Chapter 4

Molecular Machines and Motors

"*Nature, in order to carry out the marvelous operations in animals and plants, has been pleased to construct their organized bodies with a very large number of* ***machines****, which are of necessity made up of extremely minute parts so shaped and situated such as to form a marvelous organ, the composition of which are usually invisible to the naked eye, without the aid of microscope*"- Marcello Malpighi (seventeenth century);

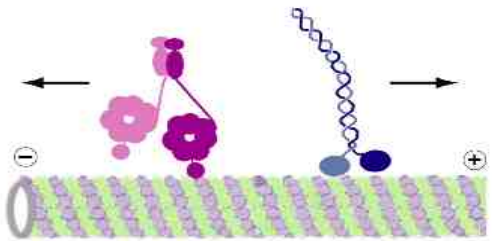
As quoted by Marco Piccolino, Nature Rev. Mol. Cell Biology 1, 149-152 (2000).

Marcello Malpighi

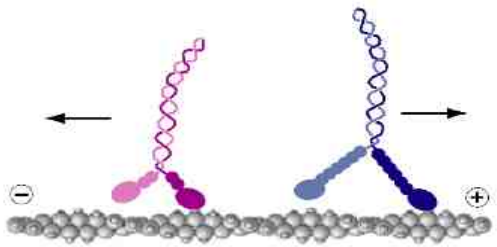
Molecular Motors and Nanomachines

Every Biological Cell Contains a Huge Number of Different Molecular Machines:

- Stepping Motors:

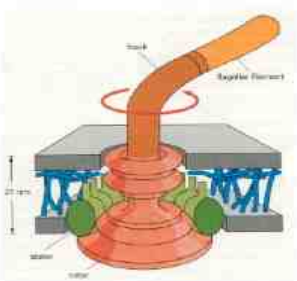


Dynein and Kinesin



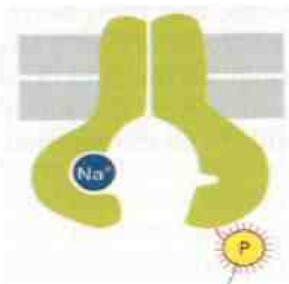
Myosin VI and V

- Rotary Motors:

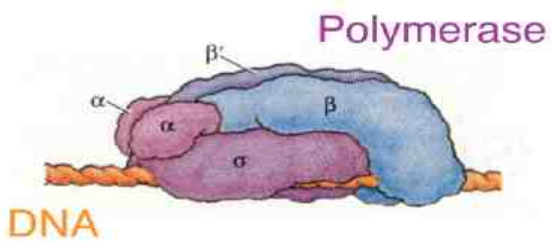


- Membrane-Pumps:

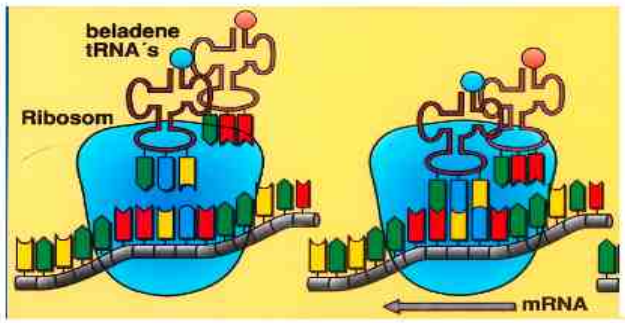
Na-K-pump



- Nano-Assemblers:

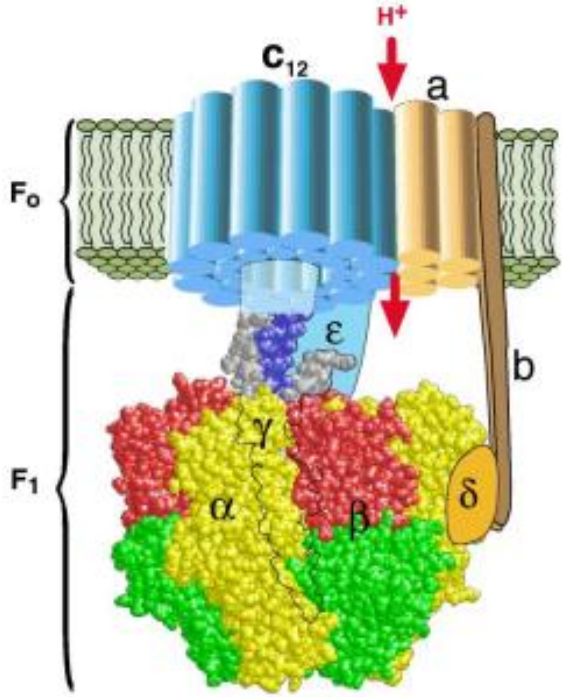


Ribosome



F0F1 ATPase

ATP synthase—also called F0F1 ATPase, or simply F-ATPase
Rotary form of Motor.
Nearly identical proteins are found in eukaryotic mitochondria and bacteria
ATP synthase utilizes the energy stored in this electrochemical gradient
Converts electromotive force into a rotary torque which promotes substrate binding and liberates ATP
Composed of at least 8 subunit types: α3, β3, γ, δ, ε, a, b, c



H. Wang and G. Oster (1998). Nature 396:279-282.

10 nm

Two regions

F0: membranous rotor. Units: c and a

F1: Cytosolic rotor: 3 units of α, β each, 1 unit of γ, δ, ε and b

γ and ε makes the stalk

c-complex rotates when a H^+ enters a-complex. This rotation drives the coupling of ADP to Pi and forms ATP

Produces 3 ATPs per twelve protons passing through it.

