

INTERACTIVE VISUALIZATION TOOL FOR TUMOR GROWTH SIMULATIONS

Rafal Wcislo

Department of Computer Science, AGH University of Science and Technology, Cracow, Poland

Keywords: Simulation, Visualization, Tumor growth, Angiogenesis.

Abstract: We present the main requirements and ready-to-use components of the interactive visualization tool for modeling of solid tumor proliferation. As the simulation engine it uses complex automata paradigm, which integrates cellular automata with particle dynamics. To make it sufficiently fast for interactive visualization we show that the system can be efficiently implemented on multicore workstations, with moderate number of processors controlled by data parallel interface such as OpenMP. In the near future the system will be empowered by a combined CPU and GPU computational environment. This in silico lab system is intended for medical laboratories doing research in oncology and/or in anticancer drug design.

1 INTRODUCTION

There are many mathematical models of tumor growth driven by the process of angiogenesis (Folkman, 1971; Castorina et al., 2009; Bellomo et al., 2003; Chaplain, 2000; Preziosi, 2003; Mantzaris et al., 2004; Lowengrub et al., 2010). The models fall into four categories: (a) continuum models that treat the endothelial cell (EC) and chemical species densities as continuous variables that evolve according to a reaction-diffusion system, (b) mechano-chemical models that incorporate some of the mechanical effects of EC-ECM (extracellular matrix) interactions (c) discrete, cellular automata or agent based models in which cells are treated as units which grow and divide according to prescribed rules (d) hybrid multiscale models involving processes from micro-to-macroscale. Multiscale and multiphysic models represent the most advanced simulation methodologies.

In (Wcislo et al., 2009) we present the concept of tumor growth model which is driven by particle dynamics (Haile, 1992; Dzwinel et al., 1999; Dzwinel et al., 2000; Dzwinel et al., 2006; Kadau et al., 2004) combined with a cellular automata paradigm (Hoekstra et al., 2007; Slood and Kroc, 2009). In this article we present a tool used for preparation and visualization of such a simulation. At a certain stage the creation of that tool became crucial due to:

- A number of simulation parameters (physical as well as chemical and biological characteristics of tissues are defined by as many as a few dozen up

to a few hundred of parameters) which became very inconvenient to modify manually in the text file.

- The simulation is expected to consist of several million of particles (depending on the modeling there shall be either single cells or their clusters together with the ECM) forming a three-dimensional fragment consisting of a healthy tissue, an array of blood vessels and a tumor. Thus a tool that would make it possible to interactively observe such a simulation would undoubtedly become a significant aid for a researcher.

2 VISUALIZATION TOOL

Figure 1 presents the view of the main screen of the visualization program.

2.1 Tissue Templates

The simulation program allows several types of tissues to be present simultaneously (a typical situation in the simulation is when there is a cancerous tissue surrounded by a healthy one and the two are interwoven with the network of blood vessels). Each tissue has an array of characteristic features such as density, an average size of cells, the rate of diffusion of particular substances (oxygen, TAF), oxygen requirements, life span, resistance to oxygen deficiency, etc.

