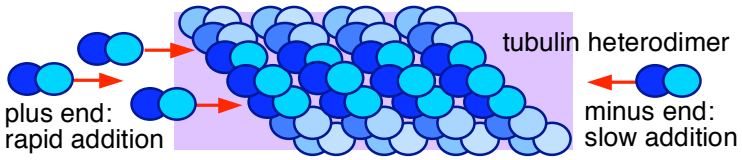
PHYS 4xx Movement in the cell

Motility and transport

- cells can actively change shape; *e.g.* cell division
- cells can locomote in search of prey or to escape from predators
- cells need a mechanism for directed transport of materials from production to consumption site. NOT diffusion via $\langle x^2 \rangle = 2Dt$
  for 10 nm proteins, $D = 10^{-10}$ m^2/s in water and 10^{-14} m^2/s in lipids
  if $\langle x^2 \rangle = 1$ μm and $D = 10^{-12}$ m^2/s ----> $t \sim 1$ second (OK for local transport)
  if $\langle x^2 \rangle = 1$ m and $D = 10^{-12}$ m^2/s ----> $t \sim 10^{12}$ secs = 30,000 years (hopeless for long transport along neurons)
- mechanisms for movement include dynamic filaments and protein molecular motors

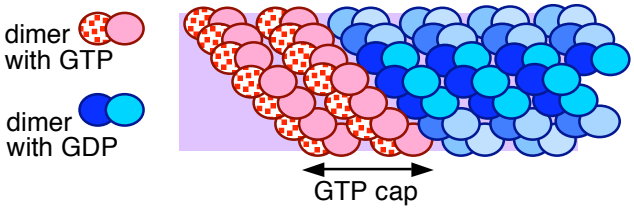
Polymerization

- characteristics of actin and tubulin monomers
  asymmetric --> filaments are oriented
  chemically inequivalent at each end because of ATP, GTP hydrolysis
- growth through polymerization occurs more rapidly at one end of filament than the other (called the plus and minus ends, respectively)



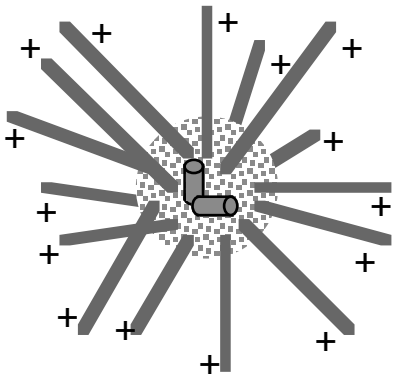
α-tubulin subunit faces towards the plus end of the filament (Oakley; 1994)

- the plus end of an actin filament resembles the feathered end of an arrow ("barbed" end), the minus end looks like the arrowhead ("pointed" end)
- actin monomer contains ATP, tubulin dimer contains two GTPs, although only GTP on β-tubulin is reactive
- both triphosphates hydrolyze after polymerization, WEAKENING the polymeric bonds and making depolymerization easier
- when tubulin heterodimers are added to a microtubule faster than the rate of GTP hydrolysis, the filament acquires a GTP-rich cap



Microtubules

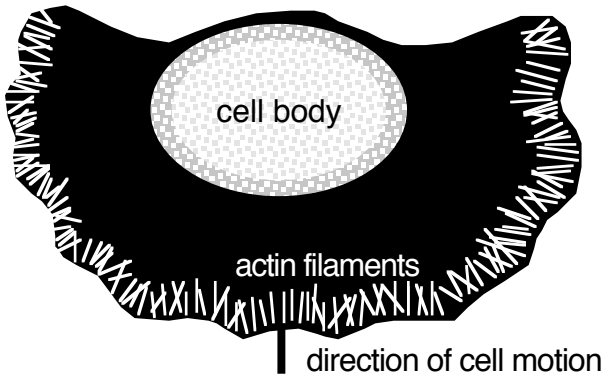
- hundreds of microtubules (MTs) radiate from the centrosome of most animal cells
- by probing the cell surface, the microtubules can push the nucleation region towards the center of the cell



- MTs are involved in separating chromosomes during cell division
- because they are relatively stiff, MTs provide highways for transport in the cell

