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Multi-Cell Tumor Growth Modeling Using CompuCell3D

Mathematical modeling and computer simulation have become crucial to biological fields from genomics to ecology. However, multi-cell, tissue-level simulations of development and disease have lagged behind other areas because they are mathematically more complex and lacked easy-to-use software tools that allow building and running in-silico experiments without requiring in-depth knowledge of programming. Recent advances in development of multi-scale, multi-cell simulation environments allow broad range of researchers to develop relatively easily sophisticated simulations of development or disease. In this talk I will present Glazier Graner Hogeweg (GGH) model, its extensions to support subcellular Reaction-Kinetics(RK) models and CompuCell3D a simulation environment supporting GGH and RK modeling. To demonstrate CompuCell3D [1] capabilities I will present a 3D multi-cell simulation of a generic simplification of vascular tumor growth [2] which can be easily extended and adapted to describe more specific vascular tumor types and host tissues. Initially, tumor cells proliferate as they take up the oxygen which the pre-existing vasculature supplies. The tumor grows exponentially. When the oxygen level drops below a threshold, the tumor cells become hypoxic and start secreting pro-angiogenic factors. At this stage, the tumor reaches a maximum diameter characteristic of an avascular tumor spheroid. The endothelial cells in the pre-existing vasculature respond to the pro-angiogenic factors both by chemotaxing towards higher concentrations of pro-angiogenic factors and by forming new blood vessels via angiogenesis. The tumor-induced vasculature increases the growth rate of the resulting vascularized solid tumor compared to an avascular tumor, allowing the tumor to grow beyond the spheroid in these linear-growth phases. In contrast to other simulations in which avascular tumors remain spherical, our simulated avascular tumors form cylinders following the blood vessels, leading to a different distribution of hypoxic cells within the tumor. Our simulations cover time periods which are long enough to produce a range of biologically reasonable complex morphologies, allowing us to study how tumor-induced angiogenesis affects the growth rate, size and. morphology of simulated tumors. At the conclusion of the talk I will show a live demo (5-10 minutes) of CompuCell3D and demonstrate how, starting from relatively simple toy-models of cell-sorting, contact-inhibited chemotaxis and nutrient-dependent cell growth/cell division, we can build a fairly realistic simulation of vascularized tumor growth. Such simulation can be further improved to produce simulation equivalent to the one published in [2].

References

[1] Multi-Cell Simulations of Development and Disease Using the CompuCell3D Simulation Environment, Maciej Swat, Susan D. Hester, Randy W. Heiland, Benjamin L. Zaitlen, James A. Glazier. In Ivan V. Maly ed., Systems Biology Series: Methods in Molecular Biology, pp. 138-190

[2] 3D Multi-Cell Simulation of Tumor Growth and Angiogenesis, Abbas Shirinifard, John S. Gens, Benjamin L. Zaitlen, Nikodem J. Poplawski, Maciej Swat, James A. Glazier, PLoS ONE 4: e7190, doi:10.1371/journal.pone.0007190 (2009).