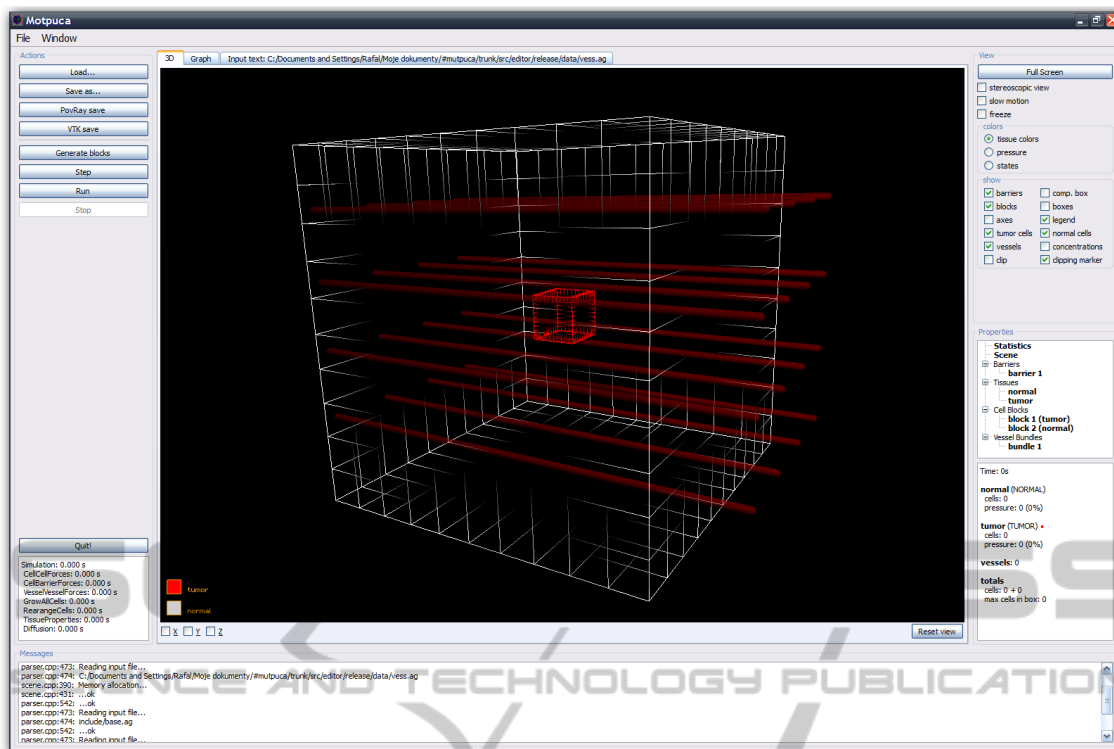


Figure 1: The main window of the visualization program.

The tool has already prepared predefined sets of data for chosen tissues so it is not necessary to define all the parameters every time for a certain tissue. These sets are prepared on the grounds of the biomedical data. During the preparatory stage when the user of this program deals with the initial values of the simulation, the data might be easily loaded and, subsequently, each parameter may be modified. This modified set of the parameters might also be saved as a template for other simulations.

2.2 Position, Rotation, Size

Due to the fact that it is impossible to reconstruct properly a process of blood vessel formation (angiogenesis) in two dimensions, all the simulations are currently carried out in three dimensions. 3D makes the simulation more accurate and consistent with reality; however, it significantly increases the time of computation and it complicates the way of defining initial tissue shape and location.

The discussed visualization tool makes it easy to position the tissues as well as adjust their size, location and space orientation so that the creation of an initial simulation state is facilitated. Such operations are mostly performed with the help of a computer mouse and a few keyboard shortcuts and func-

tion keys. The program allows the user to watch the prepared simulation from each side, zoom it, etc.

2.3 Simulation

As soon as the simulation is prepared, the program makes it possible to run the simulation. It might be run either on the single-processor computers as well as on multi-processor ones equipped with a shared memory (then the simulation program uses the OpenMP libraries). Due to the parallel execution, the time of calculation of particular steps is shortened and, therefore, the simulation is accelerated and the results are obtained earlier. At present, the research is being carried out over the implementation of the simulation on GPU devices.

If the simulation is performed locally, it might be watched on-line (Fig. 2). In that case the program shows the information concerning particular tissues (e.g. the number of cells, the number of cells in various states, pressure, O_2 concentration). The program allows to watch the tissues from any angle as well as make random cuts so that it is possible to have an insight into a tissue interior.

The visualization program makes optimizations that allow to watch the simulations - even those consisting of hundreds of thousands of particles - fluently.

