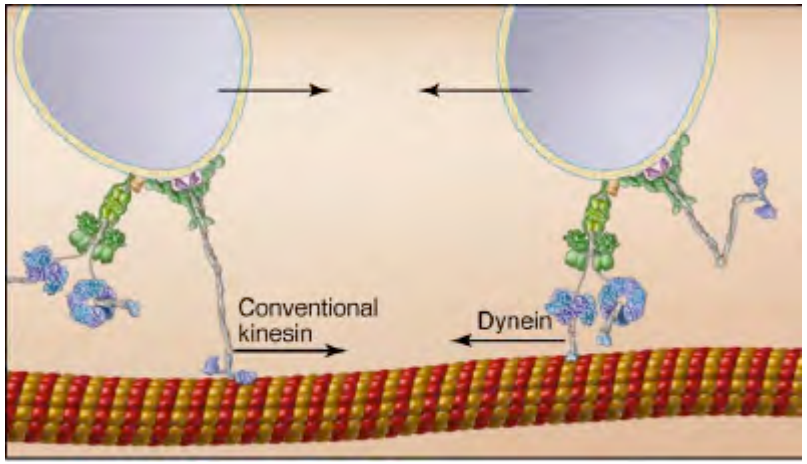
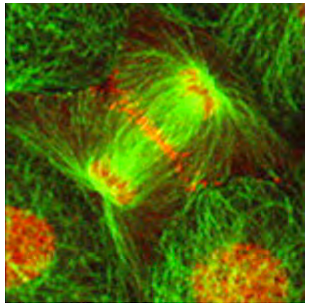
APh161 - Lecture 13: Molecular Motors



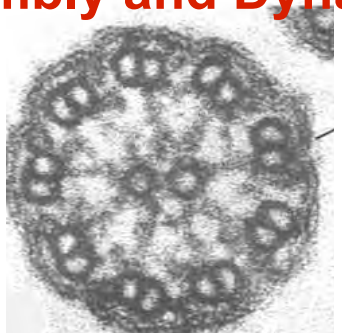
Rob Phillips
California Institute of Technology

Molecular Motors

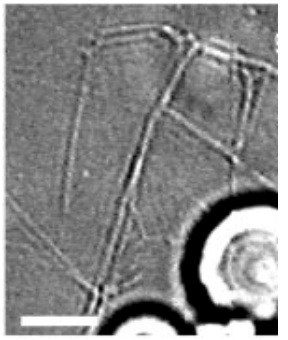
Mitotic Spindle Organization



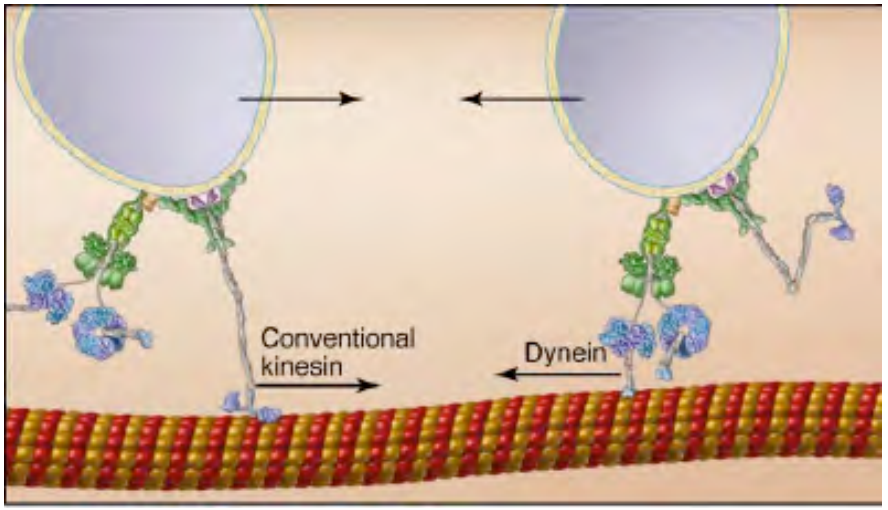
Cilia and Flagella Assembly and Dynamics



Formation o Golgi and E Networks



Vesicle Transport



Rogues Gallery of Motor Action: Rotary Motors

Show Berg movie

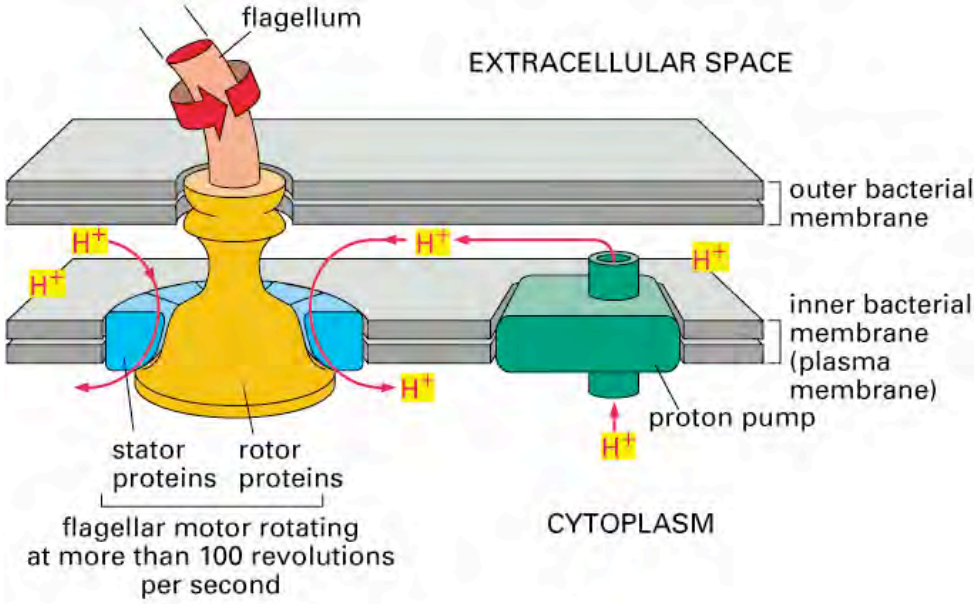


Figure 14–17. Molecular Biology of the Cell, 4th Edition.

Show Yasuda et al. movie

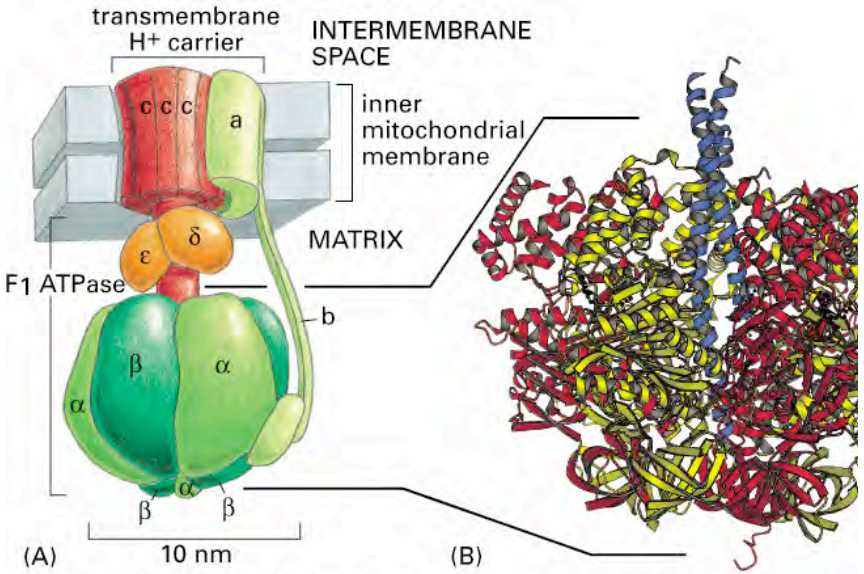


Figure 14–15. Molecular Biology of the Cell, 4th Edition.

