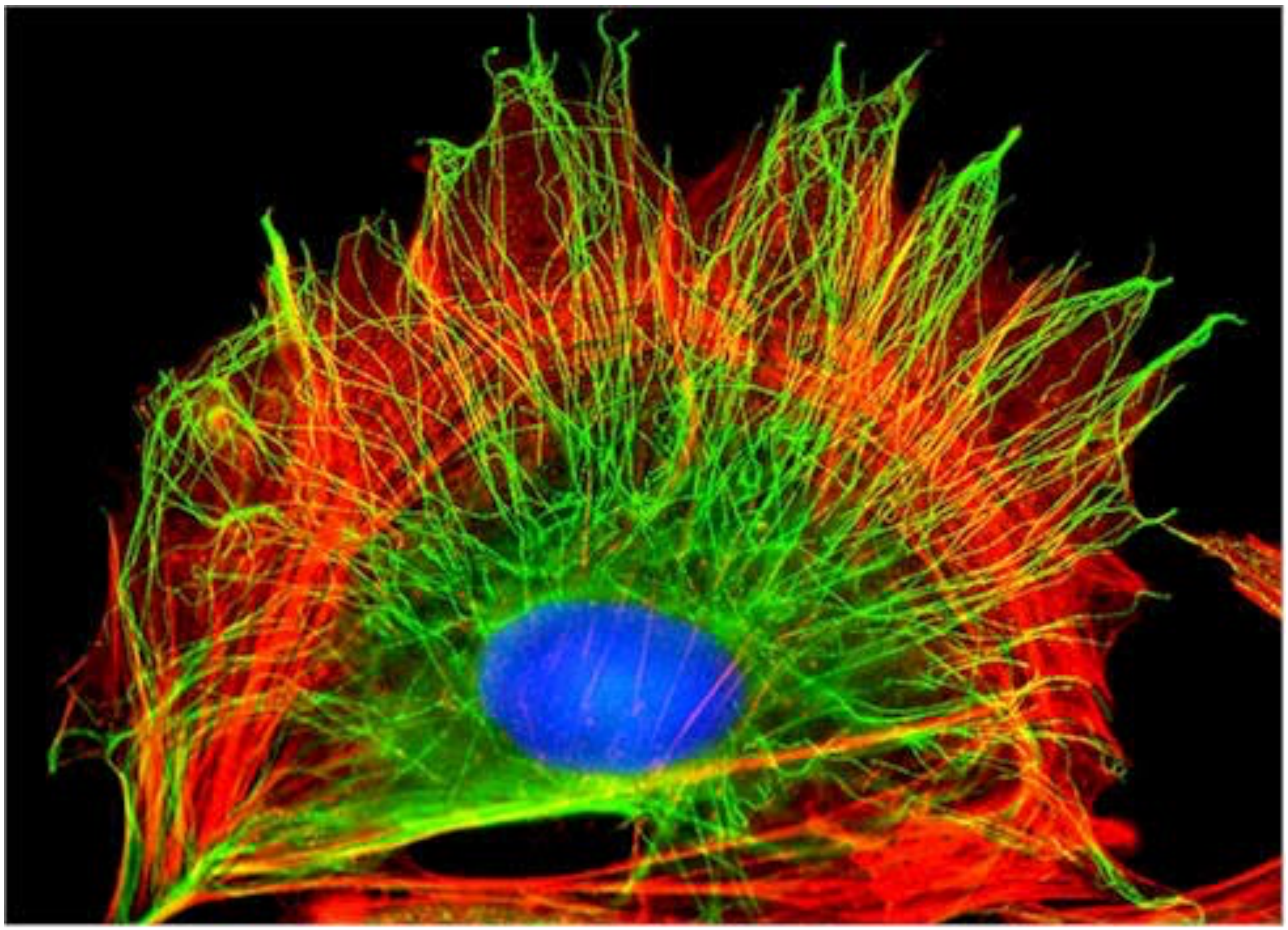
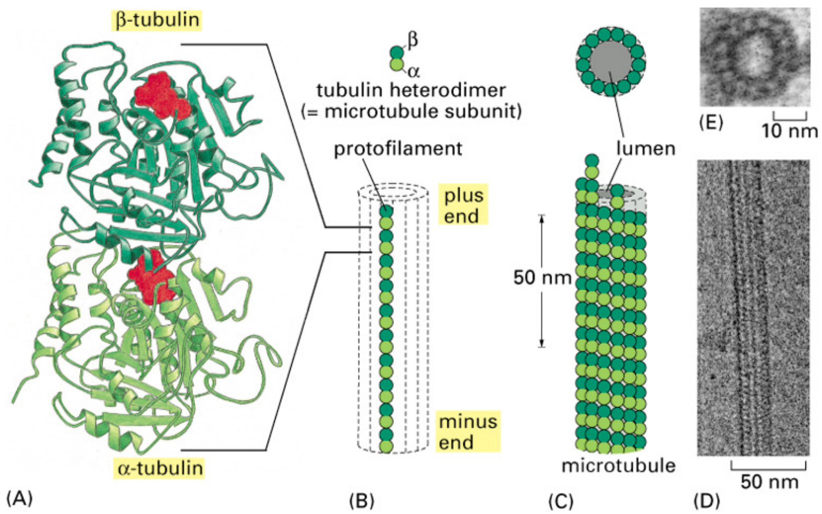
Streetfighting the cytoskeleton

