

The Interdisciplinary Center for the Study of Biocomplexity Colloquium

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Will give a lecture entitled:

High Microtubule Growth Variability Indicates Near-kHz Assembly Kinetics

Thursday, September 16th, 2010

5 PM

Location: 127 Nieuwland Science Hall

Abstract:

Microtubules are dynamic intracellular polymers that grow and shorten at their ends via the stochastic addition and loss of $\alpha\beta$ -tubulin heterodimers; this highly regulated process is fundamental to cellular organization. Previously, tubulin subunit exchange rates at the ends of growing microtubules have been estimated using a 1D linear growth theory, which assumes that tubulin dissociation occurs at a constant rate regardless of the free subunit concentration. We test this prediction experimentally via fluorescence microscopy and a laser-tweezers assay with near-molecular resolution, and find that the variance in GMPCPP-microtubule assembly rates in vitro is too high to be consistent with the previous low kinetic rate estimates. In contrast, a 2D model, with kinetic rates that are an order-of-magnitude higher than the 1D model kinetic rates, quantitatively predicts a priori the variance and its concentration dependence. We conclude that net assembly is the result of a relatively small difference between large rates of subunit addition and loss, which occur at near-kHz rates, far faster than previously believed. More generally, our theoretical analysis demonstrates that the constant off rate originally used in the 1D model, and assumed in most subsequent models, is problematic for self-assembled polymers having both lateral and longitudinal bonding interactions between subunits. In addition to fundamentally changing our understanding of microtubule dynamics, these results indicate the mechanisms available for regulating microtubule assembly by drugs and in vivo are broader and in many cases simpler than currently supposed.