Rogues Gallery of Motor Action: Translocation

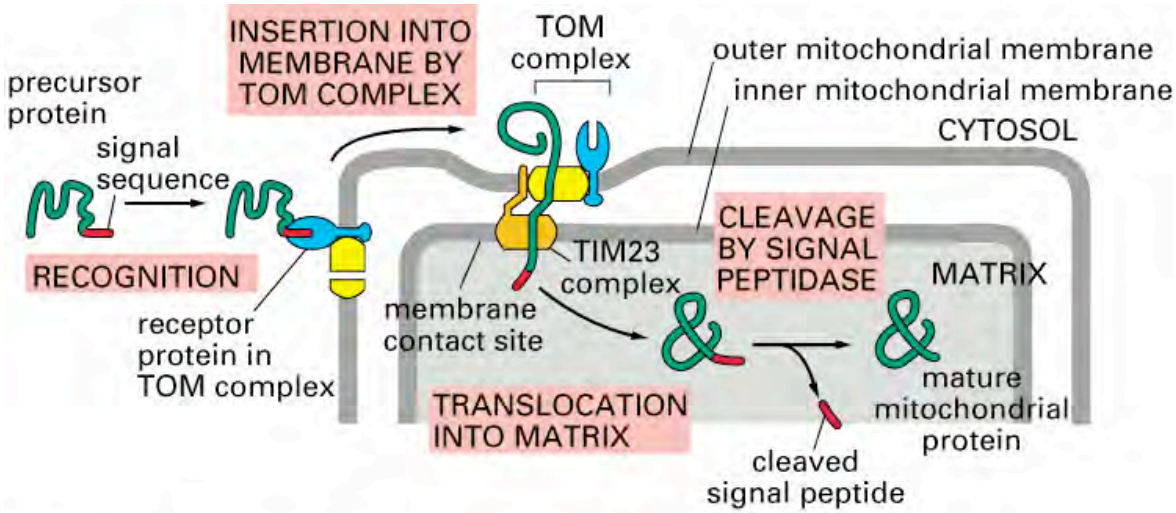


Figure 12–26. Molecular Biology of the Cell, 4th Edition.

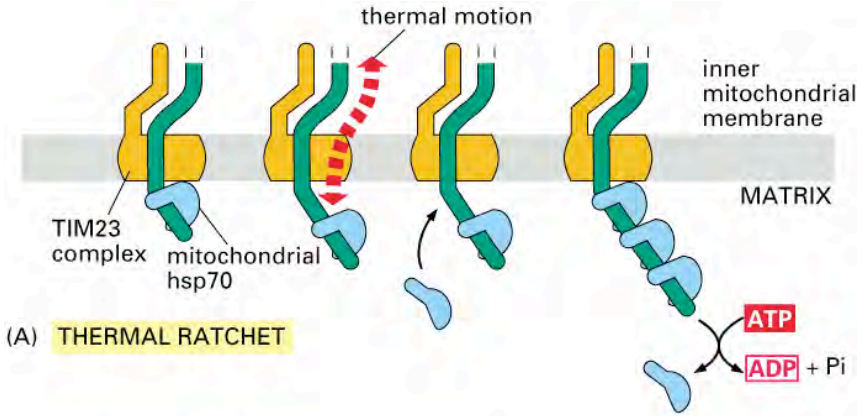


Figure 12–28 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

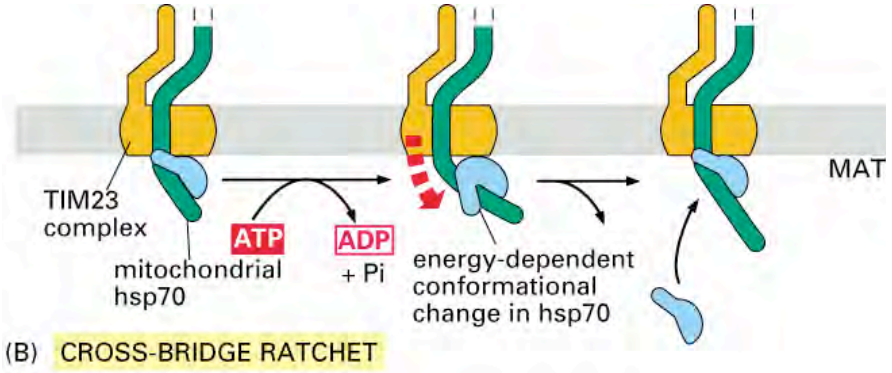


Figure 12–28 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Rogues Gallery of Motor Action: Translational Motor 1

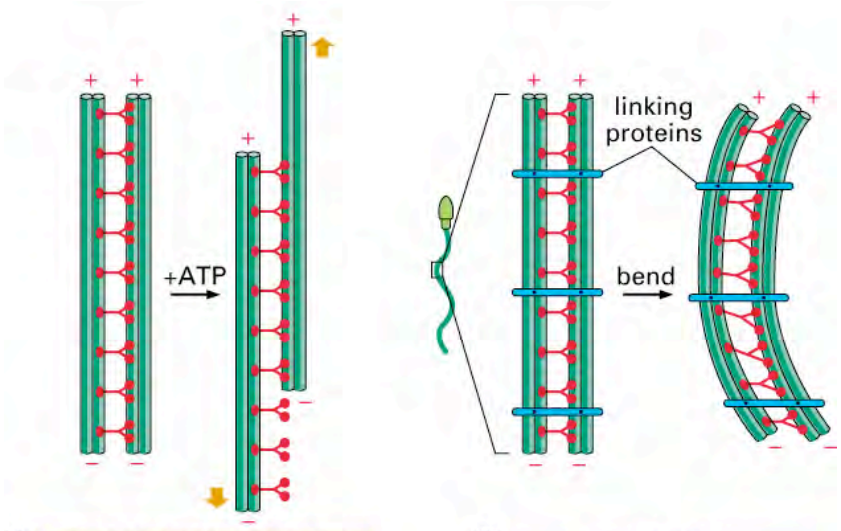


Figure 16–79. Molecular Biology of the Cell, 4th Edition.

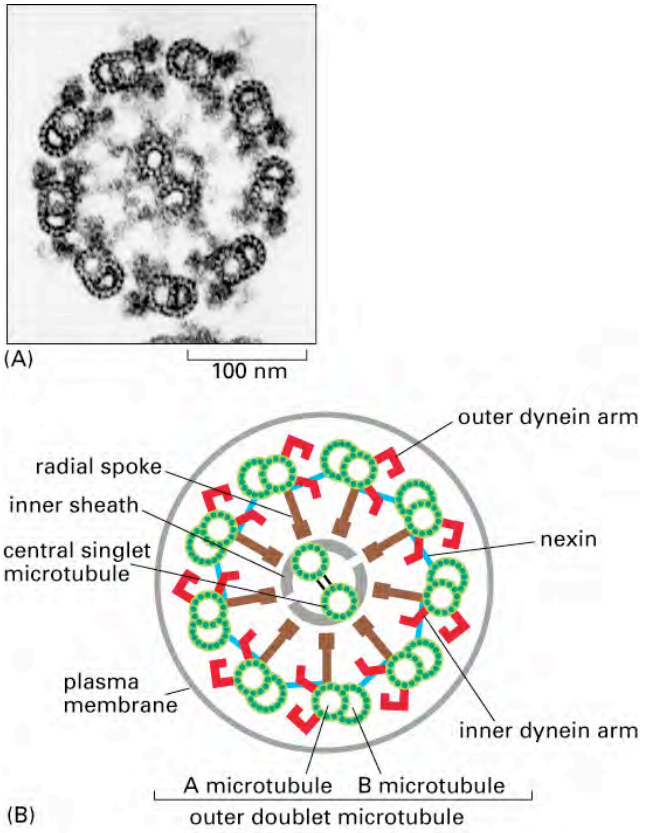


Figure 16–77. Molecular Biology of the Cell, 4th Edition.