Some times even depends on PMF from Na^+

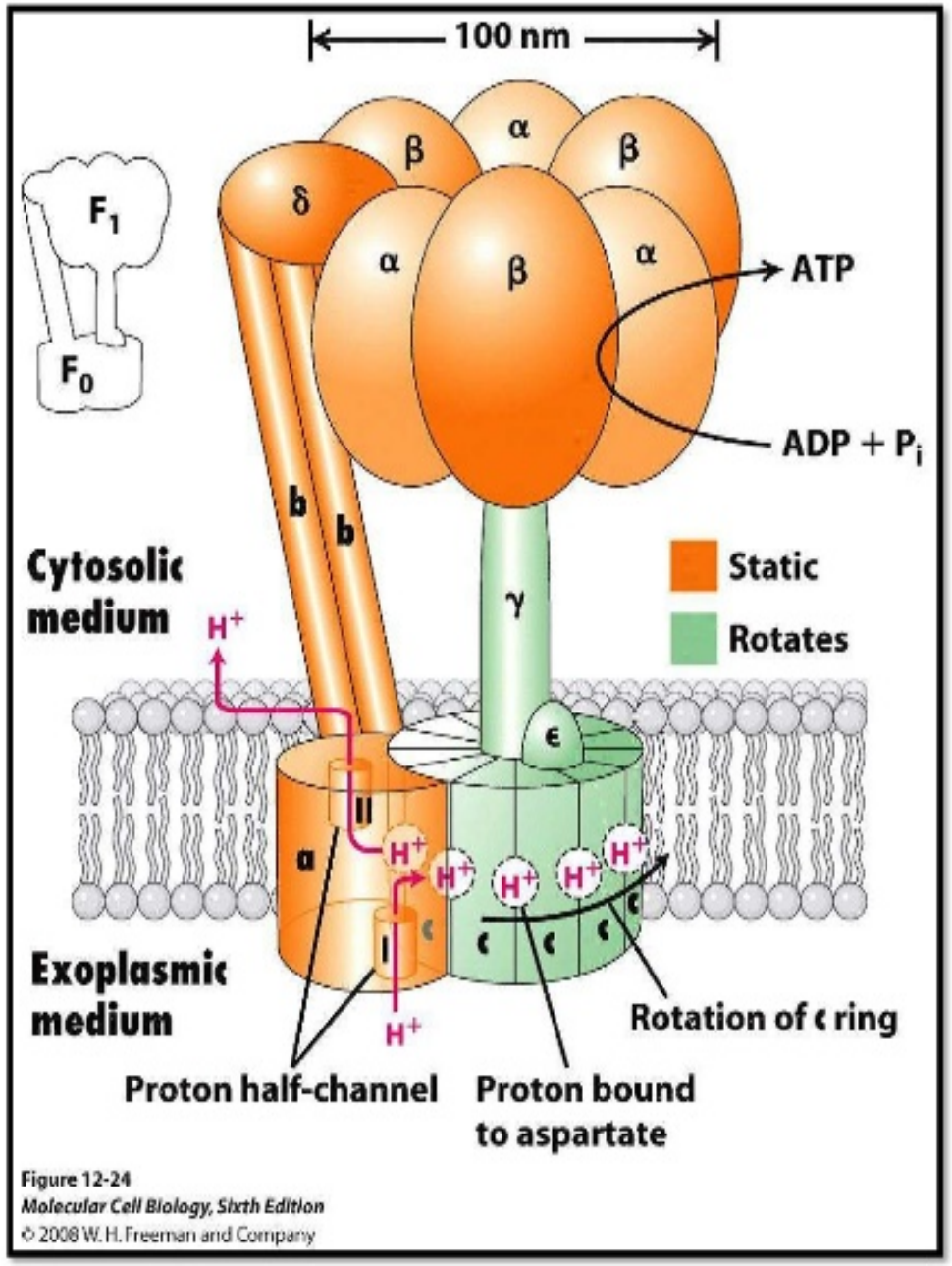