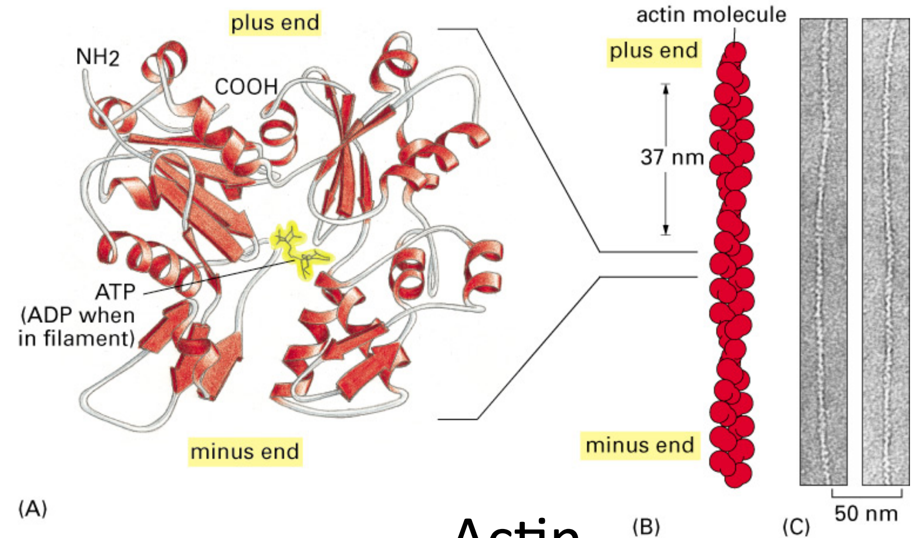


Cytoskeletal filament structures



Microtubule

persistence length ~ 1 mm



Actin

persistence length ~ 10 - 20 μm

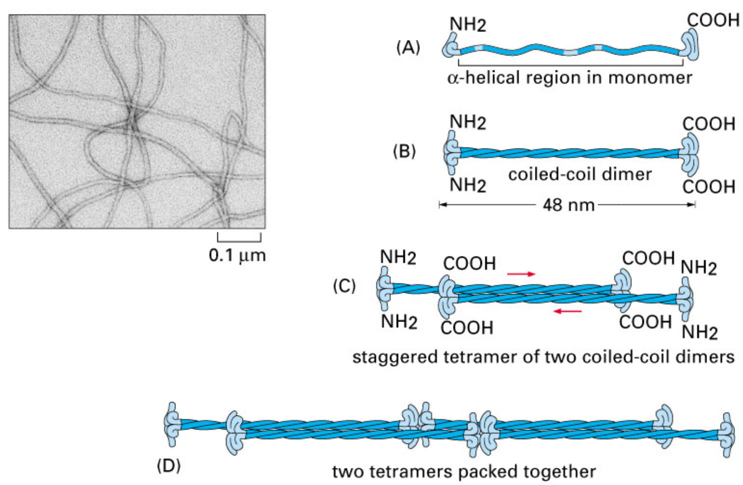
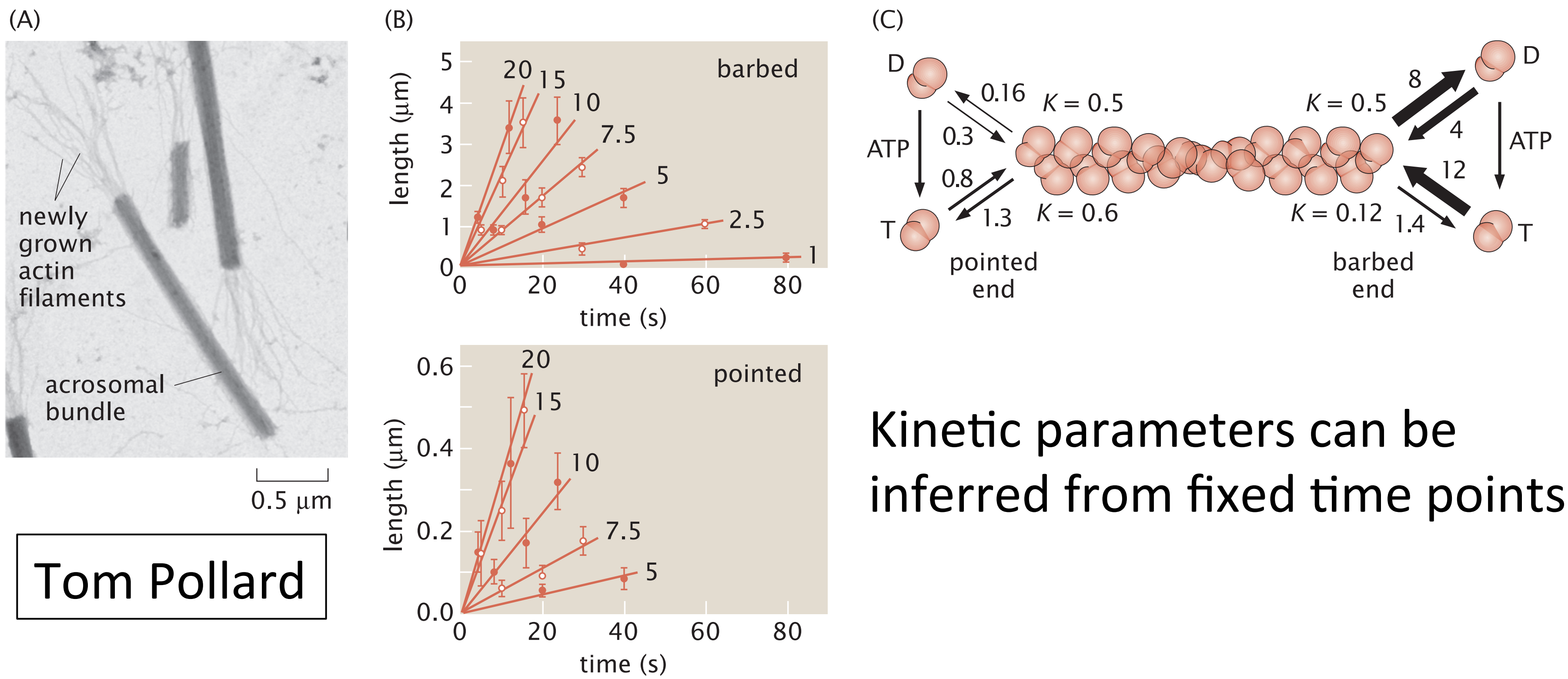