Rogues Gallery of Motor Action: Translational Motor 2 - Muscles

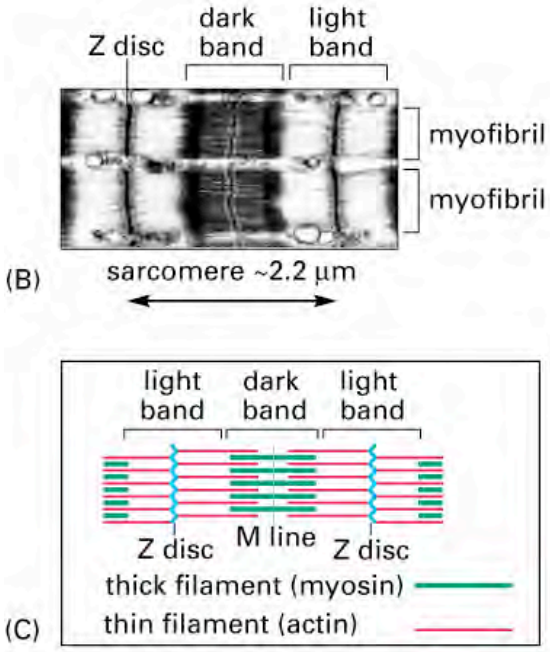


Figure 16–69 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

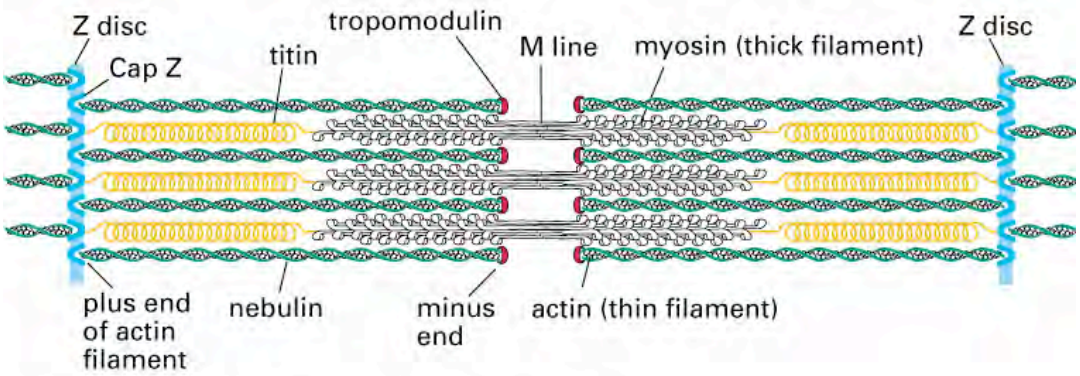
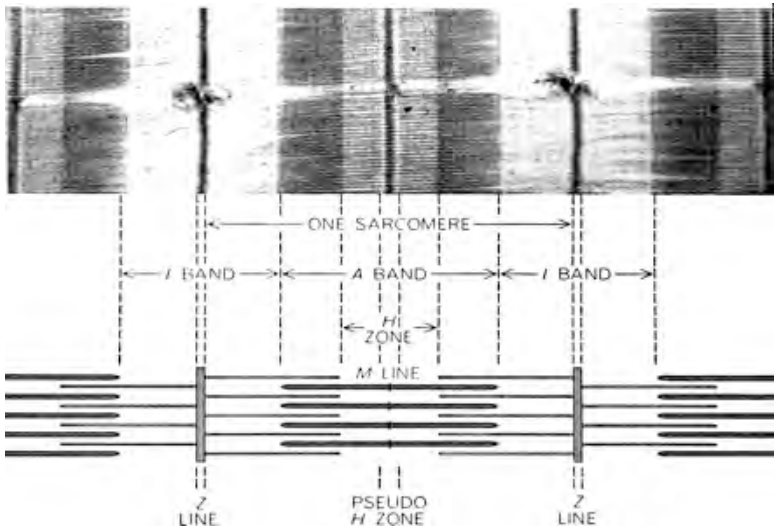


Figure 16–72. Molecular Biology of the Cell, 4th Edition.



See Hugh Huxley review on websit

Rogues Gallery of Motor Action: Translational Motor 2 - Muscles

Heuser lab – Washington University

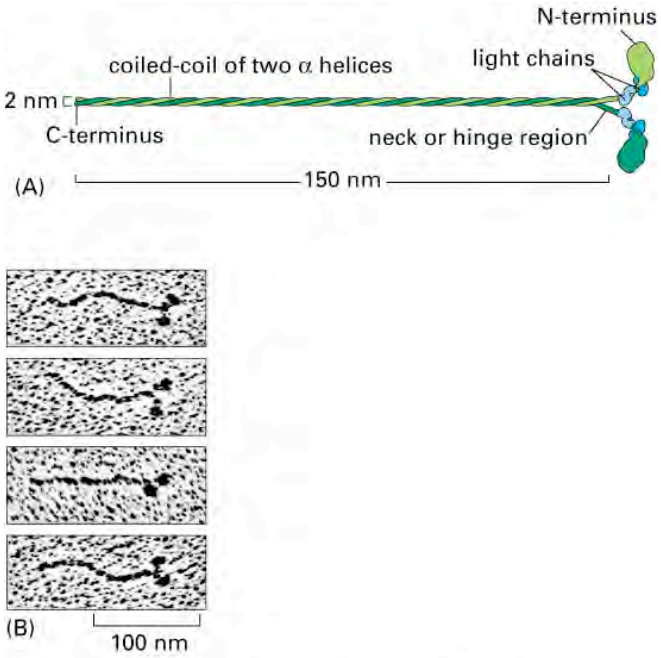
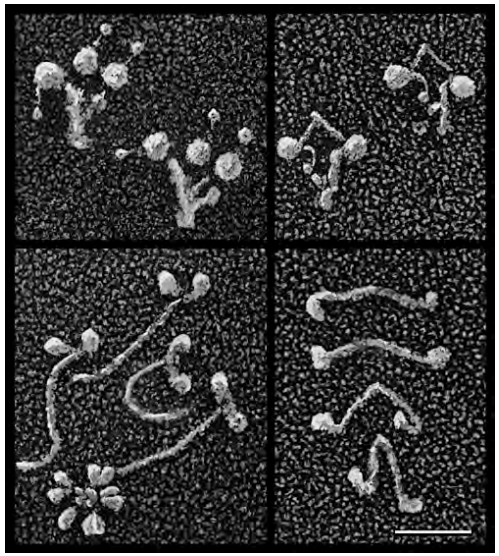
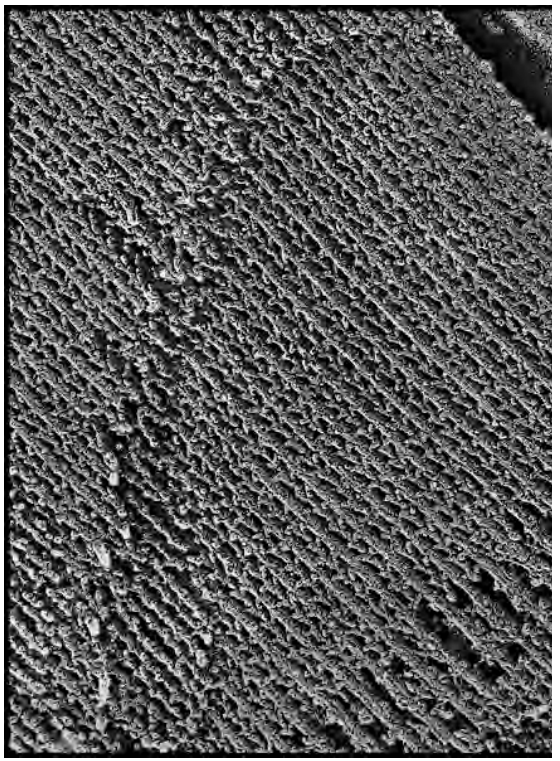