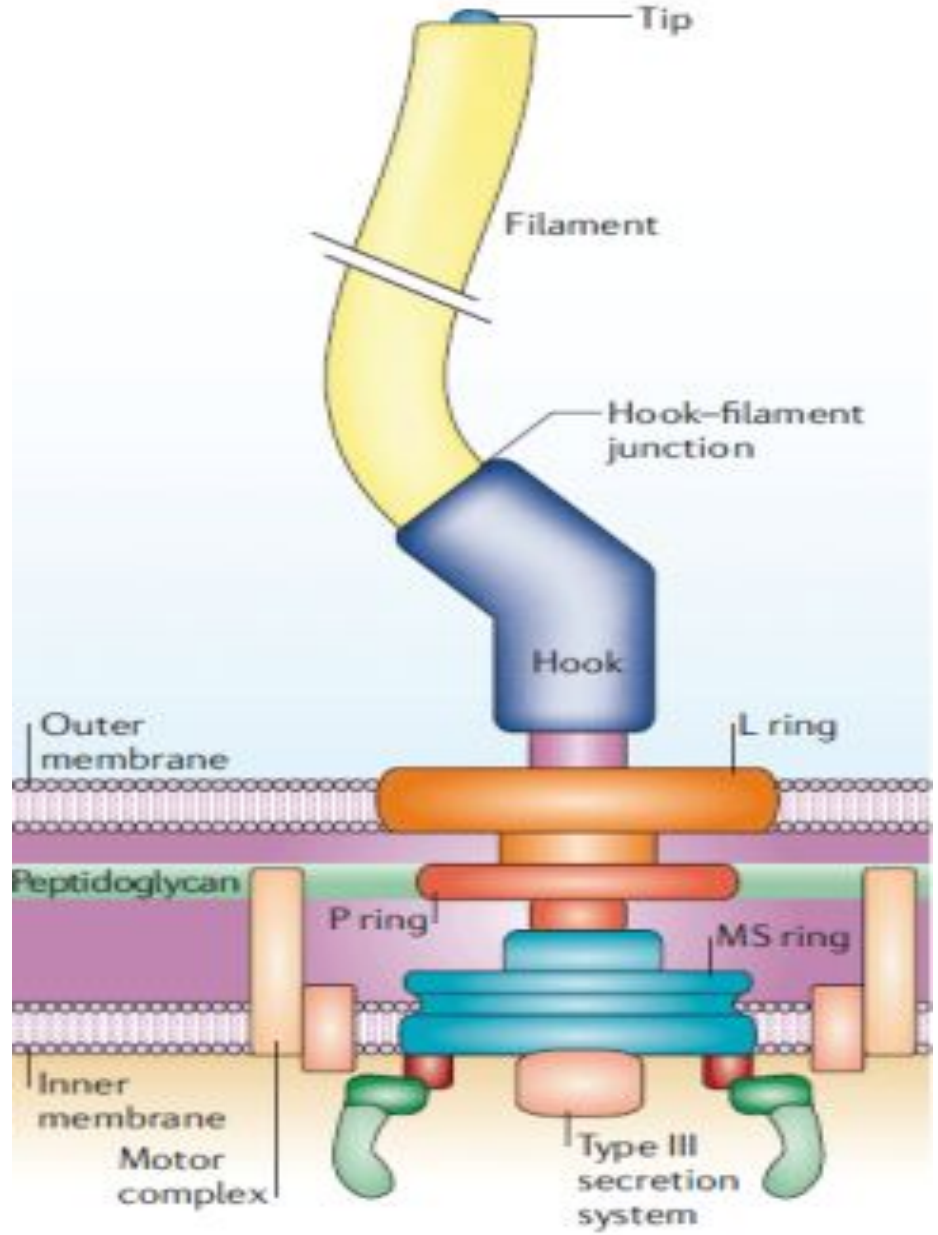
