



**L.H. BAKER CENTER FOR BIOINFORMATICS AND
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Multiple Scales in Molecular Motor Models

Molecular motors, such as kinesin and dynein, carry cargo through a cell along a microtubule network. The heads of these motors step along a microtubule and are on the order of nanometers, while the cargo size and the distance traveled can be on the order of hundreds of nanometers. Two examples of mathematical models of motors that bridge these spatial scales will be discussed.

In the first example, a stochastic model for variable-length stepping of kinesins engineered with extended neck linkers will be developed. This requires consideration of the separation in microtubule binding sites between the heads of the motor at the beginning of a step. This separation is a stationary process and can be included in the calculation of standard experimental quantities through a semi-Markov model. A corresponding matrix computational framework will be discussed for conducting computer experiments that is more computationally efficient than large-scale Monte Carlo simulation; this efficiency greatly eases sensitivity analysis, an important feature when there is considerable uncertainty in the physical parameters of the system.

The second example involves multiple motors attached to a common cargo. The behavior of intracellular cargo should depend strongly on the number of motors that attach the cargo to microtubules. However, convincing evidence for the influence of multiple motors on transport has proved elusive. In fact, some authors now claim that cargo interact with microtubules in vivo almost exclusively through one motor at a time. In order to better understand how both single and multiple motors can influence the motion of a cargo, a mathematical model for microtubule-motor-cargo dynamics is developed that emphasizes the spatial configuration and the resultant distribution of forces generated on and by the cargo. In the analysis, the comparison in performance of multiple motors versus a single motor is dependent on the applied external force. At small force regimes, multiple motors are found to move cargo more slowly than a single motor, while at high force regimes (such as near stall force) superlinear improvement in transport performance is observed. Although this phenomenon has been observed in stochastic simulation, the presented results depend on rigorous asymptotic methods that lead to the specification of explicit conditions under which different transport phenomena arise. Theoretical predictions are confirmed by experimental data from multiple sources.

Date: Wednesday, May 16

Time: 4:00-5:00 PM

Room: 1414 Molecular Biology