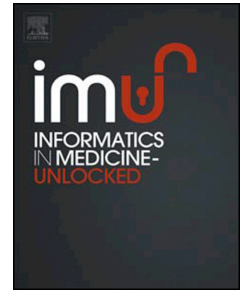# Accepted Manuscript

A stochastic cellular automata model of growth of avascular tumor with immune response and immunotherapy

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A Stochastic Cellular Automata Model of Growth of Avascular Tumor with Immune Response and Immunotherapy

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Abstract— **In this paper, a stochastic cellular automata model is presented to investigate the immunotherapy effects on avascular tumor treatment. In this model, the influence of the extracellular matrix on tumor growth is explored. To investigate the immunotherapy effect, first, the model tumor is first allowed to grow in a natural way. Then, immunotherapy is applied by increasing/decreasing the main parameters of the model, based on a threshold number of immune system cells. During the therapy period, the proliferation and escape rates of the cancer cells are decreased, with a constant step. In addition, the rate of cancer cell lysis and the rate of the binding of cancer cells are increased. These changes are continued until the number of immune cells reaches the given threshold. Results show that with a low threshold value, the tumor cell population does not change much. Moreover, by increasing the threshold value, the tumor enters the dormant state, and for the extreme threshold value, a long-term eradication of the tumor would be possible. These results are consistent with those captured by the ordinary differential equation (ODE) based models and also with experimental observations, where it has been shown that many patients can be in complete remission for 7 to 91 months.**

Index Terms—**Cancer modeling, Cellular automata, Immune system, Immunotherapy, Extra-cellular.**

I. INTRODUCTION

Cancer is a leading cause of death. It can be defined as growth, proliferation and sometimes propagation of human cells in an unnatural way. Cells of the human body grow, proliferate and finally die. If this process is carried out in its normal and stable manner, the body would be safe and maintain performance. However, problems begin when a cell involved in mutation or variation consequently morphs to a cancerous cell [1, 2].

Much of the mechanism of cancer development and proliferation is still unknown, though it has been shown that factors making changes in the DNA can lead to generation of a cancer cell. These changes cause unnatural characteristics to appear in the cell, which in turn result in an irregular cell division. When a cell is altered, the cell is different from its neighbor cells and does not perform the duty of a normal cell. Thus the changed cell does not follow controlling commands and acts arbitrarily, growing in an uncontrolled way [3, 4].

In a simple point of view, growth and development of a tumor includes three steps: first, the tumor should escape from the immune system response. Then, it needs to reduce the extracellular matrix. Finally, after sufficient growing, it should assist blood vessels to survive in its tissue [4].

Different models, including mathematical models and computer simulations, can be used to decrease the time and cost of cancer related experiments and research. In some cases, simulations can prevent futile experiments [5- 12].

A cellular automaton is a type of mathematical model that can be exploited for simulation of systems and diseases at the cell level. In addition, cellular automata are simple and discrete systems in which limited number of states are defined for one cell. Cellular automata can generate a complicated behavior based on simple and local rules. Local means determine the state of each cell, and the states of neighbor cells, while distant cells have no influence [13, 14].

Currently, there are various cancer treatment options such as surgery [15], chemotherapy [16], radiation therapy [17], and hormone therapy [18]. In many cases, the aforementioned techniques have been largely unsuccessful and may result in an unpleasant side effects [19]. Another approach is immunotherapy, involving activating or strengthening the immune system to fight the cancer itself [19- 24]. It was named "Breakthrough of the Year" in 2013, by the journal Science [19]. In this paper, we have modeled immune cell therapy. It removes cancer-fighting T-cells from the body, harvesting them in the lab, and then, reinjecting them into the patient.

So far, many models have been presented to understand cancer behavior. Most of them have modeled tumor growth and its effective factors [25- 28]. Also, in some work, competition for nutrients among normal and cancerous cells has been analyzed, as well as the influence of the immune system response on the tumor growth [29, 30].

In this paper, we have simulated the influence of immunotherapy on the treatment of avascular tumors, based on a cellular automaton. In addition, the influence of differing number of immune system cells on tumor growth is investigated.

The remainder of this paper is organized as follows. In section II, the basic concept of the cellular automata and of one of the papers related to stochastic modeling of tumors are presented. The proposed model is described in section III. The

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