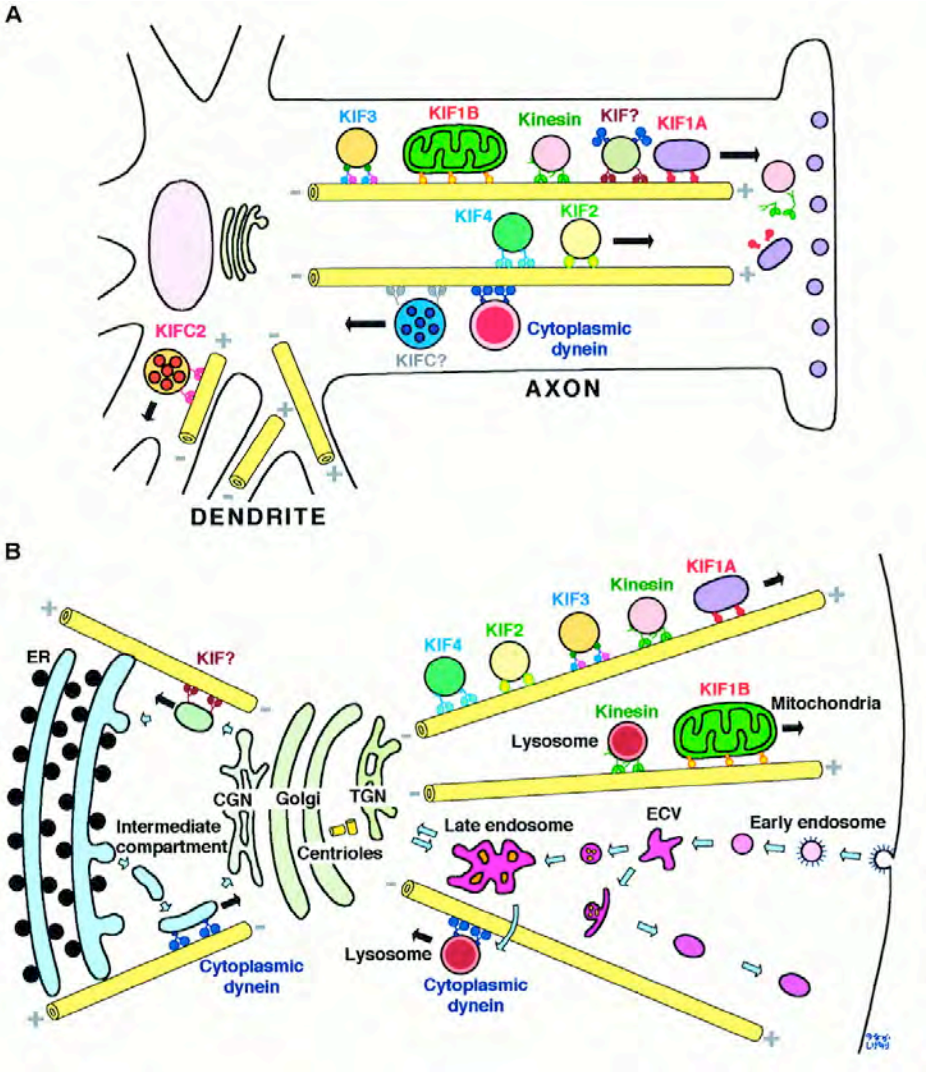
Figure 16–51. Molecular Biology of the Cell, 4th Edition.

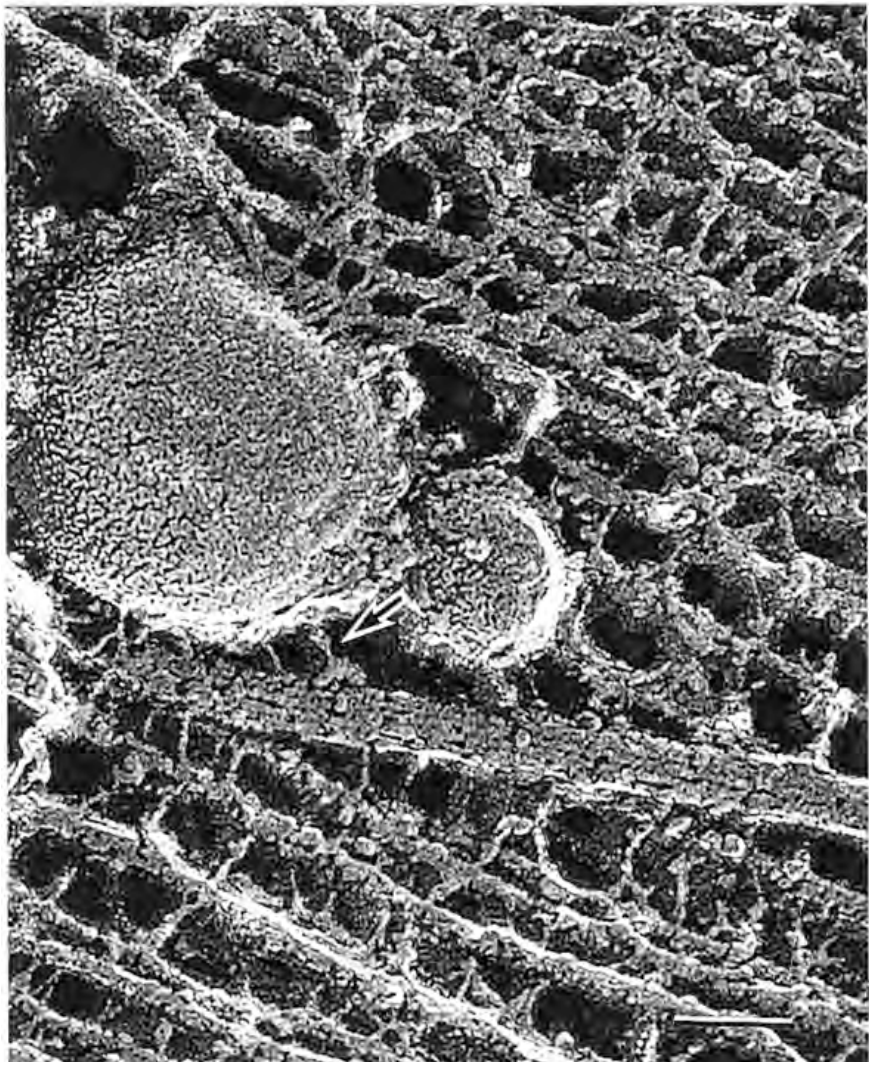




Organellar Transport

(Hirokawa, Science 1998)





