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ORIGINAL ARTICLE

Cancer cells population control in a delayed-model of a leukemic patient using the combination of the eligibility traces algorithm and neural networks

Elnaz Kalhor[1] · Amin Noori[1] · Ghazaleh Noori[2]

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Abstract
The main purpose of this paper is to provide a solution, through which one can efficiently reduce the population of cancer cells by injecting the lowest dose of the drug; therefore, reducing the side effects of the drug on healthy cells. In this paper, a mathematical model of stem Chronic Myelogenous Leukemia (CML) is used. To this aim, a hybrid method is used, that is a combination of the Eligibility Traces algorithm and Neural Networks. The eligibility traces algorithm is one of the well-known methods for solving problems under the Reinforcement Learning (RL) approach. The reason is that the population of cancer cells can be controlled with a higher accuracy and will have a significant impact on dosage of injection. The eligibility traces algorithm has the advantage of backward view, meaning it will investigate previous states, as well. That will result in improving the learning procedure, speed of reduction in cancer cells population and the total dosage of the injected drug during the treatment period, in patients with CML. Combination of the mentioned method and neural networks has provided continuous states in the considered problem. Hence, there will be no limitation for considering all possible states for solving the problem. Moreover, this can accelerate obtaining the optimal dosage with a high accuracy, which is a significant advantage of the proposed method. To show the effectiveness of the proposed method to control the population of cancer cells and obtaining the optimal dosage, it is compared with four different cases: when only the eligibility traces algorithm is employed, in the case only the Q-learning algorithm is used, when the Optimal Control is applied and in the case no dosage is injected. Finally, it is revealed that the combinatory method of the eligibility traces algorithm and neural networks can control the population of cancer cells more quickly, with a higher accuracy as well as applying a lower dosage of the drug.

Keywords Eligibility traces · Reinforcement learning · Neural networks · Chronic myelogenous leukemia · Drug therapy · CML stem cells · Optimal control

1 Introduction

Leukemia is a kind of blood disease, where the proliferation of stem blood cells is uncontrolled. In acute leukemia, the disease progresses rapidly and produces huge numbers of undeveloped nonfunctioning white blood cells. Stem-like leukemic cells are similar to normal ones. Some differences between these two types of cells lead to the generation of leukemic cells with different metabolic activities, resulting in the survival of the tumor under hard conditions, even when treating with chemotherapy drugs. Researches reveal that stem-like leukemic cells are generated under genetic changes in a cellular population. These changes can lead to the presence of excessive genes (compared with the normal case) and mitigation of other ones. In order to identify stem-like leukemic cells and differentiate them from the non-stem

✉ Amin Noori
Amin.noori@sadjad.ac.ir

Elnaz Kalhor
e.kalhor123@sadjad.ac.ir

Ghazaleh Noori
Nourigh891@mums.ac.ir

[1] Faculty of Electrical and Biomedical Engineering, Sadjad University, 9188148848 Mashhad, Iran

[2] Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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