BHE 012

Understanding Molecular, Cellular, and Physiological Interactions through Computation Biology and Nanotechnology for Disease Therapeutics and Diagnostics

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Abstract

The combination of improved understanding of nanoscience molecular systems, methods for mathematical modeling and simulation, and computing power is generating great promise for predictive models of increasingly complex cellular biological systems. Understanding the inherent molecular interactions in these spatiotemporal environment is critical with many diseases including cancer and diabetic nephropathy.

The goals of our work are to develop modeling methods that can account for these challenging spatial constraints, characterize their performance relative to space-blind differential equation models, and determine the conditions under which spatial

considerations are necessary to reliably capture self-assembly dynamics that affect disease diagnosis and treatment. To this end, we have developed a general technique for lattice Monte Carlo modeling of protein assemblies forming within spatially constrained environments. In this technique, proteins are presumed to occupy discrete points in a space and are allowed to move about the space and interact with one another according to probabilistic rules of behavior. We have initially applied this model to a system of two-dimensional linear polymer assembly that is meant to model the assembly of actin fibrils constrained to a two-dimensional surface. Comparisons of this model to a differential equation model of the same system lacking spatial constrains reveals convergence between the models under conditions of slow reaction rates, low concentrations, and large volumes, but noticeable divergence as we move to the high concentrations and small spaces one finds in physiological environments. These results suggest the need for continuing to work on exploring the effects of spatial constraints on assembly reactions, improving methods to model these effects, and characterizing where the conditions under which these methods will be necessary for reliable quantitative modeling of self-assembly dynamics in cellular environments.