Rogues Gallery of Motor Action: Translational Motor 2

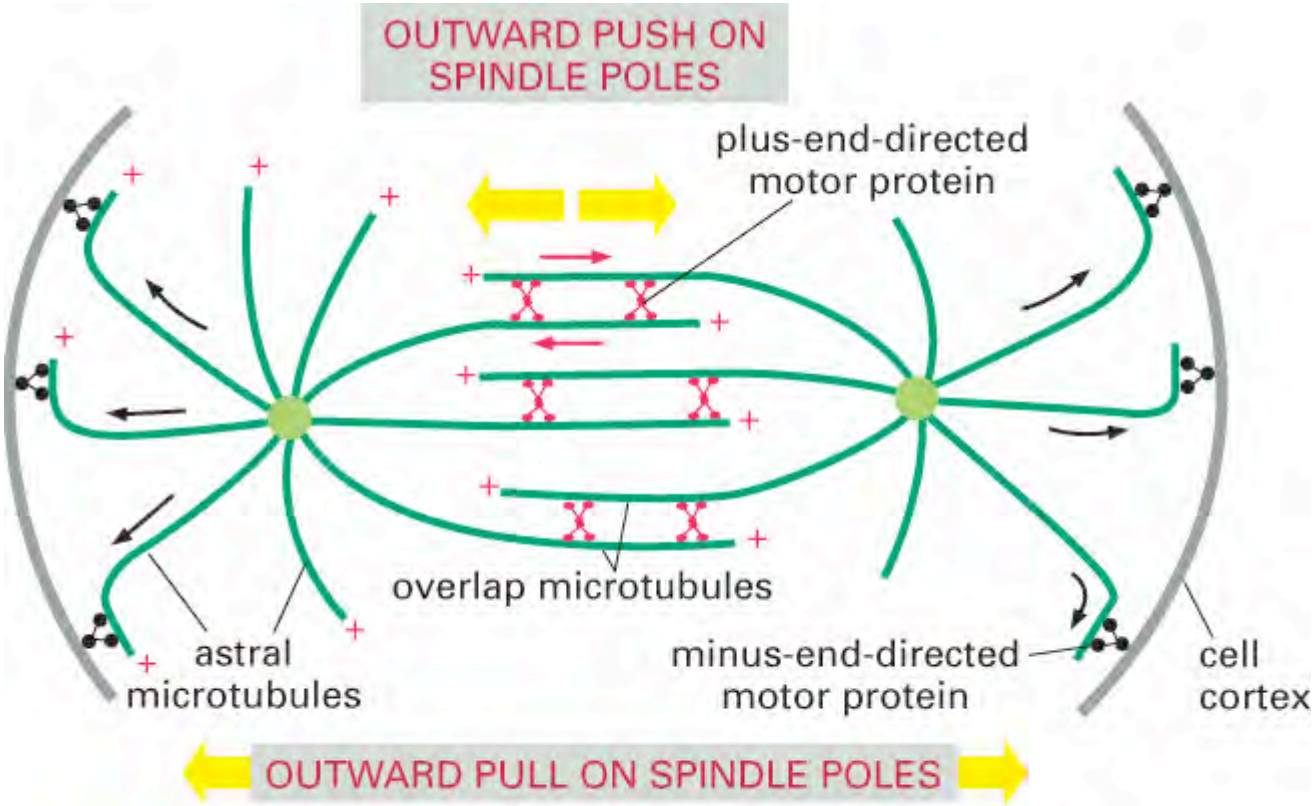
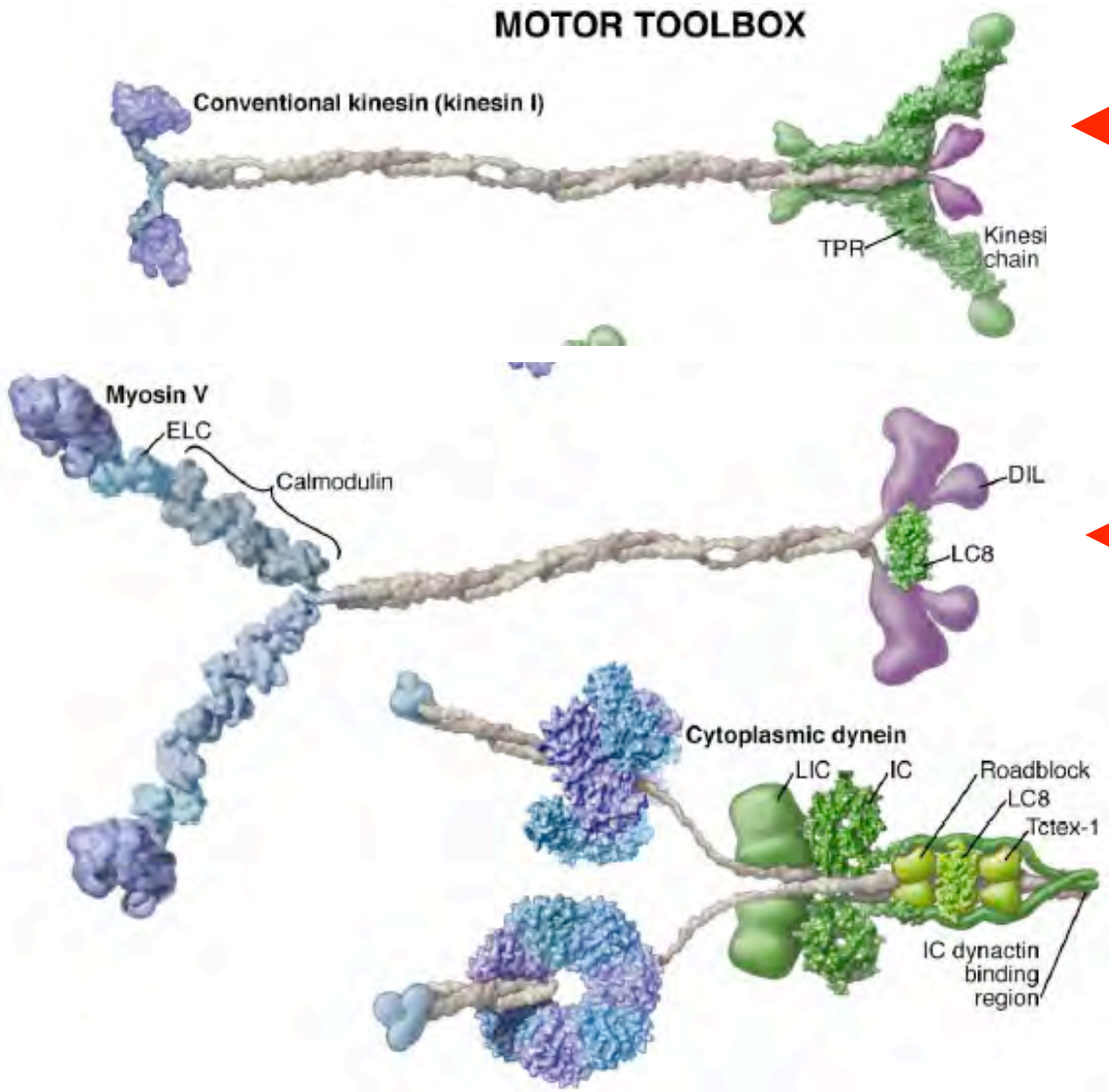


Figure 18–29. Molecular Biology of the Cell, 4th Edition.