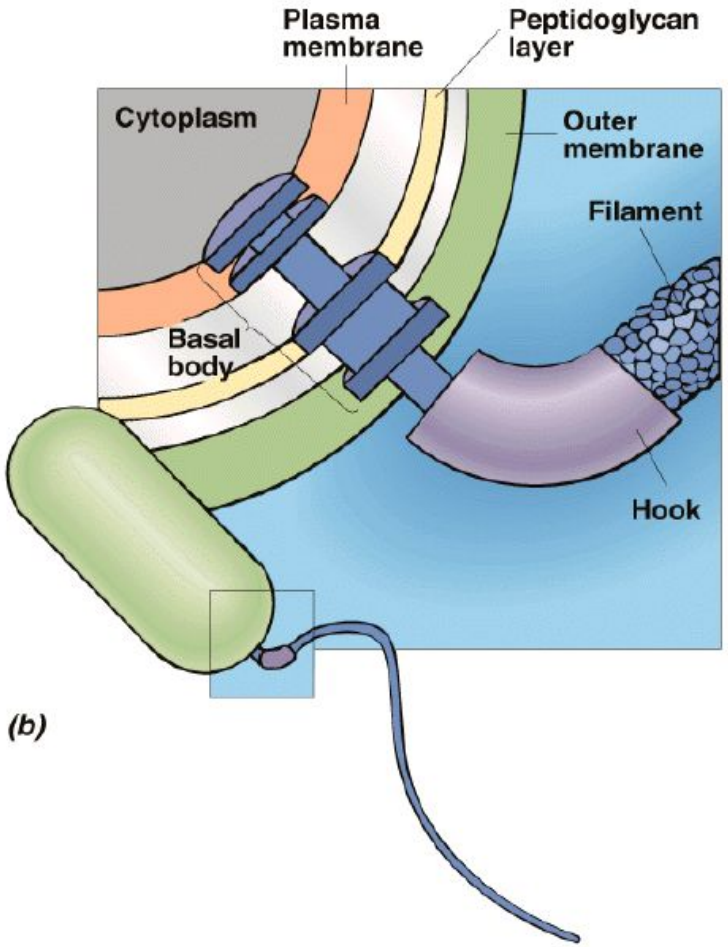
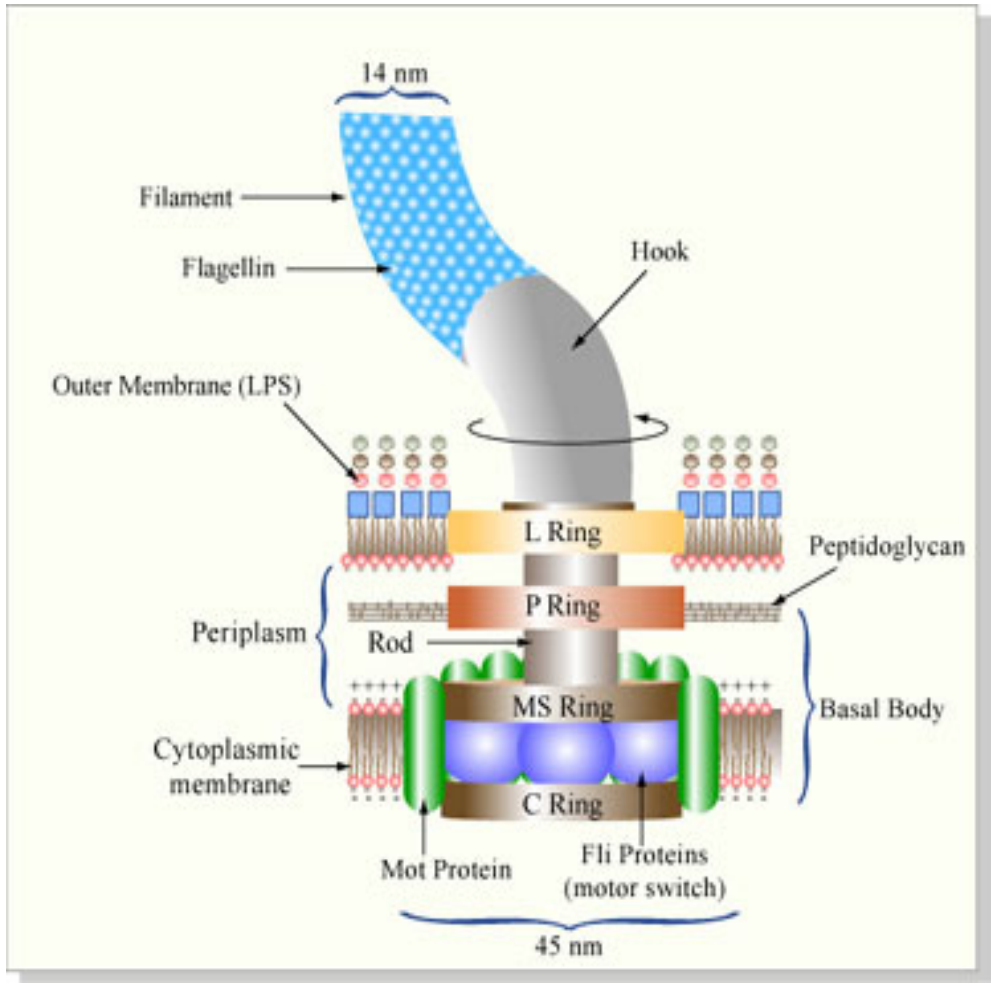