Actin

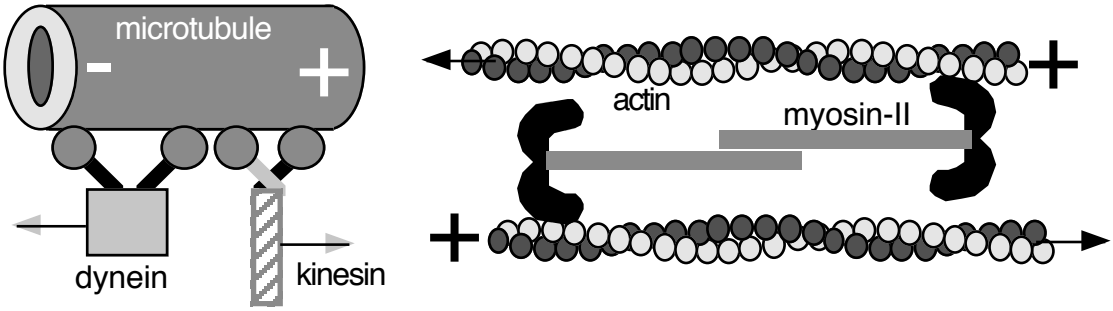
- fibroblasts move along a substrate, adhering by the sheet-like lamellipodium



- leading edge is actin-rich, with plus ends at the cell boundary
- in keratocytes, actin filaments move back through the cell body at roughly the speed of the cell (up to 0.1 μm/s), such that a given position on a filament remains roughly stationary with respect to the substrate (Theriot and Mitchison, 1991)

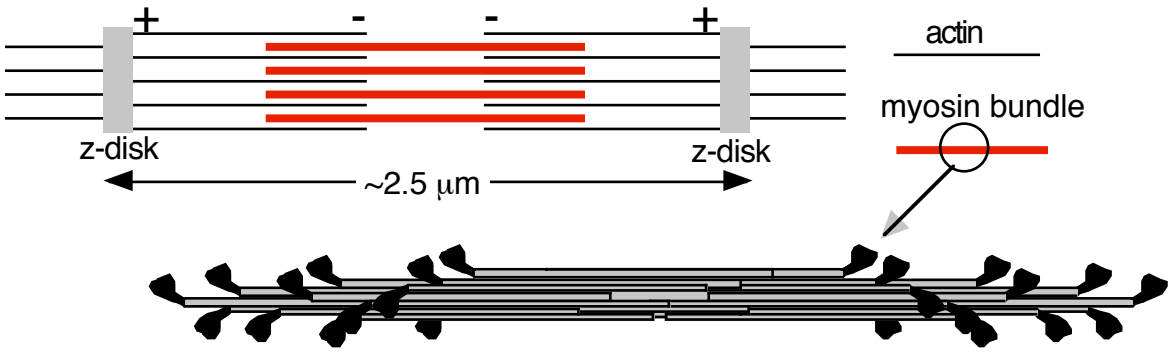
Linked filaments

- actin-binding proteins (ABPs) and microtubule-associated proteins (MAPs) link filaments together
- motor proteins move along the filaments
  myosins move on actin (to plus end)
  kinesins and dyneins move on MTs (usually plus and minus, respectively)



- e.g., at speeds up to 2-5 microns per second, a chemical cargo can be transported in 2-6 days from a production site in the brain to the end of a neuron a meter away

- actin and myosin may be organized into highly cooperative structures in our muscles
- thick filaments are bundles of more than 100 myosins
- walking towards the plus end of the actin, mysosin pulls the minus ends of the filament towards one another, contracting the muscle along the horizontal direction



- example of speeds: contraction of an arm muscle 30 cm long
  say myosin takes a step of 5 nm at a rate of 50 steps per second = 250 nm/sec
  the Z-discs move towards each other at 2 x 0.25 μm/s = 0.5 μm/s
  in a 30 cm segment of muscle there are 0.3 m / 2.5 μm ~ 10^5 actin bundles
  thus, the muscle contracts at 10^5 x 0.5 μm/s = 0.05 m/s or 5 cm/s
  (right order of magnitude)

- cilia and flagella are other mechanical structures, to be discussed later