A new model of tumor progression based on the concept of complex automata driven by particle dynamics

R.Wcisło[1*], W.Dzwinel[1], D.A.Yuen[2]

[1]*AGH University of Science and Technology, Institute of Computer Science, Al. Mickiewicza 30, 30-059 Krakow, Poland, wcislo@agh.edu.pl, dzwinel@agh.edu.pl.*
[2]*University of Minnesota. Minnesota Supercomputing Institute, Minneapolis, MN 55455-0219, USA, daveyuen@gmail.com.*

A.Dudek[3]

[3]*University of Minnesota Medical School, Division of Hematology, Oncology, and Transplantation, Department of Medicine, Minneapolis, Minnesota, MN 55455-0219, USA, dudek002@umn.edu.*

Abstract

Angiogenesis, the growth of a network of blood vessels, is a crucial component of solid tumor progression, linking avascular and the potentially fatal vascular growth phases. Existing computational models assume that the interaction between tumor and vasculature takes place mainly via two concentration fields: the oxygen originating in the vessel network and the growth factor originating in the tumor cells. The dynamics of growing tumor involving mechanical remodeling of healthy tissue and vasculature are neglected in most of the models. This is due to the lack of efficient computational framework allowing for simulation of mechanical interactions. Meanwhile, just these interactions trigger global changes in tumor growth and are responsible for its volumetric and directional progression. We describe here a novel 3-D model of tumor growth, which combines particle dynamics with cellular automata concept. The particles represent both tissue cells (spherical particles) and fragments of vascular network (tube-like particles). They interact with their closest neighbors via semi-harmonic central forces simulating mechanical resistance of the cell walls. The particle dynamics is governed by both the Newtonian laws of motion and the cellular automata rules. These rules can represent cell life-cycle and other biological interactions involving smaller spatio-temporal scales. The particles (cells) can replicate by a simple mechanism of division, similar to that of a single cell reproduction and die due to apoptosis or necrosis. We introduce also diffusive substances (such as nutrients or signaling cues) which are described by means of continuum fields. We use Kirchoff's laws to calculate the hydrodynamic quantities in each blood capillary. In this sense, our model represents extension of cellular automata paradigm (CA) to the complex automata (CxA), where the CxA nodes correspond to moving particles while their states evolve both accordingly to the regular CA rules and with dynamically changing continuous fields. We conclude that our concept can serve as a general framework for designing advanced multiscale models of tumor dynamics and is very competitive to the approaches presented before. The CxA particle based model can reproduce realistic 3-D dynamics of the entire system consisting of the tumor, normal tissue cells, blood vessels and blood flow. It can explain such the phenomena like: inward cell motion in avascular tumor, stabilization of its growth due to external pressure, trapping of healthy cells by invading tumor, remodeling of tumor vasculature due to the pressure inside the tumor, influence of external (boundary) conditions on the direction of tumor progression. We concluded that this computational framework can be used for developing computational models reproducing multi-scale dynamics of the particle ensembles in sub-scales ranging from diffusion of cytokines, blood flow up tumor growth and vascular network expansion.

Keywords tumor progression, angiogenesis, computer simulation, complex automata, particle model

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[*]*Corresponding author*