

Possible Java Mini-Projects:

- (1) Actin filament population dynamics: The idea here would be to create a population of actin filaments that grow and shrink, monomer-by-monomer, with the experimentally measured rate constants. This would be a biochemical simulation only, i.e. there would be no rigid body dynamics. New actin seeds would be created with some concentration dependent rate from a depletable monomer pool. With this model you might study the steady-state filament length distribution, and how that distribution changes over time.
Reference: Kuhlman PA, Dynamic Changes in the Length Distribution of Actin Filaments During Polymerization Can Be Modulated by Barbed End Capping Proteins, Cell Motility and the Cytoskeleton 61:1-8 (2005).
- (2) Concentration Dependence of Filament Seed Formation: It is known that the stable seed for establishing a de novo actin filament in purified g-actin is a trimer. This project would detect collisions between a large static population of monomers. Collisions between monomers would create a dimer. Collisions between a dimer and a monomer would create a stable seed from which filament growth would then proceed by the measured rates. These filaments would not exist explicitly in the model; trimer creation would increment a counter keeping track of the number of filaments. Another scalar value (number) would be a measurement of the total filamentous actin, which is a function of the number of filaments, monomer concentration, and polymerization rates. This model can be used to explore the concentration dependence of f-actin growth.
- (3) Brownian ratchet model: Our own Garry Odell was an author on an early paper applying the idea of a Brownian ratchet to actin-based motility. The concept has been extended in more recent work. In this project we would simulate the monomer-by-monomer addition to a single filament, which could be rigid or flexible, whose tip is in proximity to a load undergoing Brownian motion in 1D.
References: Peskin, Odell, and Oster, Cellular Motions and Thermal Fluctuations: the Brownian Ratchet, Biophys. J. 1993.
Mogilner and Oster, Force generation by actin polymerization II: the elastic ratchet and tethered filaments, Biophys. J. 2003.
- (4) MCAK and/or Kip3p on a microtubule. The idea here is to build a single cylindrical filament... this will be our microtubule. We could populate the space about it with some moderately large number of diffusing motor proteins. When the motors collide with the MT they will do a 1D random walk (like MCAK) or highly processive motoring (like Kip3p). We could explore the accumulation on the ends, the effect on depolymerization of the MT, and the rebinding probabilities if they dissociate while on the MT lattice (this was one of Garry's questions in Joe Howard's lecture today).
Reference: Helenius J et al., The depolymerizing kinesin MCAK uses lattice diffusion to rapidly target microtubule ends, Nature 2006.

- (5) A 1D+ model of spindle oscillations: We've heard a lot about these spindle oscillations of late. This project would build a barbell-shaped spindle that can move in 1D in the direction orthogonal to the spindle. The spindle will also rotate as a result of net torques (this is the + in the 1D). The elements attaching each centrosome of this rigid spindle will be endowed with the general features of the microtubule/dynein/cortex attachments discussed in Pecreaux et al. and by Joe Howard during his visit.

Reference: Pecreaux et al, Spindle oscillations during asymmetric cell division require a threshold number of active cortical force generators, Curr. Biol. (to appear).