A branching process model of hematopoiesis with applications to Chronic Myeloid Leukemia

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***Short Abstract* — An age-dependent reducible branching process model is proposed to model hematopoiesis and the genesis and relapse of chronic myeloid leukemia stem cell populations. The model attempts to determine the probability of nonextinction of a population and the amount of time until a population reaches a specific size. The model is motivated by a pseudo-stochastic model that introduces within-tissue plasticity although it does not account for cell death, removing part of the variability due to stochasticity in small populations.**

***Keywords* — reducible branching processes, hematopoiesis, stem cell plasticity, chronic myeloid leukemia.**

I. Introduction

Roeder and Loeffler propose a pseudo-stochastic model of hematopoietic stem cell organization and proliferation accounting for plasticity within functionally similar stem cells prior to differentiation [6, 7]. The model relies on an amended definition of tissue stem cells formulated to account for plasticity within the tissue while relying on the functionality of stem cells. A stem cell is defined by its capabilities rather than properties of the cell, including the ability to self-maintain, self-renew, and the residence in a growth or quiescent environment [3, 5].

According to the model, as cells remain in the growth environment, they divide at every time step into 2 daughter cells with a propensity to differentiate. However, with some probability the cells can enter a quiescent environment and lose the propensity for differentiation, bringing them back toward an earlier state. Once differentiated, a cell exits this cycle and can enter the peripheral system, preparing it for maturity and eventual cell death [6]. The authors show the application of their model and simulation to the study of chronic myeloid leukemia, its treatment and the potential for relapse [2].

Simulations of CML treatment include the effect of cytostatics such as imatinib or hydroxurea which reduce the number of leukemic stem cells (and normal stem cells with treatment of HU). However after the treatment period is finished, there is a potential for CML stem cells to self-renew their population count and relapse to occur, which is a common situation. The model does not account for cell death, and at low population counts, the associated stochasticity is not considered which could lead to extinction of the CML population of cells instead of a relapse. Variability of the time until relapse may also vary due to the stochasticity of cell fates. Both should be considered after treatment [2, 6].

II. Branching process model and its predictions

We propose an age-dependent multitype branching process model as a stochastic model of hematopoiesis with within-tissue plasticity. Such a model will allow us to account for variability during the genesis of CML and after therapy. We can determine the probability of nonextinction of leukemic cells and the time until a sizable population has been achieved (as in a relapse event). Our model assumes stem cells exist in a growth or quiescent environment proliferating until exiting a final state to become fully differentiated. Once differentiated, cells are no longer stem cells and continue into maturity before death, so the process is reducible. Since we are dealing with a potentially large population of cells, asymptotics and large number approximations of the process are determined [1, 4].

At the present stage, the results include determination of feasible range of parameters and a sensitivity study of the model. This will be followed by calibration to existing experimental and clinical setups.

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