Translational Motors



Kinesin

Speed: 850 nm/s
ATPase: 44.0 1/s

Myosin V

Speed: 350 nm/s
ATPase: 5.0 1/s

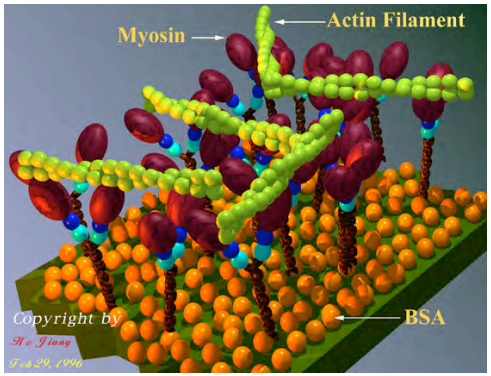
Dynein

Speed: -1250 nm/s
ATPase: 2.0 1/s

****ALL INVOLVED IN VESICLE TRANSPORT**

How We Know: Gliding Motility Assays

Show Vale movie



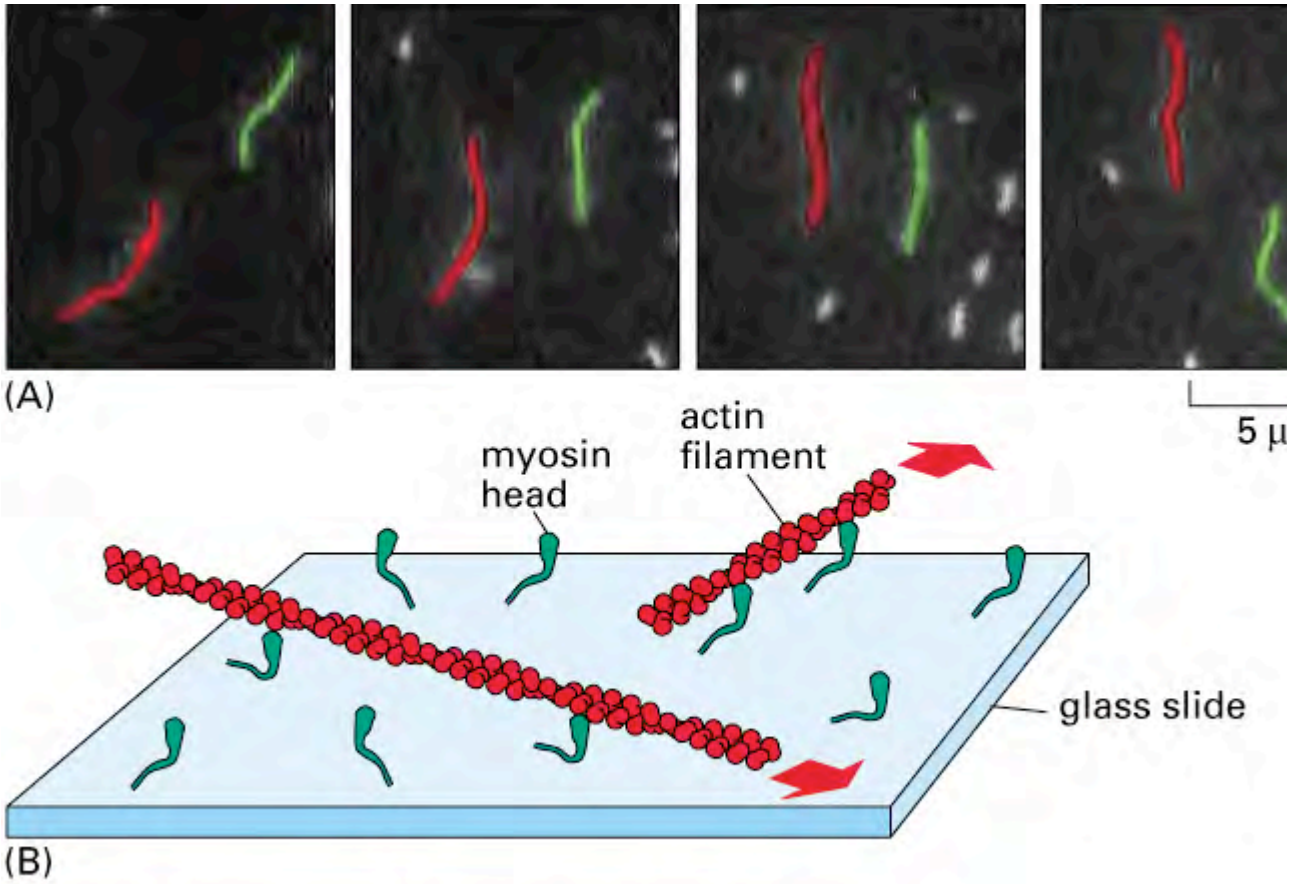
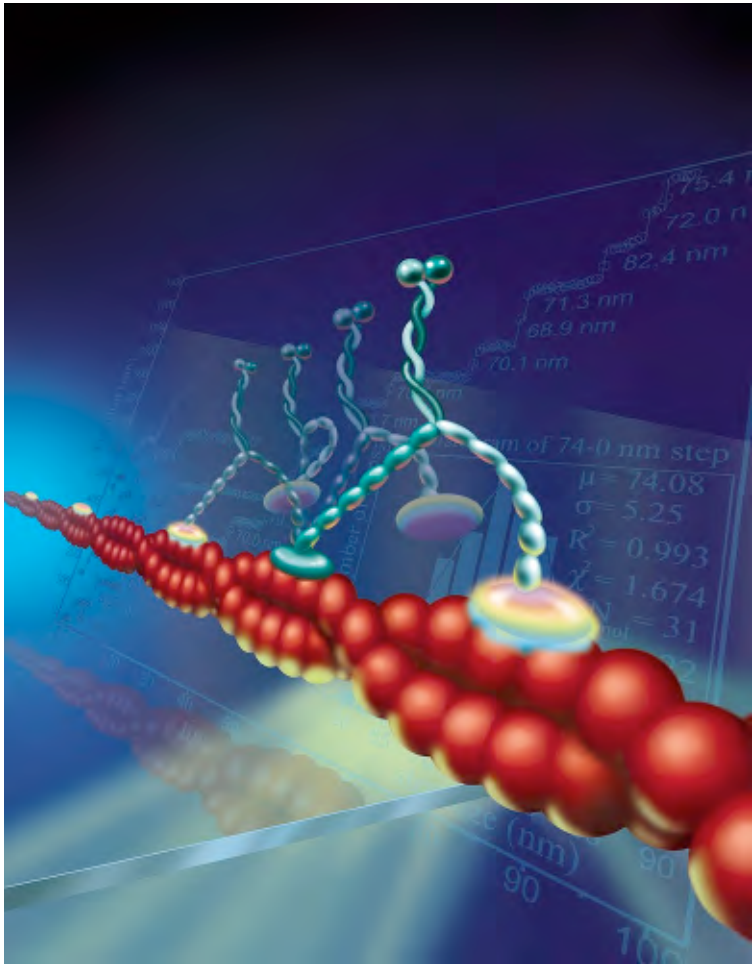
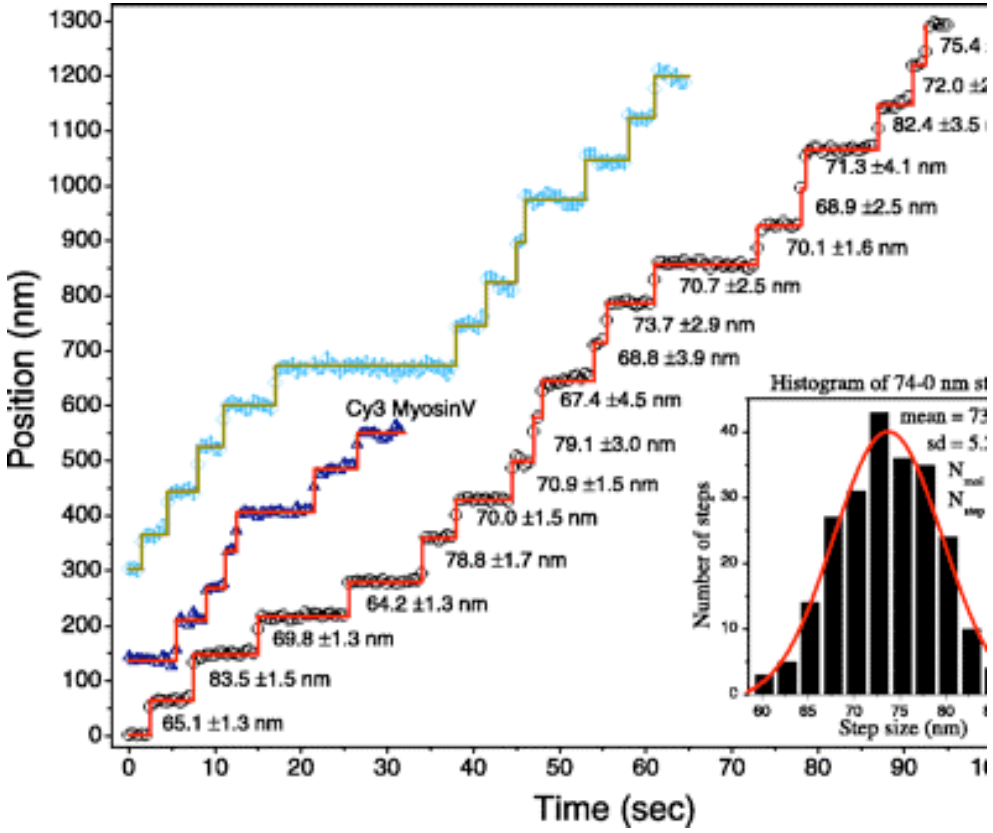


Figure 16–53. Molecular Biology of the Cell, 4th Edition.