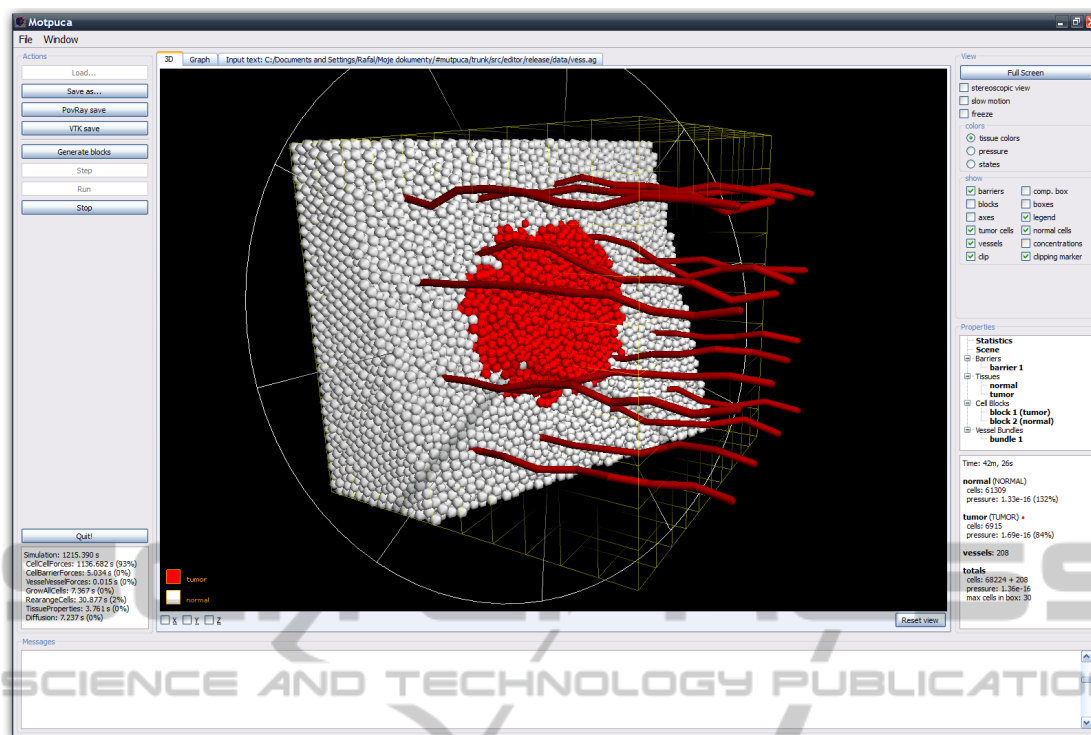


Figure 2: Simulation visualization. Normal cells are marked in white, tumor cells – in red. Tissue section is visible.

It is also possible due to the fact that it has the access to all the parameters of the simulation. This program, thus, holds an advantage over other visualization programs intended for general use.

3 CONCLUSIONS

It should be taken into account that during the creation of simulation programs, tools that could be used consecutively in *in silico* experiments should also be prepared. It is particularly crucial in the case of preparing a simulation of complex processes during which it is necessary to deal with hundreds of parameters and analyze the results from various dimensions. Such a convenient and intuitive tool allows to do the research undoubtedly more effectively as well as to verify one's hypothesis quicker.

ACKNOWLEDGEMENTS

This research is financed by the Polish Ministry of Higher Education and Science, project N N519 579338 and partially by AGH grant No. 11.11.120.865.

REFERENCES

Bellomo, N., de Angelis, E., and Preziosi, L. (2003). Multiscale modeling and mathematical problems related to tumor evolution and medical therapy. In *J Theor Med.*, volume 5/2, pages 111–136.

Castorina, P., Carc, D., Guiot, C., and Deisboeck, T. (2009). Tumor growth instability and its implications for chemotherapy. In *Cancer Res*, volume 69 (21).

Chaplain, M. (2000). Mathematical modelling of angiogenesis. In *J Neuro-Oncol*, volume 50, pages 37–51.

Dzwiniel, W., Alda, W., Kitowski, J., and Yuen, D. (2000). Using discrete particles as a natural solver in simulating multiple-scale phenomena. In *Molecular Simulation*, volume 20/6, pages 361–384.

Dzwiniel, W., Alda, W., and Yuen, D. (1999). Cross-scale numerical simulations using discrete-particle models. In *Molecular Simulation*, volume 22, pages 397–418.

Dzwiniel, W., Yuen, D., and Boryczko, K. (2006). Bridging diverse physical scales with the discrete-particle paradigm in modeling colloidal dynamics with mesoscopic features. In *Chemical Engineering Sci.*, volume 61, pages 2169–2185.

Folkman, J. (1971). Tumor angiogenesis: Therapeutic implications. In *N Engl J Med*, volume 285, pages 1182–1186.

Haile, P. (1992). *Molecular Dynamics Simulation*. Wiley&Sons, New York.

- Hoekstra, A., Lorenz, E., Falcone, L., and Chopard, B. (2007). Towards a complex automata framework for multi-scale modeling: Formalism and the scale separation map. In *Lect Notes Comput Sci*, pages 1611–3349.
- Kadau, K., Germann, T., and Lomdahl, P. (2004). Large-scale molecular-dynamics simulation of 19 billion particles. In *International Journal of Modern Physics*, volume 15(1), pages 193–201.
- Lowengrub, J., Frieboes, H., Jin, F., Chuang, Y.-L., Li, X., Macklin, P., Wise, S., and Cristini, V. (2010). Non-linear modelling of cancer: bridging the gap between cells and tumours. In *Nonlinearity*, volume 23.
- Mantzaris, N., Webb, S., and Othmer, H. (2004). Mathematical modeling of tumor-induced angiogenesis. In *J Math Biol*, volume 49/2, pages 1432–1416.
- Preziosi, L., editor (2003). *Cancer modelling and simulation*. Chapman & Hall/CRC Mathematical Biology & Medicine.
- Sloot, P. and Kroc, J. (2009). *Complex Systems Modeling by Cellular Automata, Encyclopedia of Artificial Intelligence*. Informatio SCI, Harshey-Nedw York.
- Wcislo, R., Dzwinel, W., Yuen, D., and Dudek, A. (2009). A new model of tumor progression based on the concept of complex automata driven by particle dynamics. In *Journal of Molecular Modeling*, volume 15/12, pages 1517–1539.