Math 218 - Seminars on Mathematics for Complex Biological Systems

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Multiscale Molecular Kinetics by Coupling Markov State Models and Reaction Diffusion Dynamics

Abstract:
A novel approach to simulate simple protein-ligand systems at large time and length-scales is to couple Markov state models (MSMs) of molecular kinetics with particle-based reaction-diffusion (PBRD) simulations; this approach is named MSM/RD. Current formulations of MSM/RD lack an underlying mathematical framework to derive coupling schemes; they are limited to protein-ligand systems, where the ligand orientation and conformation switching are not taken into account; and they lack multiparticle extensions. In this work, we develop a general MSM/RD framework by coarse-graining molecular dynamics into hybrid switching diffusion processes, a class of stochastic processes that integrate continuous dynamics and discrete events into the same process. With this MSM/RD framework, it is possible to derive MSM/RD coupling schemes as discretizations of the underlying equations. It also allows conformation switching and the inclusion of all the rotational degrees of freedom. Given enough data to parametrize the model, it is capable of modeling protein-protein interactions over large time and length-scales, and it can be extended to handle multiple molecules. We derive the MSM/RD framework, and we implement and verify it for two protein-protein benchmark systems and one multiparticle implementation to model the formation of pentameric ring molecules.

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(Contact Bo Li at bli@math.ucsd.edu for the Zoom info)