Agent-Based Multicellular Modeling for Predictive Toxicology

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Biological modeling is a rapidly growing field that has benefited significantly from recent technological advances, expanding traditional methods with greater computing power, parameter-determination algorithms, and the development of novel computational approaches to modeling biological systems. Agent based models (ABMs) such as CompuCell3D (CC3D; developed at the Indiana Biocomplexity Institute) often use a traditional lattice-based cellular automata method to simulate the collective behavior of cellular systems. CompuCell3D runs three interactive modules, written in Python and C++, to simulate cellular structure, biochemical gradients, and cell state-type changes. A biological 'cell' is defined as a connected domain of lattice nodes (pixels in 2D, voxels in 3D) of the same type and identity. The CC3D model evolves by updating pixels based on the total Hamiltonian energy of the system at every Monte Carlo Step. A number of signaling fields can be superimposed onto the lattice, via systems of partial differential equations as the basis for cellular behavior. The biochemical fields can be morphogens, signaling molecules, components of the extracellular matrix, metabolites or environmental factors. Thus a cell's behavior in the system is determined by many individual and possibly independent parameters. As such, the ABM has the potential to identify moments in time when interventions may have phenotypic consequences. Rather than focusing on stable states, this approach considers a complex system's robustness and ways that it might adapt to perturbations. Embryonic vascular development is one biological system modeled using an ABM approach. Chemical disruption of vascular plexus formation is a potential adverse outcome pathway (AOP) of potential significance, and multicellular modeling approaches are being used to create *in silico* assays for predictive toxicology. *This abstract does not necessarily reflect US EPA policy.*