Figure 12-24
Molecular Cell Biology, Sixth Edition



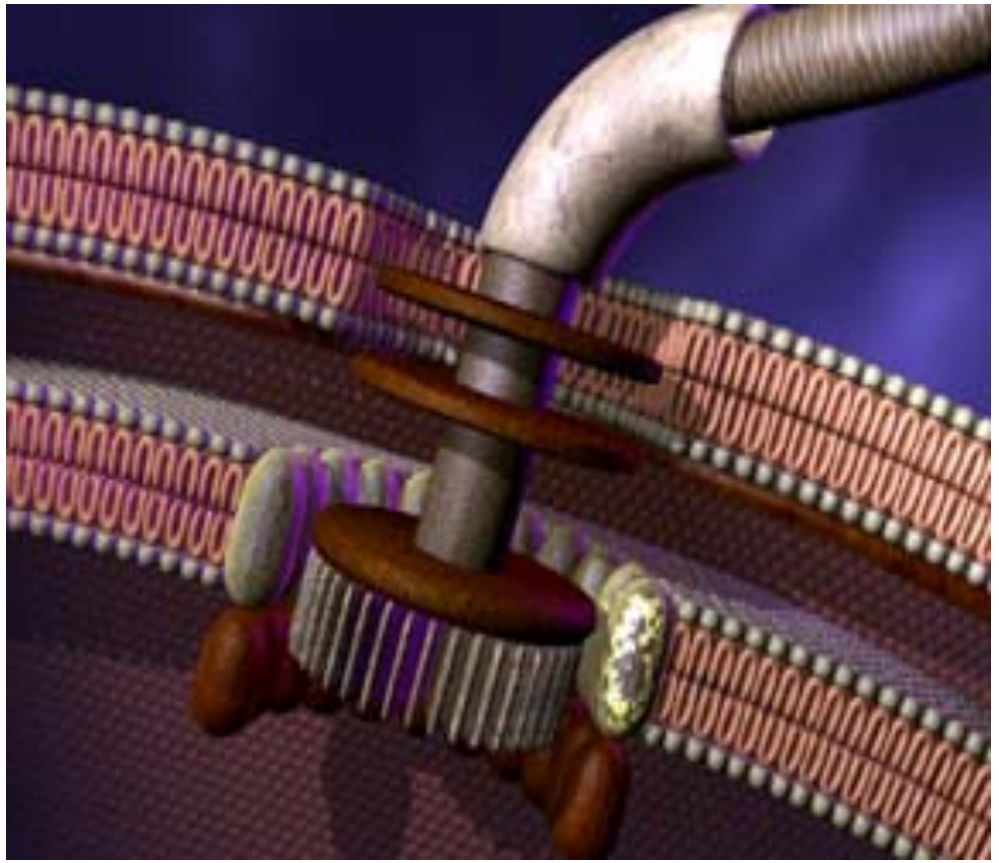
Bacterial Flagella





Bacterial Flagella

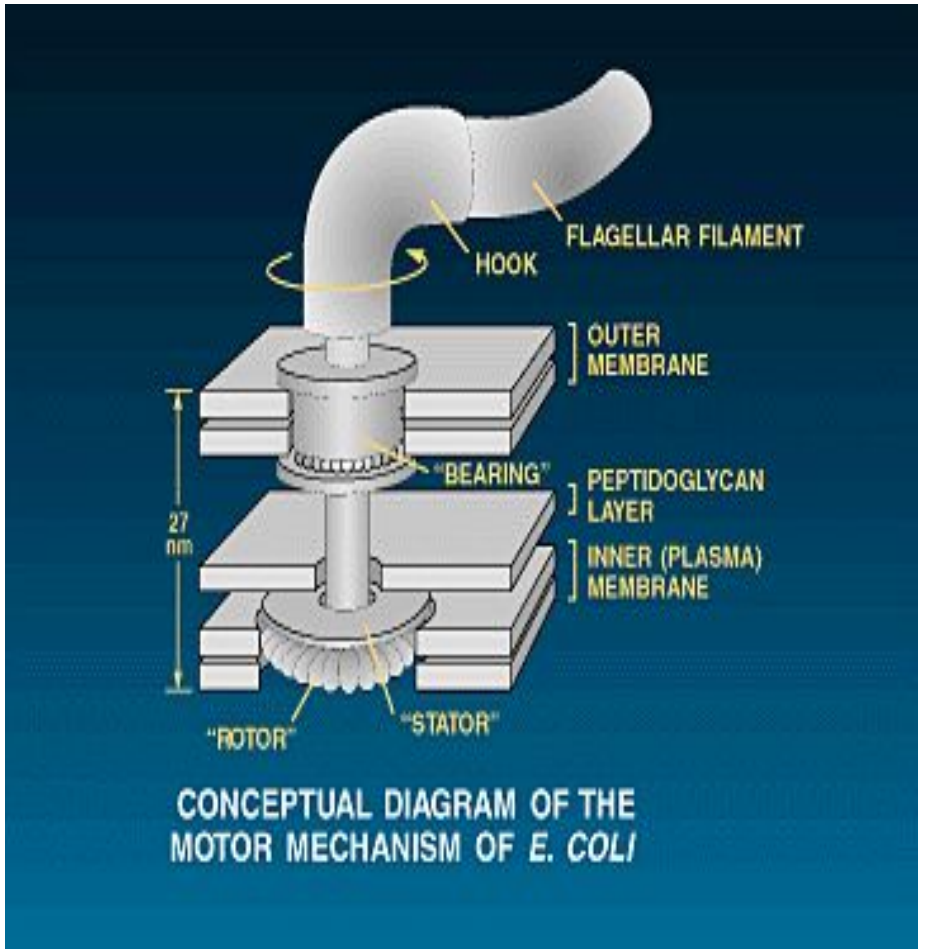
- Molecular engine powered by the flow of ions across the inner, or cytoplasmic, membrane of a bacterial cell envelope
- Each motor drives a protruding helical filament, and the rotating filaments provide the propulsive force for cells to swim.



