Simulating the behaviour of cancer cells in the microfluidic chip

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Abstract: One of the newly emerging experimental setups in biomedical experiments are the three-dimensional culture models, the so-called lab-on-chip systems, or microfluidic chips. They ensure a more realistic physiological experimental conditions by using a chamber with cells and microchannels that imitate the capillary network and ensure a better diffusion of nutrients. In this study a hybrid numerical model is presented that is capable of simulating the behavior of cancer cells in a microfluidic chip. The model combines the agent-based model (ABM) and the lattice Boltzmann method (LBM) and is capable of predicting the change of number of cells over time. The presented model can be helpful for a more thorough analysis of behavior of cancer cells under diverse drug treatments and can be an efficient support to experiments. Experiments can be used as the basis for the estimation of parameters of the numerical model and this information can provide quantitative insight into influence of diverse considered drug treatments on the behavior of cancer cells, which can further help plan future experiments accordingly.

Keywords: hybrid numerical model, cancer cell cycle dynamics, agent-based modeling, lattice Boltzmann model

1. Introduction

Different experimental setups are employed within experiments in biomedical science. Two-dimensional (2D) in vitro cell culture models are commonly used, but they have limitations, such as the fact that they involve monolayer cultures, that limit the effectiveness of these systems for per example testing of potential drug therapies for cancer. The alternative emerged through the use of three-dimensional (3D) culture models, the so-called lab-on-chip systems [1]. In these systems there is a chamber with a hydrogel matrix where the cells are seeded. There are specifically designed microchannels that imitate the capillary network and connect this chamber with a peristaltic pump, which ensures better diffusion of nutrients. This way a more realistic

physiological experimental conditions are ensured [1] and studies in literature have shown that these systems are more efficient and superior to 2D cell culture models, where there is only a static flow of nutrients [2].

However, experiments performed in such 3D microfluidic systems can be expensive and time-consuming and could benefit from additional information, to help guide more specific experimental research. For this purpose, numerical simulations have proven to be a useful additional tool [3]. They can help to determine additional quantitative data that can help to define future experiments or predict the behavior of cells under varied conditions without the need to perform all experiments. In this study a hybrid numerical model is presented that is capable of simulating the behavior of cancer cells in a microfluidic chip.

2. Methods

The hybrid numerical model used in this study was previously presented in [4]. It combines the agent-based model (ABM) and the lattice Boltzmann method (LBM). ABM is used to simulate the behavior of individual cancer cells within the considered domain, by using a decision scheme that is shown in Figure 1. LBM is used to simulate the distribution of nutrients within the considered domain. The main difference in comparison with the model presented in [4] is that in this case, the simulation involves a 3D microfluidic chip, which means that the diffusion and flow of nutrients must be modelled differently. Instead of a diffusion equation, here the advection-diffusion equation has to be solved. This equation is given by:

$$\frac{\partial \omega}{\partial t} + \nabla(\mathbf{v}\omega) = D\nabla^2\omega - \kappa\omega\delta(\mathbf{x} - \mathbf{x}_{Ci}) \tag{1}$$

For solving this equation the LBM method and the D3Q27 lattice structure are used. The voxelized domain is created by using the data for the microfluidic chip that was applied in experiments. All quantities in the simulation are taken in their dimensionless form, as it was also performed in literature [4,5]. The ABM model contains several parameters that describe the behavior of cancer cells. The values of these parameters are taken from literature and are also given in Table 1.

Table 1. Values of the parameters of the ABM model

Parameter	Value
Average cell cycle length	16
Average hypoxia duration	9
Average necrosis duration	48
Average apoptosis duration	48
Spontaneous apoptosis probability	0.01
Quiescence threshold	0.5
Hypoxia threshold	0.3
Nutrient consumption	0.02