Figure 16–16 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Intermediate filament

persistence length ~ 2 μm

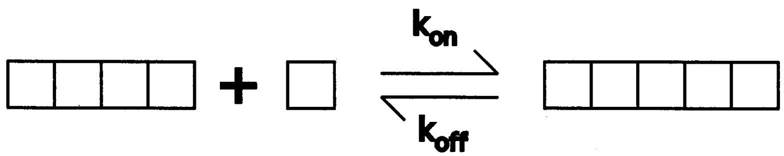
Cell behaviors that depend on the cytoskeleton usually require polymerization and depolymerization



Tom Pollard

Kinetic parameters can be inferred from fixed time points

Polymerization can generate force



Growth speed v = δ * ([m]k_{on} - k_{off})

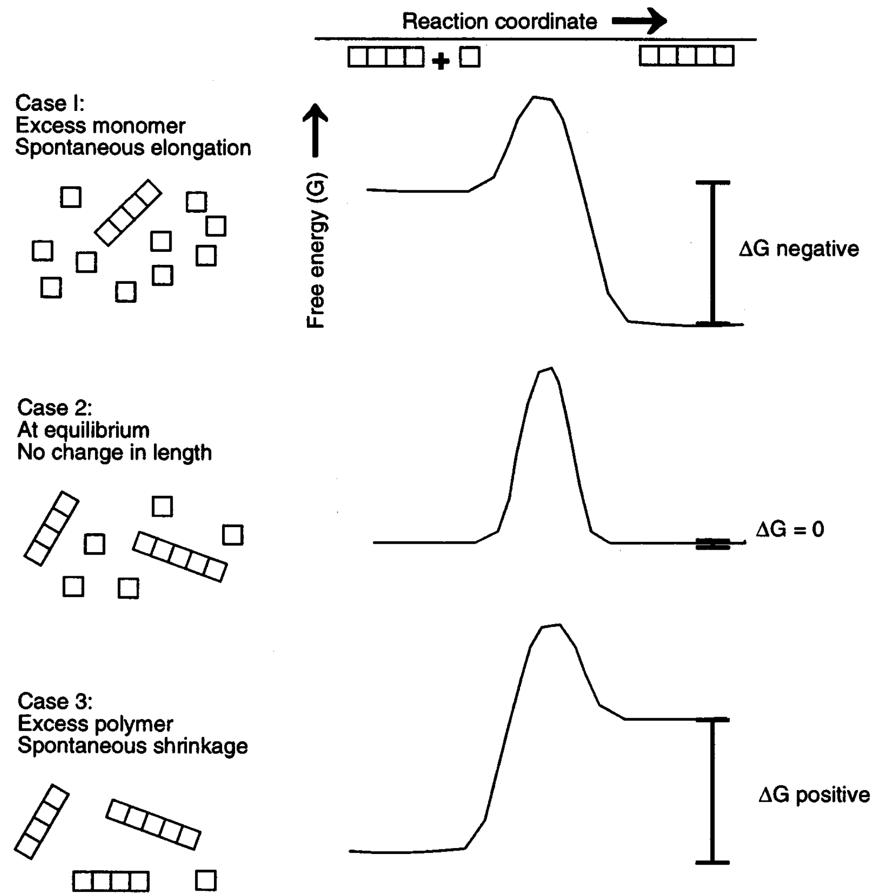
remember:

