

# **Comprehensive interactive modeling (Reactive animation) of the vascular system during insults and inflammations.**

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In the past year, with the aid of the fund from the Slezak foundation, we built version 1.0 of CellStudio, a Hybrid software of simulations of biological and biophysical interactions. The system features a graphical user interface to generate an experiment and displays an animated graphical representation of the experiment. The user may control the timeline of the experiment as well as intervene to affect the experiment itself (e.g. inject molecules). Two modes of operation are developed for the system: (a) A "batch mode" is used to run multiple instances of the simulation with different parameters. The output is textual, including events and quantities from the experiment. It can easily be parsed, manipulated using "big data" tools, and graphed. (b) A real time (3D) animated view mimicking microscopy imaging of the cells, of membranal proteins are visible as they diffuse and migrate on the surface. The "live" animation (not a movie, but a clip of simulation results!) allows to control the timeline of the experiment or the zoom and angle of the "microscope camera". Hundreds of cell can be modelled, all operating in parallel, within a grid of 1 mm<sup>3</sup> tissue segment. Cells are 'decorated' by thousands of receptors and membrane proteins. Coding uses C++ and CUDA and the Unity3D game engine with its physics engine, scripting environment and GUI creator.

We suggest the system for preliminary testing of hypotheses, optimization of experiments on neural systems (prior to "wet" experiments) and understanding of scenarios in which the exact spatial organization of the network is critical. Modeled biophysical and molecular mechanisms include: membrane excitability, release and diffusion of ions, apoptosis, release of cytokines or other proteins, and more. Cellular actions are directed by state machine that defines signaling and response to environmental cues. This may allow the analysis of pathological events such as inflammatory responses, ischemic events, etc.

Our vision is that Cell Studio will become a 'game-changer' in experimental biology. The same way simulations are used in engineering, physics and structural chemistry: it will allow run virtual experiments, before the 'real' costly experiments, and will allow testing biological hypotheses.

Publications. A paper was lately submitted for publication (my students in asterisk): Liberman A\*, Kario D\*, Mussel M\*, Buetow K, Efroni S, Nevo U. Cell Studio: A Platform for 3D Graphical Simulation of Biological and Biophysical Processes.

Further funding: via collaboration with Arizona State University, we now negotiate support from the Bristol Myers Squibb (BMS) pharma company, to further continue this research.