ML-14
The Cell as a Machine

Filament Dynamics (Nucleotide Hydrolysis, Polarity and Treadmilling)

Actin monomer contains a bound ATP and tubulin dimer contains a bound GTP that are hydrolyzed after polymer formation. The rate of hydrolysis follows a first order decay process after the subunits assemble in the polymer. After hydrolysis, the ADP or GDP forms of the subunits have a much higher K_d for binding (weaker binding) which results in an instability of the filaments and increases disassembly.

Filaments are polar in several respects: 1. the rate of polymerization is greater at one end than the other, 2. the subunit structure is polar, and 3. the ends are dramatically different in the components that bind to them. Because subunits polymerize onto one end faster than they do on the other, the subunits on the fast end are more likely to contain ATP than the slow end. Thus, the slow end is most likely to have an ADP or GDP containing subunit and to depolymerize. Situations can arise where ATP subunits can add onto the fast end (barbed end for actin filaments or plus end for microtubules) and ADP subunits can leave the slow end, giving rise to treadmilling.

Description of filament systems (for tubulin: the critical concentration is 5 μM and the concentration in cells is on the order of 20 μM, for actin: the critical concentration is 0.1 μM and the concentration in cells is on the order of 200 μM).

Problems:

1. If the K_d for the actin subunit-subunit interactions along a strand is 0.1 mM and the K_d for subunits at the ends of two-stranded filaments is 0.03 mM, then what is the K_d for a single inter-strand bond (assume that subunits that bind at the ends are bound by one intra- and one inter-strand bond).

2. A classic experiment in the microtubule field involved the dilution of the microtubule solution and the subsequent changes in microtubule number and length. The observation was that the dilution of an equilibrium solution of monomer and polymer resulted in the decrease in the number of microtubules and a slight increase in their length. How can you explain this result based upon the GTP hydrolysis after polymerization?