ΔG_0 = -RT*ln K_{eq}

ΔG = ΔG_0 + RT*lnQ

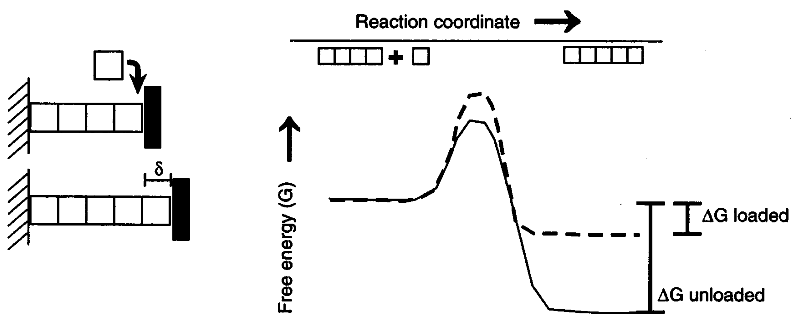
Q = ratio of concentrations of products over reactants

k_B = R (gas constant) / N_A

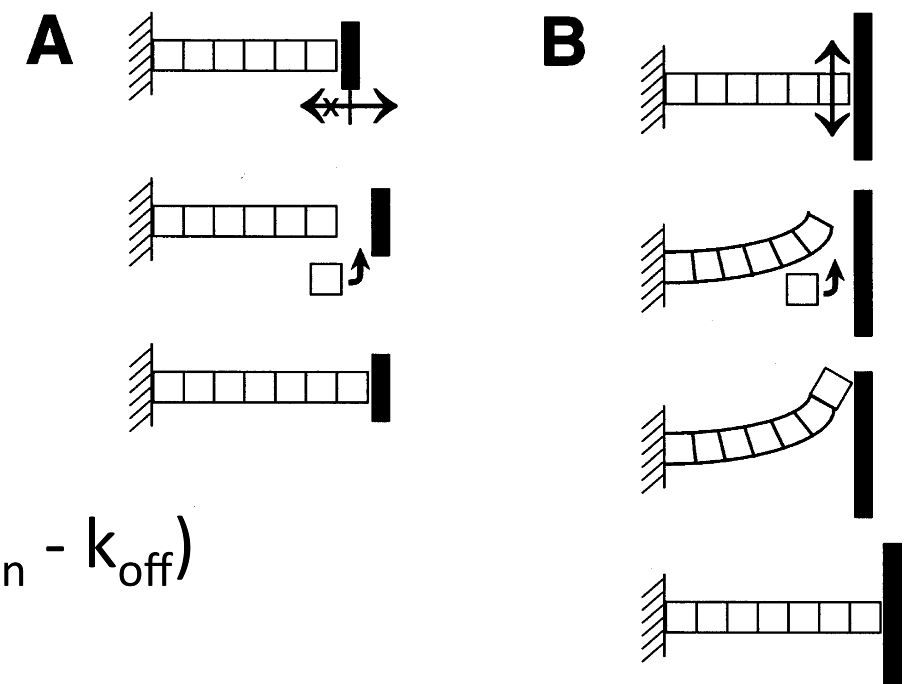


Force should slow polymerization until stall occurs

$F_{max} = (k_B T/\delta)\ \ln([m]/C_c)$



Possible kinetic mechanisms:

