Stochastic simulations of cellular processes: From single cells to colonies

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High-performance computing now allows integration of data from structural, single-molecule, and biochemical studies into coherent computational models of cells and cellular processes. Here we analyze the stochastic reaction-diffusion dynamics of selected biochemical pathways in *Escherichia coli* to show how individual cells vary expression of a set of genes in response to an environmental signal. The whole cells, simulated under *in vivo* conditions, include ribosomes, DNA, and large protein complexes, which take up 30-50% of the cell volume and are placed according to data from cryoelectron tomography and proteomics. Using our GPU based Lattice Microbe software, we simulate the dynamics for an entire cell cycle and compare the mRNA/protein distributions to those observed in single molecule experiments. We show how such distributions can be used to derive additional kinetic parameters and integrate effects of cell-to-cell variations into flux balance analysis of genome scale models of metabolic networks. The distribution of growth rates calculated for a colony of bacteria are analyzed and correlated to changes in fluxes through the metabolic network. Animation of reaction trajectories involving millions of particles is facilitated using a plugin to the VMD visualization and analysis program.

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