A stochastic Cellular Autotmata Model of tumor-immune interaction with therapy intervention

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Introduction

Cellular automata (CA) are mathematical models that describe in simple mathematical formalism a highly complex phenomenon. CA theory is related to several disciplines such as the graph theory, finite algebras and stochastic processes. In systems theory, a major interest is taken to this type of models that offer a powerful approach to represent complex phenomena which are difficult to model using conventional approaches (ODE, PDE etc.). The objective of this work is to use a stochastic cellular automata model [4] in order to simulate a primary tumor growth and its interaction with immune cells, and also to introduce to [4] the immunotherapy intervention and shedding light on the factor which may play a major role in the immunotherapy effectiveness. The nutrients (oxygen, amino acids, glucose, etc.) necessary for cell proliferation and motility are diffused from a capillary vessel and governed by a reaction-diffusion model [4].

Methods

The cancerous cells grow and divide with probability P_{div}, as long as oxygen and nutrients are present in their micro-environment [1], however they migrate with probability P_{mov} from the low nutrient concentration areas or from the areas where there are a high number of tumor cells. Tumor cells may also be die when they are in contact with immune cells with probability P_{imdth}, or when they are in high therapy concentration zones, or when the nutrient elements are insufficient with probability P_{dth} .
Two types of immune cells are considered in this work: NK cells and CTL cells; they migrate randomly about the domain of interest and look for tumor cells, if NK cell is in contact with tumor cell, it will be destroyed along with it, however if CTL cell is in contact with tumor, then, the surrounding normal cells are sampled for CTL induction with probability P_L. CTL cells are assumed to die if there are no tumor cells in the domain of interest with probability P_{LD}.
Immunotherapy intervention with IL-2 (interleukine-2) leads to activate NK and CTL cells, in addition to stimulate the CTL proliferation. The effect of IL-2 on CTL cells is presented with term probability P_{IL2}.

Results

Tumor migration process plays a central role in many levels of cancer growth; when the migration is high, the tumor morphology is more disconnected, however, if the migration is not considered, the tumor morphology is compact. The migration process has also an impact on immunotherapy effectiveness, for high migration cell, tumor is dispersed in tissue and may also migrate to a distant sites and grow, which increases the chance of metastases, in this case, immunotherapy intervention was not powerful against the cancer. On the other side, for low cell migration, tumor cells are localized in primary tissue and the intervention of immunotherapy has remarkably decreased the tumor mass. The simulation results have been compared with experimental results [10],[8] and they show a great agreement.

Conclusion

A cellular automata model for the growth of tumor and its interaction with immune cells in addition to the immunotherapy intervention was investigated by numerical simulations including tumor cell division, migration and death as well as the immune cells migration, death and CTL induction. Tumor motility process has an effect on tumor morphology and also on the therapy effectiveness.

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