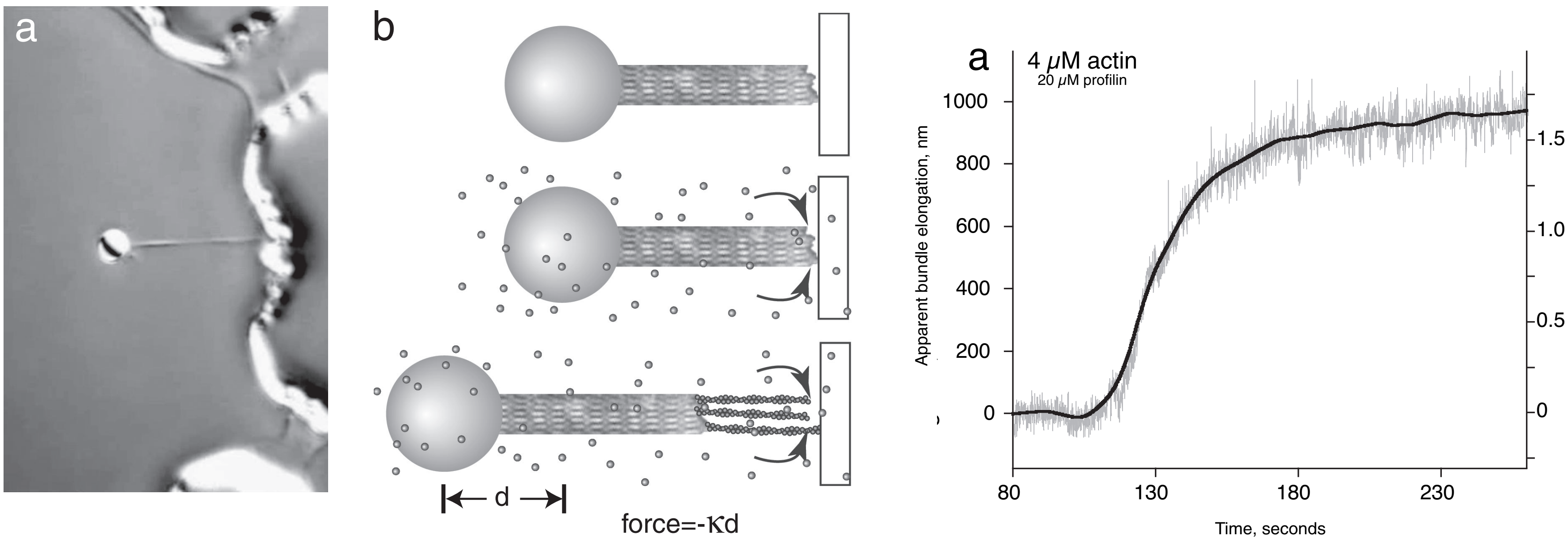


Growth speed $v = \delta * ([m]k_{on} - k_{off})$

Expect growth to slow with applied force:

$v(f) = \delta*([m]k_{on}*e^{-(f\delta/k_B T)} - k_{off}])$

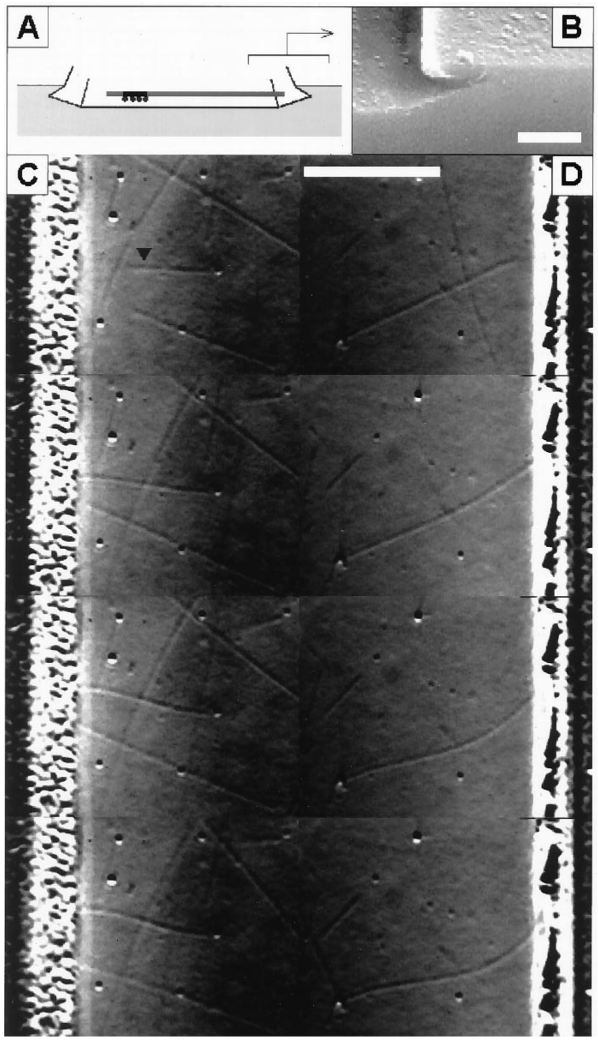
Direct measurement of actin polymerization force with an optical trap



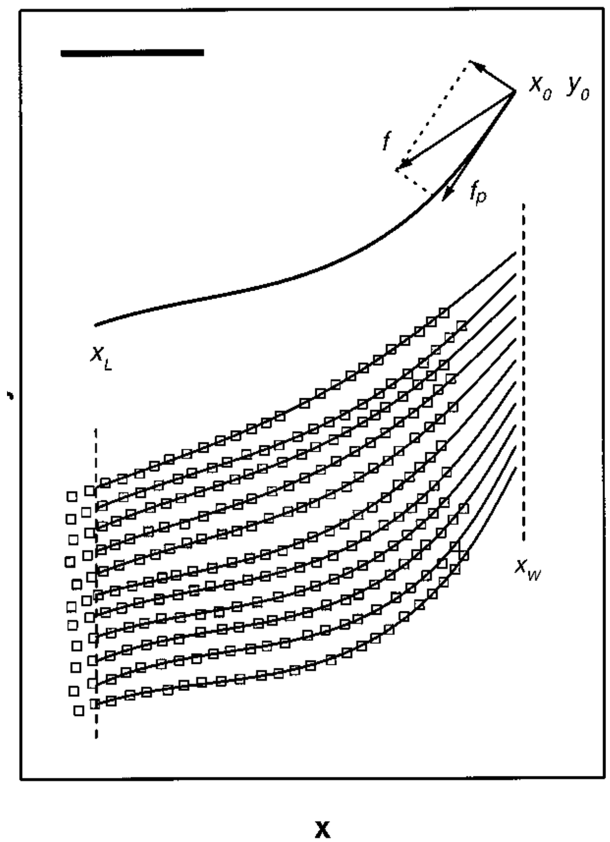
$$F_{max} = (k_B T/\delta) \ln([m]/C_c)$$