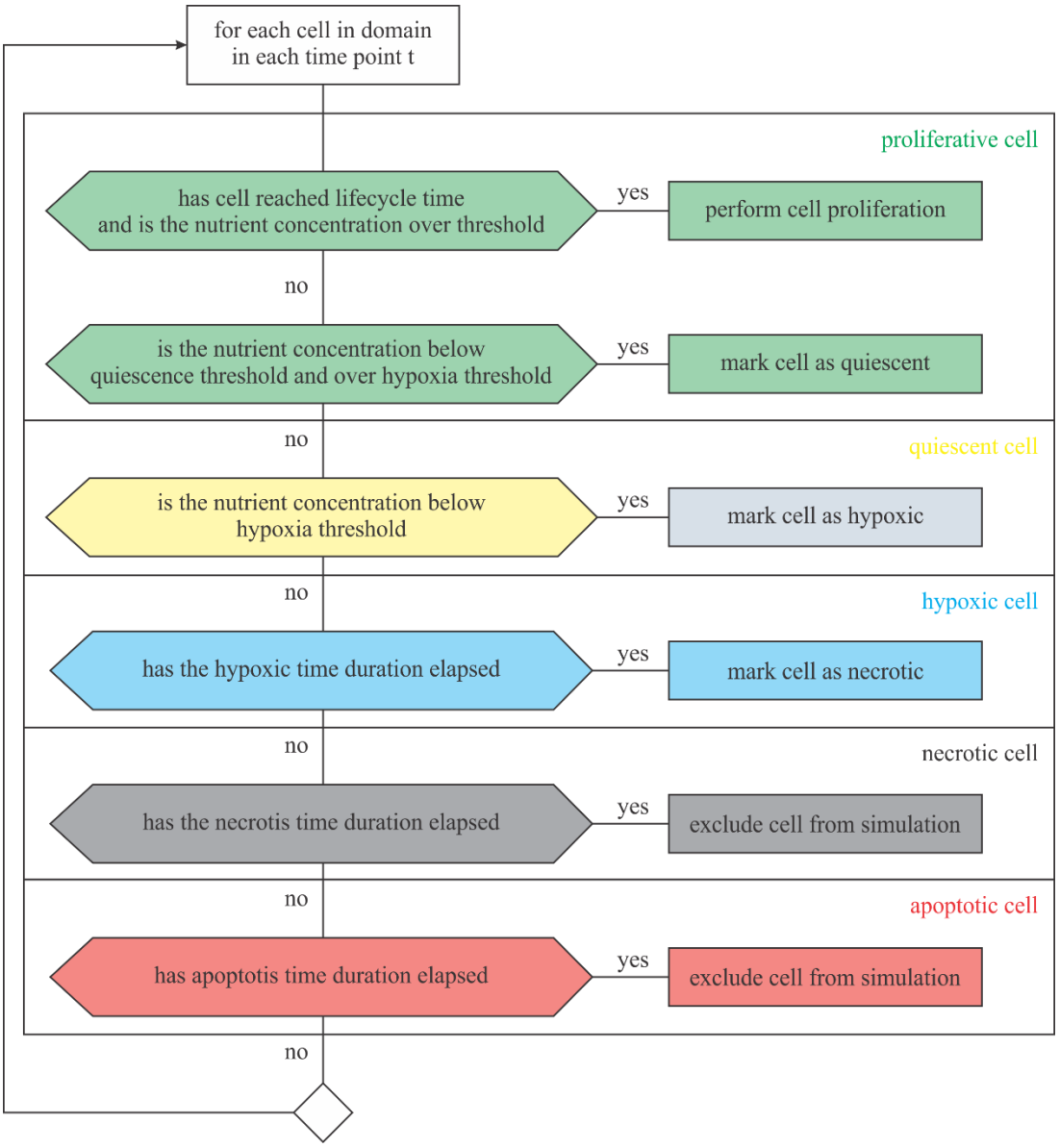

Figure 1. Decision chart for the ABM model

3. Results

Figure 2 shows the results of one simulation. The distribution of nutrients is shown together with the distribution of viable cells in the domain, for two chosen moments in time (24 and 72 hours after the start of the simulation). As it can be seen, the number of viable cells increases over time and the concentration of nutrients decreases. It should be noted that the nutrients are also constantly renewed thanks to the 2 microchannels whose entrances are located in left and right central region of the chamber (regions with maximal concentration).

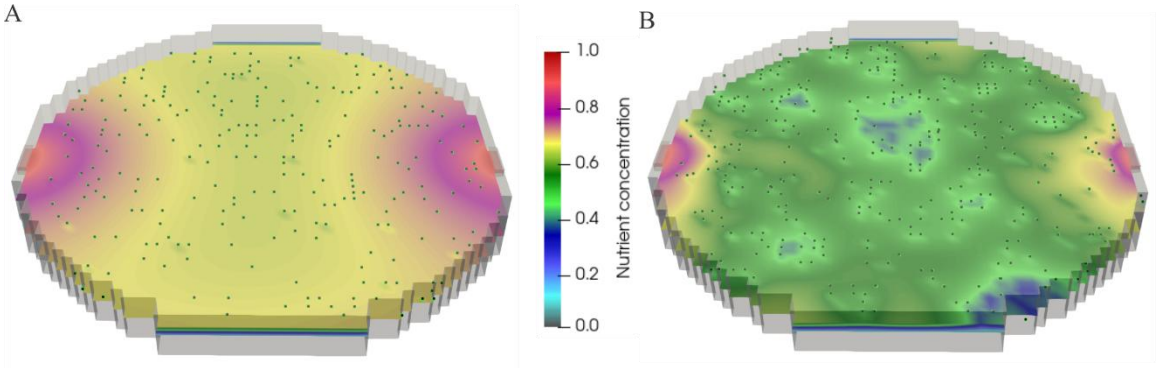

Figure 2. Results of a simulation of progression of cancer cells in a microfluidic chip. A – 24 hours after the start of the simulation; B – 72 hours after the start of the simulation

4. Conclusions

Numerical simulations using the hybrid model presented in this study can be helpful for a more thorough analysis of behavior of cancer cells under diverse drug treatments and can be an efficient support to experiments. Experiments can be used as the basis for the estimation of parameters of the numerical model and this information can provide quantitative insight into influence of diverse considered drug treatments on the behavior of cancer cells, which can further help plan future experiments accordingly.

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