Modeling of avascular tumor growth by reaction-diffusion equations and cellular automata

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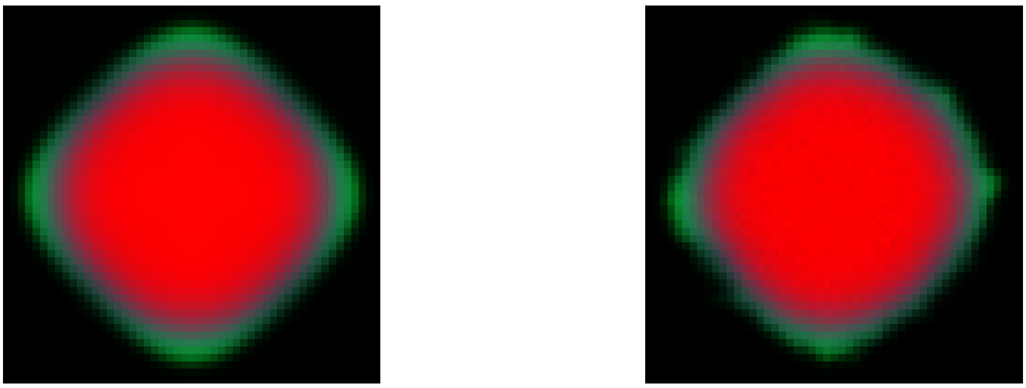
Abstract – The development of a macroscopic tumor can be divided into three subsequent stages: (1) avascular, (2) vascular, and (3) metastatic. In the avascular stage the tumor receives nutrients by diffusion from the surrounding tissue. In the vascular stage the tumor has triggered the growth of vessels in order to improve its nutrient supply. Finally parts of the tumor separate from the main bulk leading to metastases.

There are two classes of mathematical models for the description of the avascular stage. In the first class the cell density $c(x,t)$ is regarded as a continuous quantity subject to a differential equation of the reaction-diffusion type:

$$\frac{\partial}{\partial t}c(x,t)=f\left(c(x,t)\right)+D\frac{\partial^2}{\partial x^2}c(x,t)$$

The reactive term $f\left(c(x,t)\right)$ accounts for the cell proliferation, the diffusive term $D\partial^2 c(x,t)/\partial x^2$ for the spatial propagation of the tumor. The differential equation can be solved analytically or numerically. The second class of models includes cellular automata. A cellular automaton consists of spatial cells (voxels), each voxel can contain a certain discrete number of tumor cells. At each time step of the simulation the state of the automaton is updated according to deterministic or stochastic rules.

The aim of our work is to bridge the gap between both classes. For this purpose we developed two models. The first model consists of a set of reaction-diffusion equations which are solved numerically on a two-dimensional lattice. The second model is an automaton with discrete cell number. The cells proliferate stochastically and perform a random walk between adjacent voxels. Both models yield comparable simulation results (Fig. 1). This indicates the equivalence of both approaches in the limit of large cell numbers.



(a) (b)

Fig.1: Simulation results. Proliferating cells (green), quiescent cells (blue), necrotic cells (red). (a) Numerical solution of linearized and discretized differential equations, (b) Cellular automaton