Footer, et al., 2007, *PNAS*, **104**: 2181

Measurement of microtubule polymerization force by bending



Expect growth to slow with applied force:
$v(f) = \delta^*[k_{on}{}^*e\text{-}(f\delta/k_BT)[m] - k_{off}]$



Dogterom & Yerke, 1997, *Science*, **278**: 856

Measurement of microtubule polymerization force by bending

flexural rigidity
κ = 34 ±7 pN*nm^2

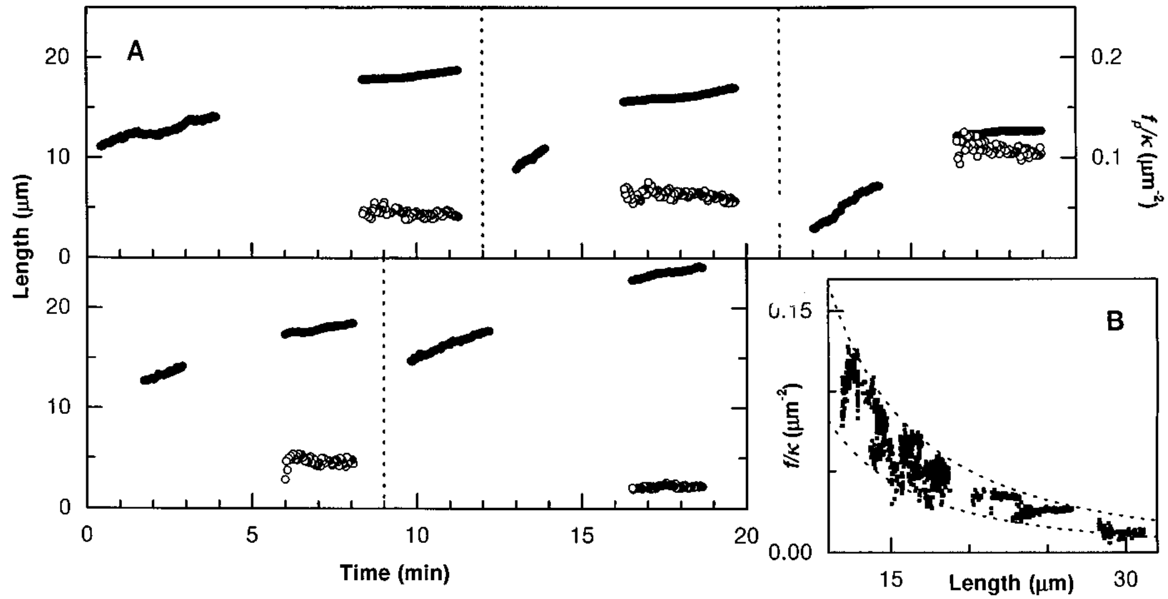
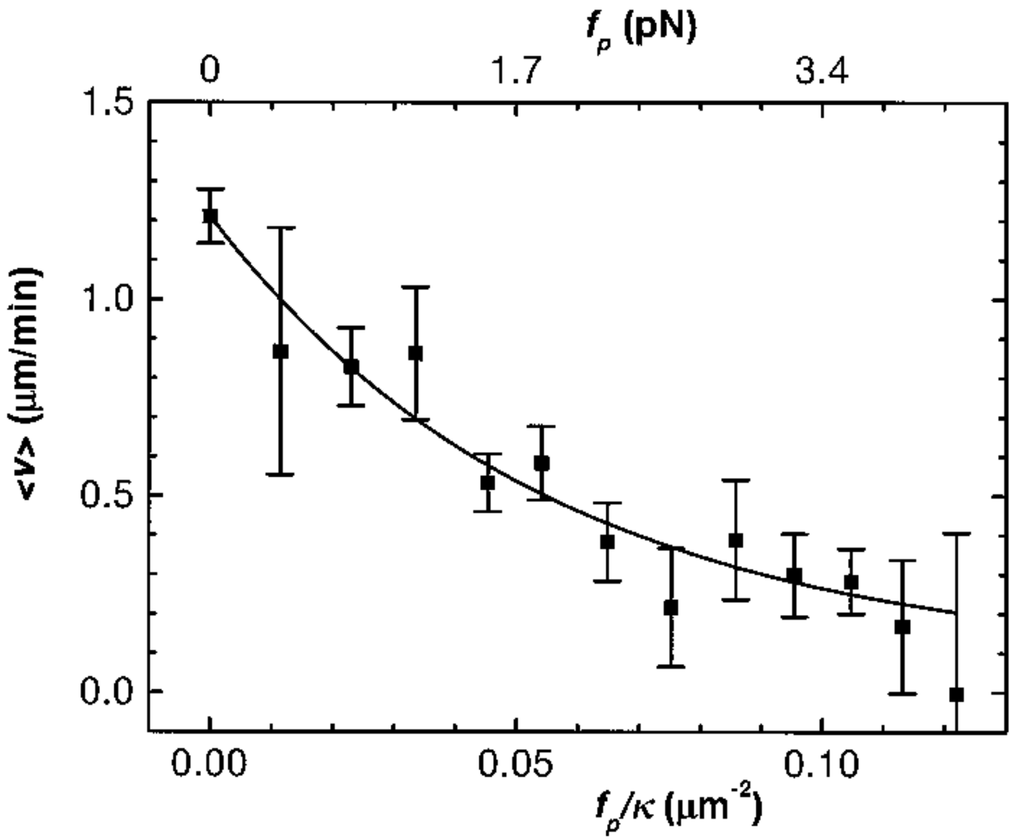


