Title: CompuCell3D – A Component-Based Simulation Environment for Developing and Running Multi-Scale Virtual-Tissue Simulations

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Multi-scale Virtual-Tissue simulations of tissue and organ development, homeostasis and disease can aid researchers in hypothesis generation and validation, and in interpreting experiments. However, the difficulty of building such simulations has limited their use to the small subset of researchers who are simultaneously biologically sophisticated and accomplished software developers. Simplifying simulation development by strictly separating simulation specification scripts from the simulation execution engine, so that the same engine can execute a limitless variety of simulations, has greatly expanded the community of researchers able to take advantage of the insights Virtual-Tissue simulations provide. Environments supporting the creation, execution and analysis of Virtual Tissue simulations, such as CompuCell3D, greatly lower the barriers to new users wishing to develop sophisticated simulations by simplifying their design, shortening their development time and reducing the degree of programming expertise required. While graphical simulation definition tools are popular and practical for simulations of problems with fairly consistent architectures, like molecular reaction kinetics, such tools are unwieldy for the definition of highly complex and heterogeneous Virtual Tissues. Our experience developing the Twedit++ editor for CompuCell3D has shown that an intermediate automated scripting layer, which serves to define the interactions among high-level computational modules implementing abstractions of natural biological objects and behaviors (like cells or cell-cell adhesion), simplifies simulation construction while maintaining the flexibility necessary to allow the construction of highly diverse simulations. This component-based architecture permits clear encapsulation of submodels operating at different length and time scales and enables reuse of prewritten software components as well as simulations that use these components. The library architecture also allows the extension of supported methodologies by inclusion of additional library-packaged methods. CompuCell3D currently supports submodel definition and execution of: reaction-kinetics, using RoadRunner (written by Dr. Herbert Sauro, of the University of Washington), PDEs describing reaction and diffusion (using custom-written solver suites), complex PDEs including fluid dynamics and solids modeling, using the Finite-Element dolphin library and the Cleaver mesh generator (written by Jonathan Bronson, University of Utah) and GGH/CPM and Center Model descriptions of cell movement, growth, death and interactions. CompuCell3D also provides a graphical Player to visualize, store and post-process simulation results.By designing all modeling environment components to maximize their reusability, we are able to significantly reduce software development cost and time, improve the quality and reliability of our simulation tools, simplify users' adherence to best-practice modeling standards and improve the user experience. This reusable component architecture allows us to focus on making Virtual Tissues useful and accessible to all scientists.