Artistic version of flagella motor

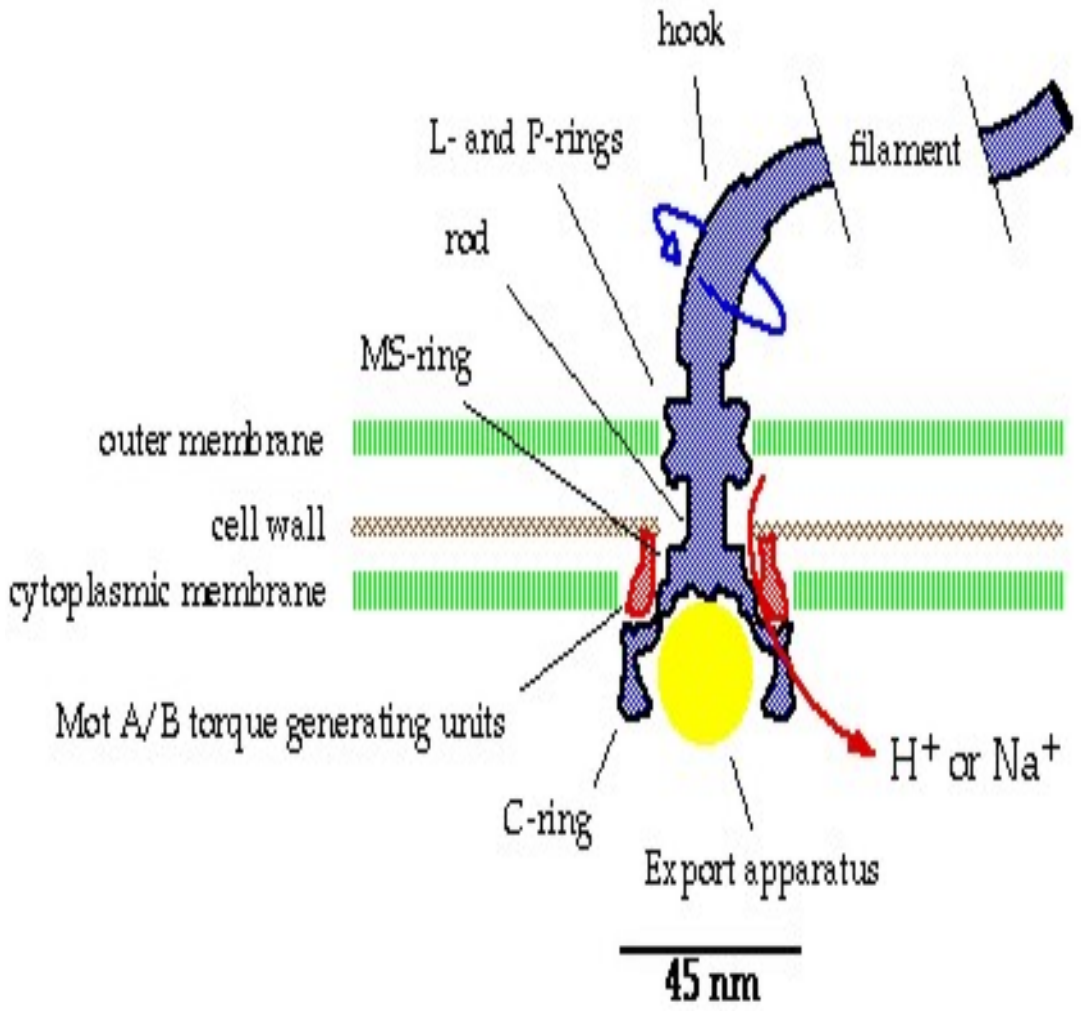
Bacterial Flagella

- Ion flux is driven by an electrochemical gradient controlled by H+ and Na+
- This gradient consists of a voltage component and a concentration component
- The inside of the cell is typically at an electrical potential about 150mV below the outside and has a slightly lower concentration of H+ or Na+

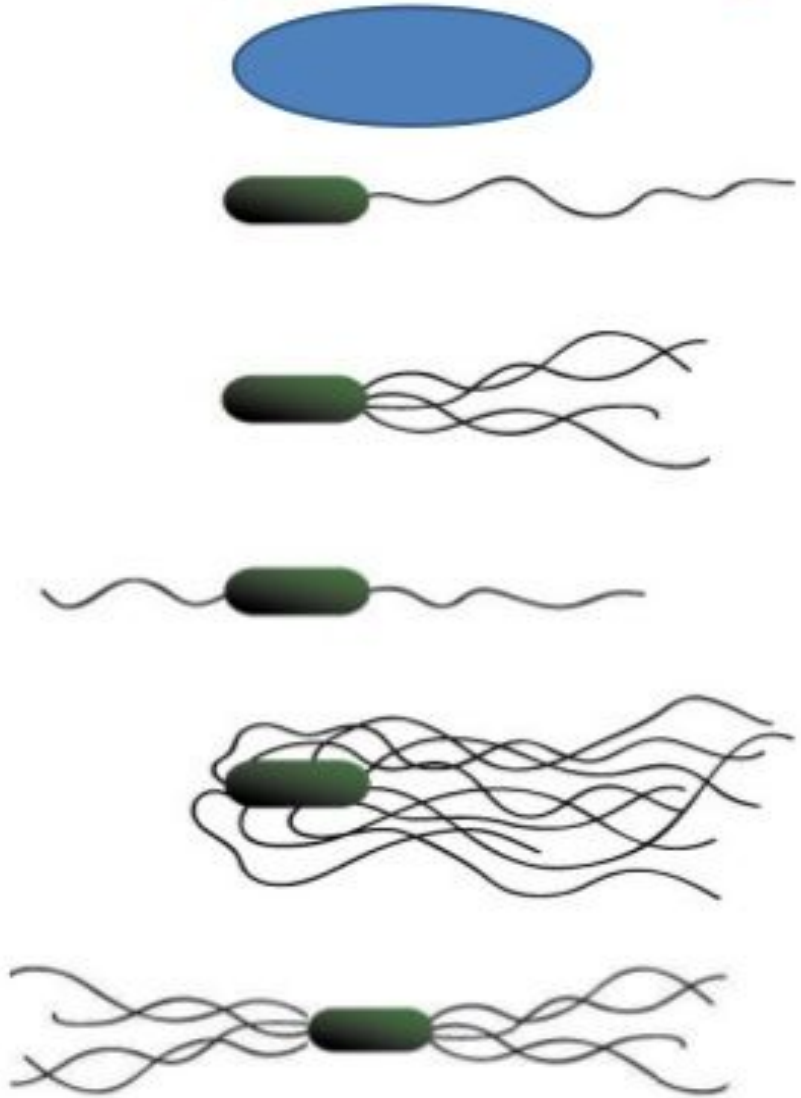


Bacterial Flagella

- This rotor is surrounded by 8-16 torque generators, proteins MotA and MotB, anchored in the cell wall
- Filaments rotate at speeds up to 1000 Hz in swimming cells
- The rotating heart of the motor is a set of rings in the cytoplasmic membrane



