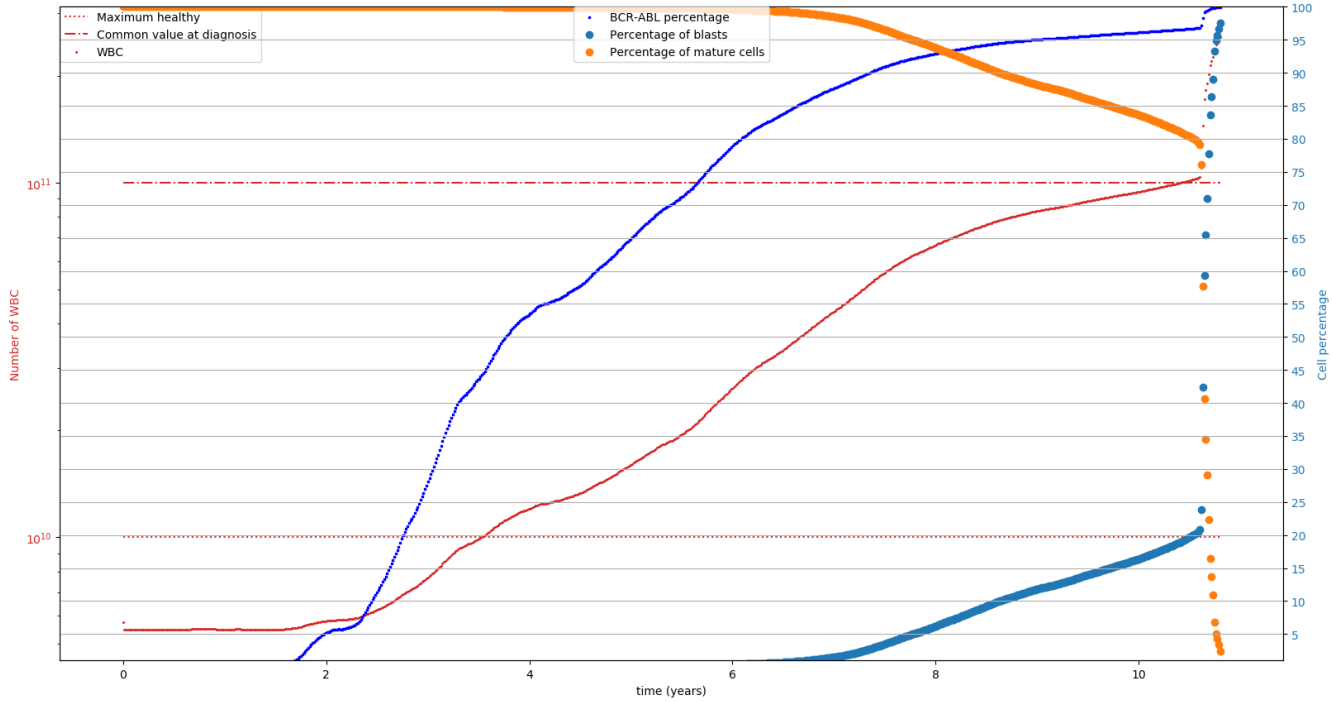

Figure 1: On the left vertical axis shows total number of white blood cells, used for progression disease monitoring. On the right vertical axis the percentage of BCR-ABL cells and blast cells in blood.

still not the desired ones. We will be working with different leaking profiles to obtain the desired results. In Figure 1 we show the latest available results.

3 Attended courses

- Reconstructing evolutionary history from molecular sequences
- Evoultionary game theory

4 Conferences

Accepted to participate and present a poster in the Evolution and Ecology of Cancer Conference to be held from 17 to 19 of July in Hinxton England.