AN EFFICIENT HYBRID STOCHASTIC-DETERMINISTIC SIMULATION TECHNIQUE FOR LIVING CELLS

Research Challenge

The Chemical Master Equation and the Reaction–Diffusion Master Equation are descriptions of cellular processes where the system is considered to follow a Markov jump process on the state space of particle numbers in time. Gillespie's Stochastic Simulation Algorithm provides a method for obtaining unbiased realizations of these Markov processes. This algorithm is limited by the fact that reaction events are accounted for explicitly, making simulations of highly reactive systems computationally expensive.

Methods & Codes

At each time step the LSODA solver is updated with the species counts from the stochastic regime simulated with SSA, and then takes adaptive time steps to evolve the high particle number species through time in the deterministic regime. Then the stochastic rates involving low particle number species interacting with high particle number species are updated with the counts found by the ODE solver. The hybrid algorithm also updates species counts generated from reactions in the CME regime to the ODE regime at this time.

Results & Impact

Simulations enabled by this type of hybrid algorithm will allow researchers to study larger and more detailed systems, capturing the effects of reactions involving high particle count species such as metabolites, which have a crucial role in systems such as the genetic switch studied in this work. This hybrid approach was used to perform a spatially resolved RDME–ODE study of the galactose switch system, experiencing similar speedup to that seen in the CME implementation.

Why Blue Waters

Blue Waters was essential to generate thousands of replicate hybrid simulations over the simulation time of 750 minutes and a range of concentrations. Only then did the study have sufficient data to make the results statistically reliable and to determine the optimal communication time.