Types of flagellar arrangement



Atrichus: No flagella

Polar/ Monotrichous – single flagellum at one pole

Lophotrichous – tuft of flagella at one pole

Amphitrichous – flagella at both poles

Peritrichous – flagella all over

Amphilophotrichous – tuft of flagella at both ends

Superfamilies of Cytoskeletal MOTORS

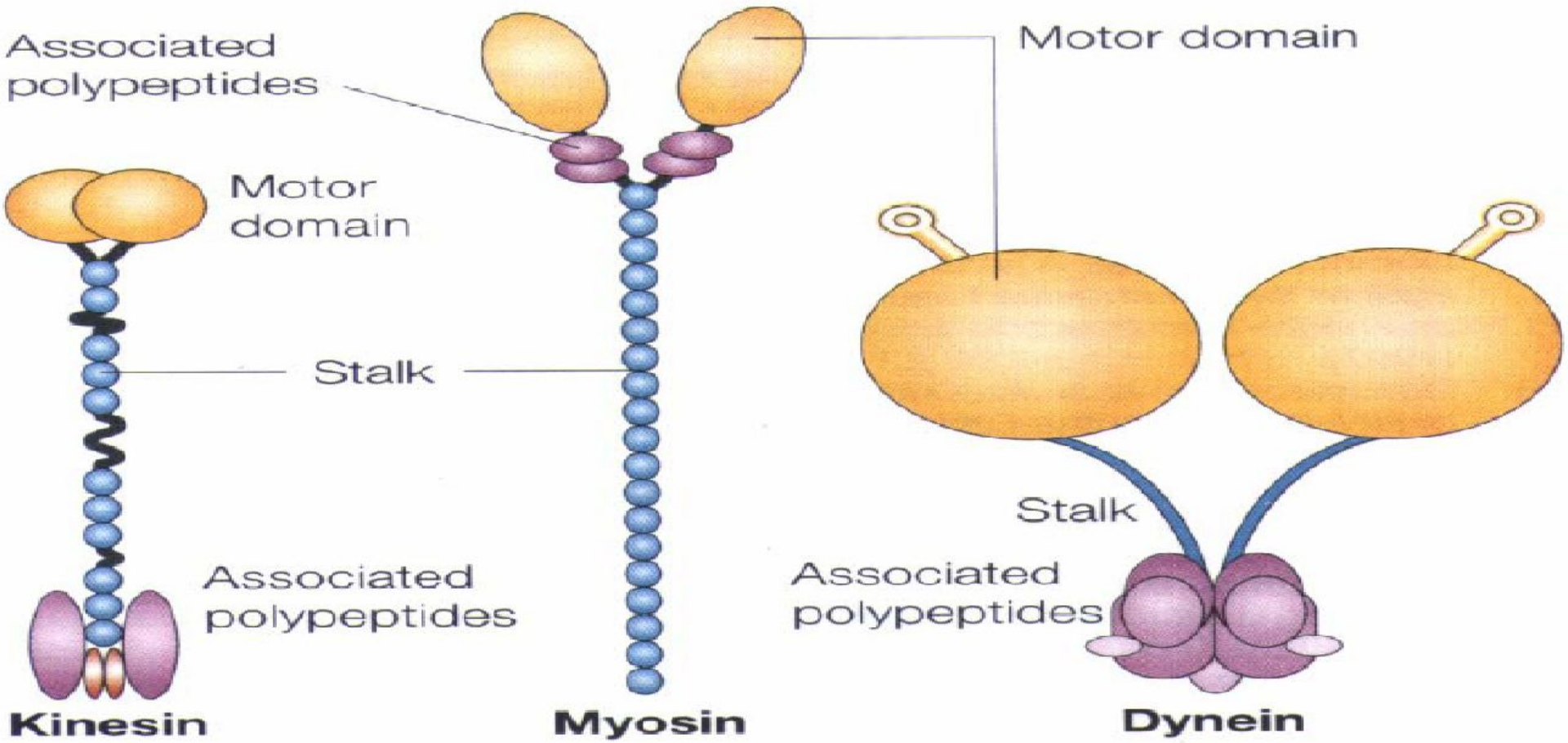


Figure 1 | **Overview of three molecular motor**

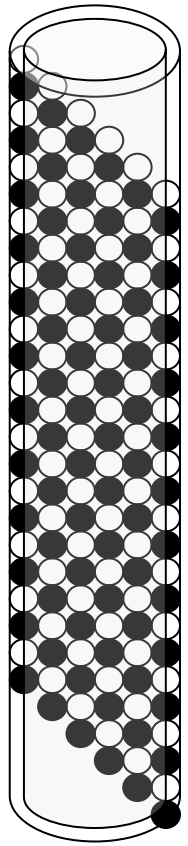
Cytoskeleton Motor

Thick Filaments:Microtubule

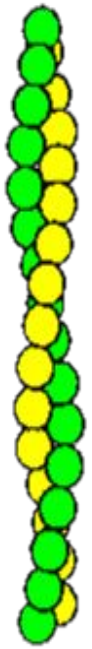
α-β dimer

