An analytical spatially-based approach to study cancer cell population evolutions

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Motivations

The evolution of many biological dynamics is strongly related to the spatial composition of the tissues where it takes place. It becomes of paramount importance, not only the knowledge of the type and the number of different biological entities involved, but also their position and their distribution in space. Spatial techniques are particularly useful to investigate the mechanisms affecting tumor growth and maintenance upon vaccination or drug treatment. However not many techniques have been studied to tackle the spatial definition of the environment in addition to the densities of the various elements. This is mainly due to the difficulties of modeling a spatial distributed system using conventional techniques.

Methods

In this work we present a new approach, based on an evolution of the mean field analysis that exploits some of the features of the ""Markovian agents"" performance evaluation formalisms. This new technique allows to study the system evolution through a sound analytical treatment of the spatial dependency. In particular, we focus on the study of tumor progression, showing that the growth and progression of many cancers are driven by small groups of Cancer Stem Cells (CSCs). The CSC tumor model presents a hierarchically structured organization similar to that found in normal tissues: CSCs are self-renewing, capable of tissue regeneration and of giving rise to non-CSCs, the latter being more differentiated and largely lacking in tissue-regeneration ability. Considering this hierarchical structure, the response to drug treatments on the several cell populations that compose the cancer will produce different effects depending on the characteristics of the cancer subpopulation. For this reason, the CSCs are believed to be the cause of failure of conventional therapies, since effective drug treatments able to eliminate all the CSCs, hence to avoid relapses, are not easy to find. Based upon this model we study the cancer progression, the drug or DNA-vaccination effects, that locally administered, at predefined time periods, can slow down the expansion of the tumor. The considered tissue is divided in small areas, each characterized by its own parameter. The evolution in one area can affect the neighbor: this allows modeling the propagation of both cancer growth or the therapeutic effects of drugs or vaccination. Our approach will aggregate similar cellular population, using differential equations, rather than modeling all the involved entities separately, in order to reduce the model complexity.

Results

We expect to model the evolution of the cancer in a volume, taking into account the total number of the different cellular population involved and their spatial distribution. The results will be compared with similar approaches in the literature based on cell automata. We show the spatial behavior of the well known therapy, and how the framework proposed could be a basic step for an optimization algorithm that will determine the best time instants in which administer the drug or vaccination, and the best locations where it should be inoculated. The solution of the model can support the in vitro/in vivo experiments for testing new biological hypothesis. Furthermore, our approach can be extended to consider the immunological tumor micro-environment by adding more details on the immunological system involved on the drug/vaccination treatments. This might be particularly interesting in the area of combined treatment development. Tumor vaccination alone is not sufficient to eradicate the disease, but combined with other immuno-pharmacological treatments, affecting the CSC differentiation rate might represent an interesting approach in the area of tertiary cancer prevention.