Dynamics of Molecular Motors

Science, Vol 300, Issue 5628, 2061-2065, 27 June 2003 - Yildiz

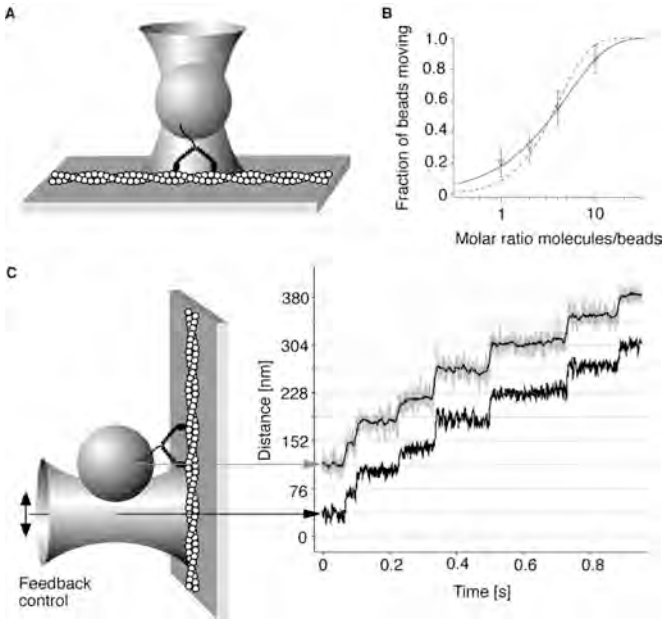


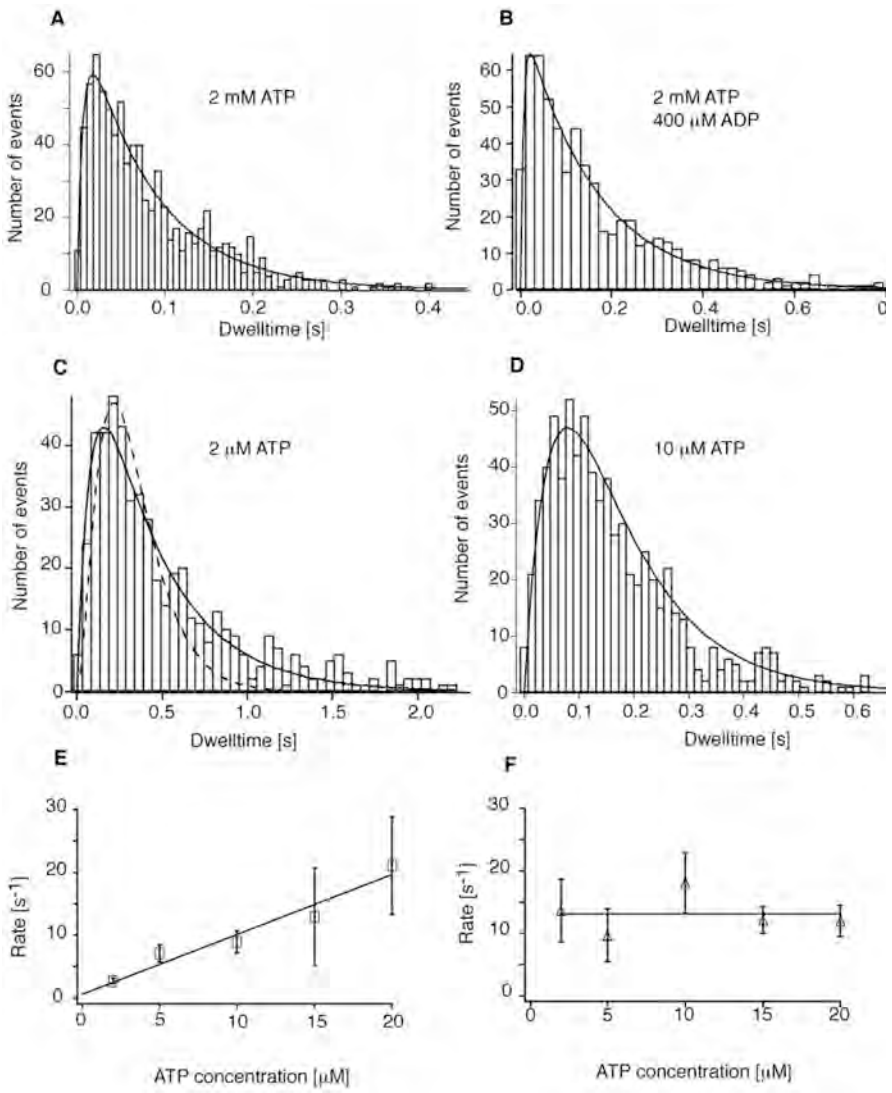


Show Gelles, Selvin movie

Stepping Kinetics

Spudich et al., PNAS 2000





Kinesin Data

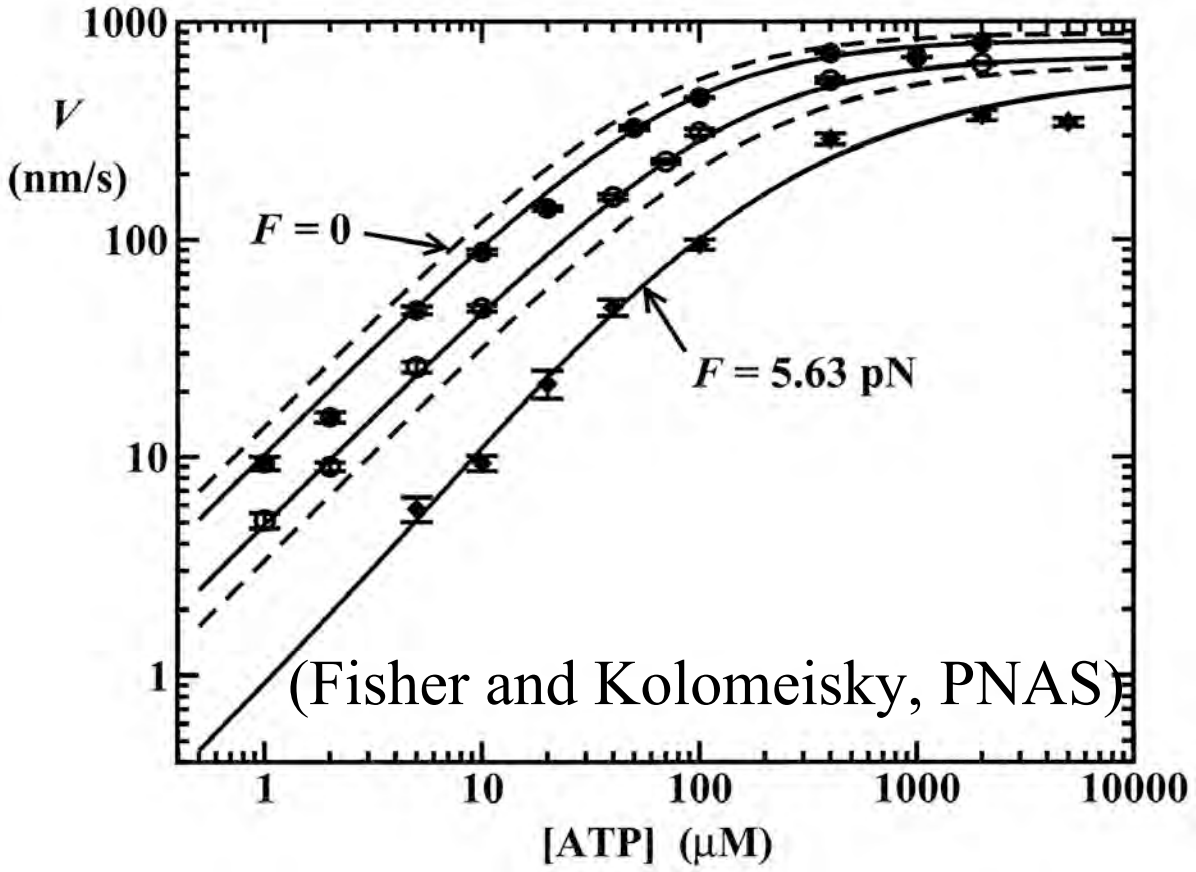
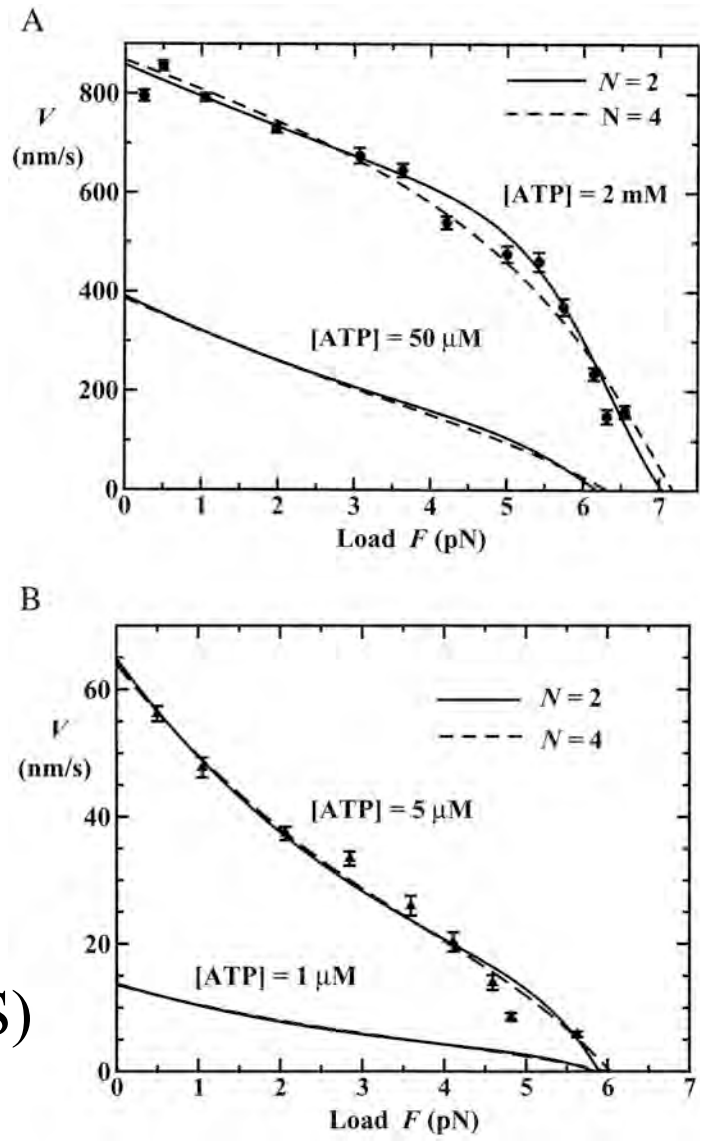


