A HYBRID STOCHASTIC-DETERMINISTIC SIMULATION METHOD ENABLES FAST SIMULATION OF CELLULAR PROCESSES IN EUKARYOTES

Research Challenge
Many processes in living cells, especially gene expression, are characterized by low particle numbers, low reaction rates, spatial heterogeneity, and a high degree of randomness. Simulations of such processes must track the random diffusion and reactions of each particle. Such simulations become prohibitively expensive in systems with many frequently-reacting particles. A hybrid method is required to combine both fast and slow processes in a single model.

Methods & Codes
The Reaction-Diffusion Master Equation is solved by the Stochastic Simulation Algorithm to explicitly model low-concentration chemical species. A deterministic ordinary differential equation model of the high-concentration chemical species is linked to the stochastic explicit model. The Lattice Microbes software suite and its pyLM problem-solving environment provide a convenient way to set up simulations of complex biological systems.

Results & Impact
Hybrid simulations are a factor of 50-100 faster than pure stochastic methods in simulating a well-studied galactose switch in S. cerevisiae (yeast). Researchers can now simulate larger cells, in greater detail, with a large number of species types, many cellular components, and high concentrations of metabolites (sugars, etc.) inside and outside the cell.

Why Blue Waters
Blue Waters was essential to generate over 1,000 replicate hybrid simulations over a simulated time of 750 minutes and a range of concentrations. This was needed to provide sufficient data to make the results statistically reliable and to determine the optimal coupling interval between the stochastic and deterministic models.