Fig. 3. MT length and applied force obtained from the analysis of MT buckling shapes such as shown in Fig. 2. (**A**) For five different MTs, the length L as a function of time (at 2-s intervals) is shown both before and after contact with the wall (solid symbols). A segment of time is missing in each case, during which the end of the growing MT was obscured by the presence of the overhang on the wall. Open symbols show the parallel component of the normalized force, f_p/κ . The lower left curve corresponds to the MT shown in Figs. 1D and 2. The upper right curve corresponds to the MT shown in Fig. 1C. (**B**) Total normalized force, f/κ, as a function of MT length for all MT shapes analyzed (n = 1316). Each point corresponds to one MT shape. The dashed lines indicate the theoretical length dependence of f_c in two limiting cases: $f_c/\kappa = 20.19/L^2$ for a MT with a seed that acts as a perfect clamp (upper curve) and $f_c/\kappa = \pi^2/L^2$ for a MT with a seed that acts as a perfect hinge (lower curve). In the experiments, the seeds behaved in an intermediate way and, as expected, the forces obtained from the fits fall between these two limiting curves.

Dogterom & Yerke, 1997, *Science*, **278**: 856

Measurement of microtubule polymerization force by bending

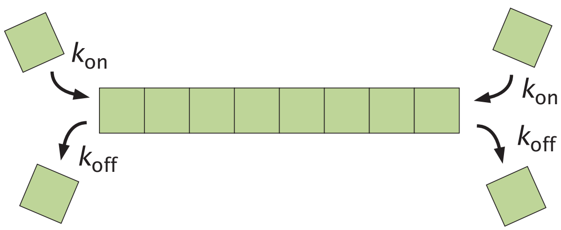


Dogterom & Yerke, 1997, *Science*, **278**: 856

Expected length distribution at steady state

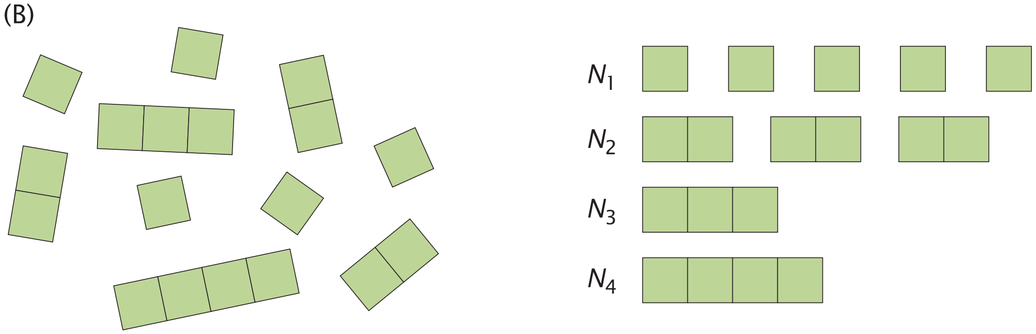
Spreading the cytoskeletal butter:

(A)



$$\mathrm{P}_n + \mathrm{P}_1 \overset{K_\mathrm{d}}{\rightleftharpoons} \mathrm{P}_{n+1}$$

(B)