Fig. 3. Kinesin velocity as a function of [ATP] under external loads, F, fixed by a force clamp. The plots, from the top down, are for $F = 0$, 1.05, 3.59, 4.60, and 5.63 pN respectively. Data from Block and colleagues (9): solid curves, $N = 2$ fits; dashed curves, $N = 2$ predictions (see text)

Kinesin Data continued

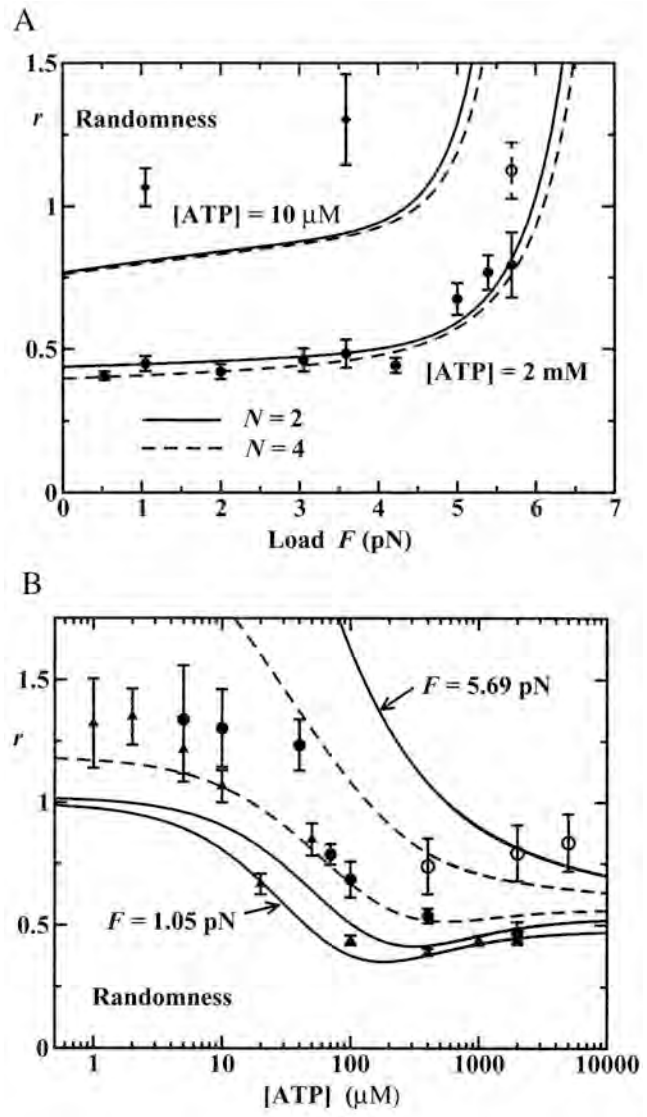
Fig. 4. Fits to the data of Block and colleagues (9) (and predictions) for velocity as a function of load for fixed concentrations of ATP. Note the inflection points at low [ATP] and convex profile at saturating [ATP].



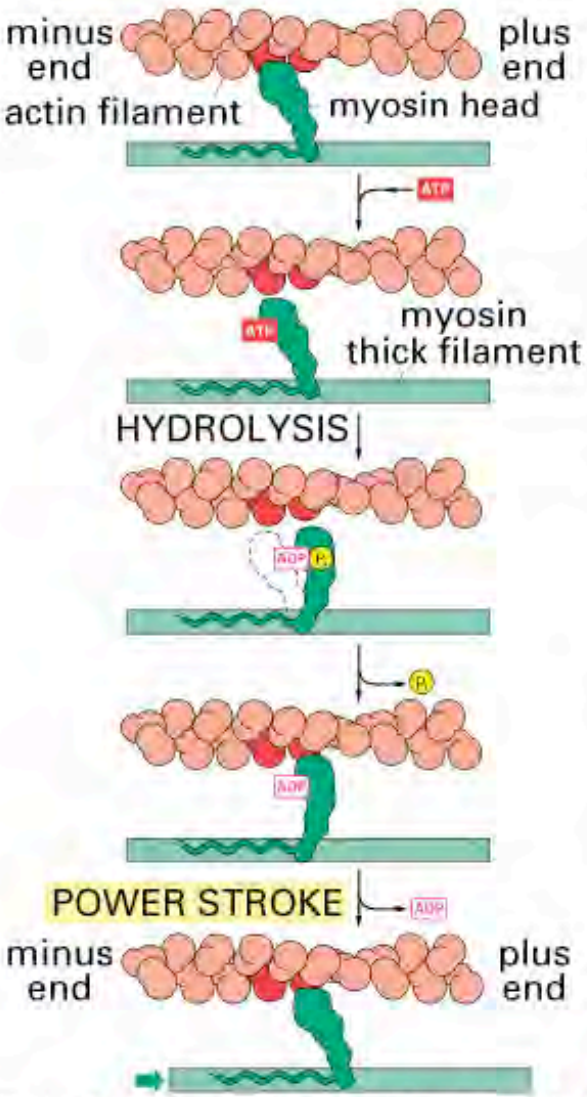
(Fisher and Kolomeisky, PNAS)

Kinesin Randomness Data

Fig. 5. Randomness data from Block and colleagues (9) and theoretical fits (*A*) as a function of external load, *F*, at fixed [ATP] (note that the two data points at *F* 5.7 pN and [ATP] = 2 mM appear separately in Block and coworkers: see figure 4 *a* and *b* of ref. 9, respectively) and (*B*) as a function of [ATP] at fixed loads of, from top down, *F* = 5.69 pN ( ), 5.35 and 4.60 pN (dashed-line predictions), 3.59 pN ( ), and 1.05 pN ( ).



What do we mean by the states?



ATTACHED At the start of the cycle shown in this figure, a myosin head lacking a bound nucleotide is locked tightly onto an actin filament in a *rigor* configuration (so named because it is responsible for *rigor mortis*, the rigidity of death). In an actively contracting muscle, this state is very short-lived, being rapidly terminated by the binding of a molecule of ATP.

RELEASED A molecule of ATP binds to the large cleft on the "back" of the head (that is, on the side furthest from the actin filament) and immediately causes a slight change in the conformation of the domains that make up the actin-binding site. This reduces the affinity of the head for actin and allows it to move along the filament. (The space drawn here between the head and actin emphasizes this change, although in reality the head probably remains very close to the actin.)

COCKED The cleft closes like a clam shell around the ATP molecule, triggering a large shape change that causes the head to be displaced along the filament by a distance of about 5 nm. Hydrolysis of ATP occurs, but the ADP and inorganic phosphate (P_i) produced remain tightly bound to the protein.

FORCE-GENERATING A weak binding of the myosin head to a new site on the actin filament causes release of the inorganic phosphate produced by ATP hydrolysis, concomitantly with the tight binding of the head to actin. This release triggers the power stroke—the force-generating change in shape during which the head regains its original conformation. In the course of the power stroke, the head loses its bound ADP, thereby returning to the start of a new cycle.

ATTACHED At the end of the cycle, the myosin head is again locked tightly to the actin filament in a rigor configuration. Note that the head has moved to a new position on the actin filament.

Figure 17-45 Essential Cell Biology 2/e. (© 2004 Garland Science)