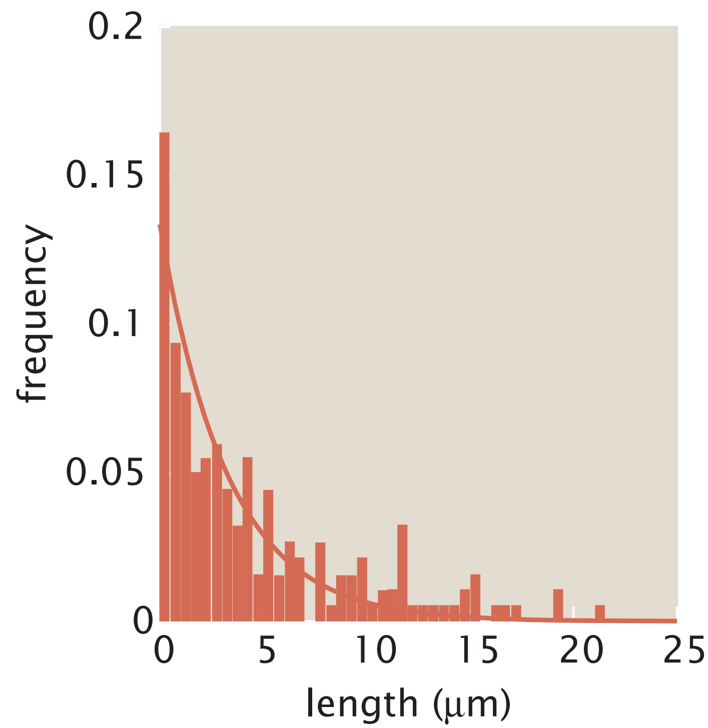
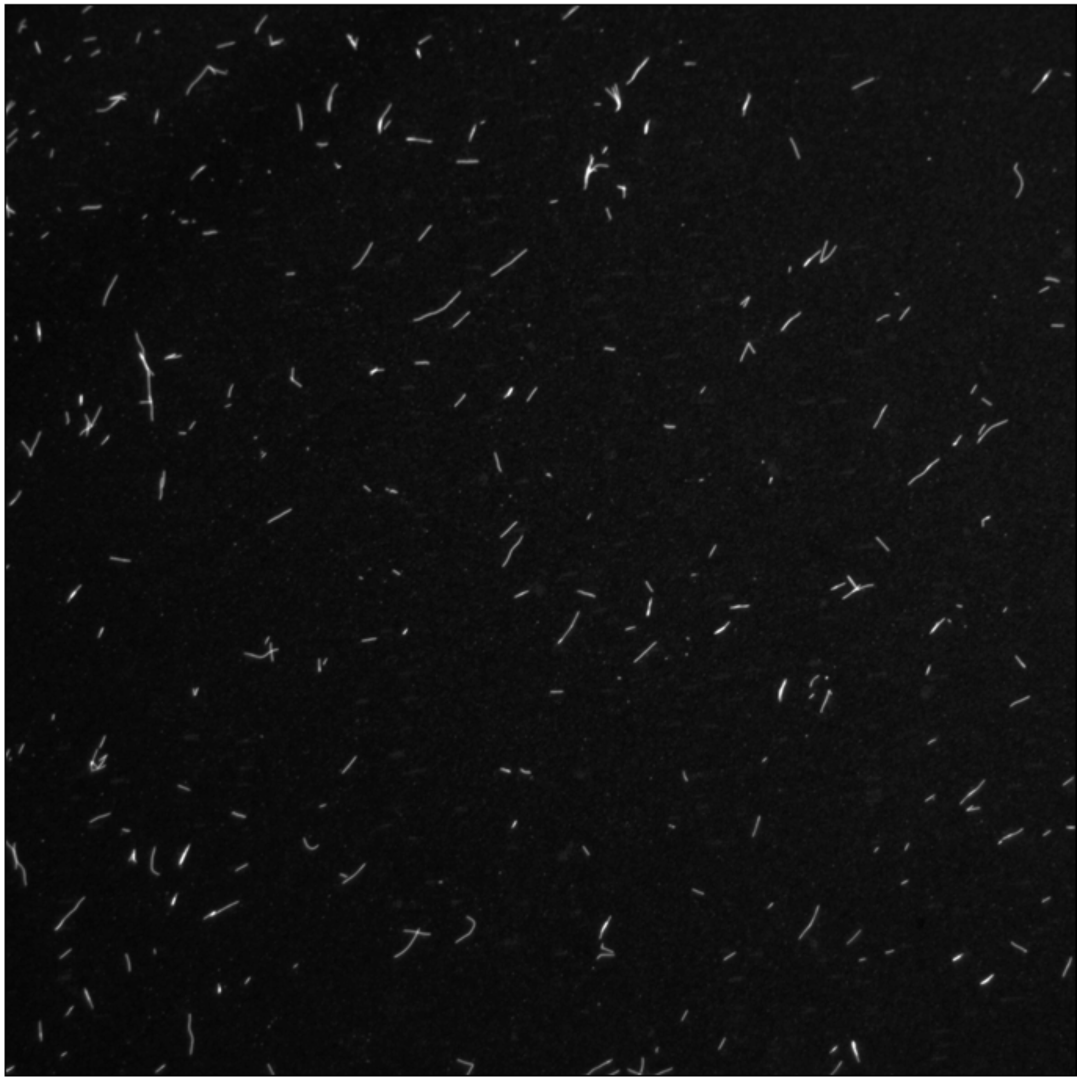


Figure 15.23: Distribution of filament lengths for actin filaments. (Adapted from S. Burlacu et al., *Am. J. Physiol.* 262:C569, 1992.)

$$[\mathrm{P}_n] = K_\mathrm{d}\mathrm{e}^{n\ln([\mathrm{P}_1]/K_\mathrm{d})} = K_\mathrm{d}\mathrm{e}^{-\alpha n}$$

Can we simulate this computationally?

An experimental data point



Tubulin
20 μM
+DMSO
80 minutes

Geoff