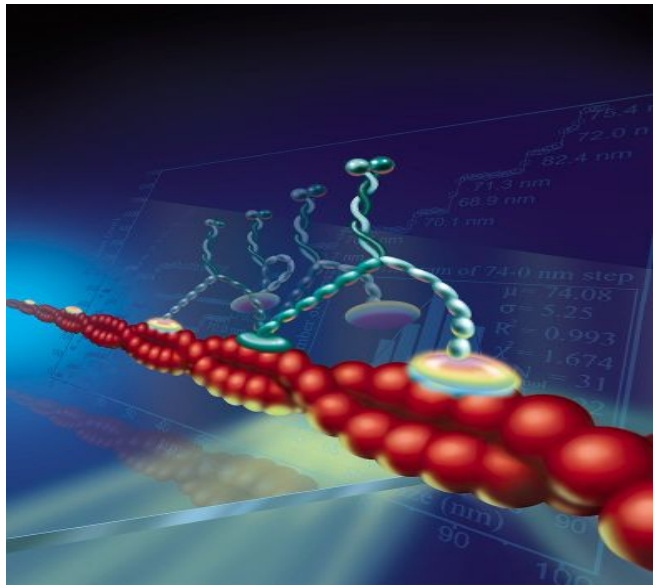
Protofilament

Diameter ~ 25 nm.



Thin Filaments: actin

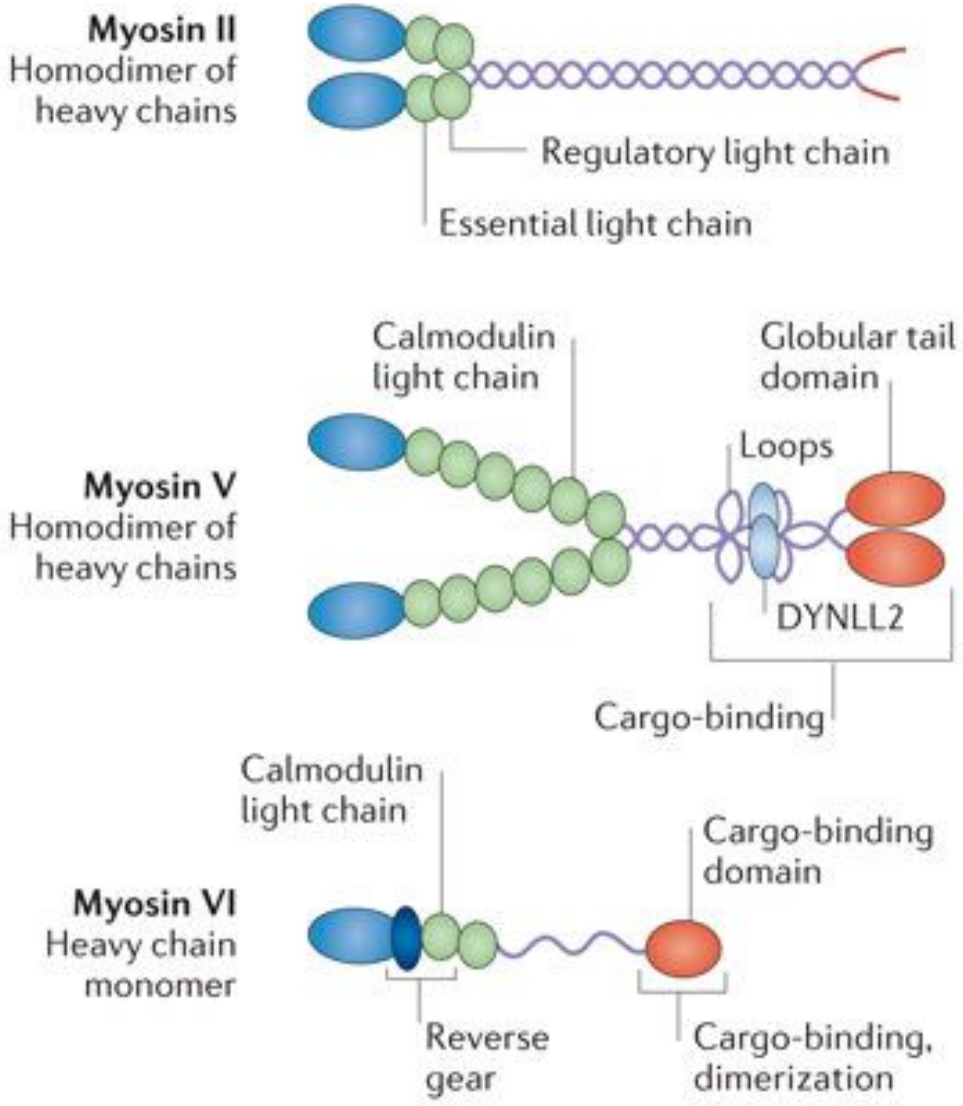




Myosin linear Motor

Myosins

- Are a family of motor proteins that bind to & move along actin filaments toward the + ends.
- Large globular heads bind and split ATP
- Undergo a configurational change that changes the angle of the head with respect to an α-helical tail. E.g. Myosin II
- Eg: Muscular contractions and Relaxations



Myosin linear Motor

The Actin myosin complex basically have two regions:

A-band and I-band

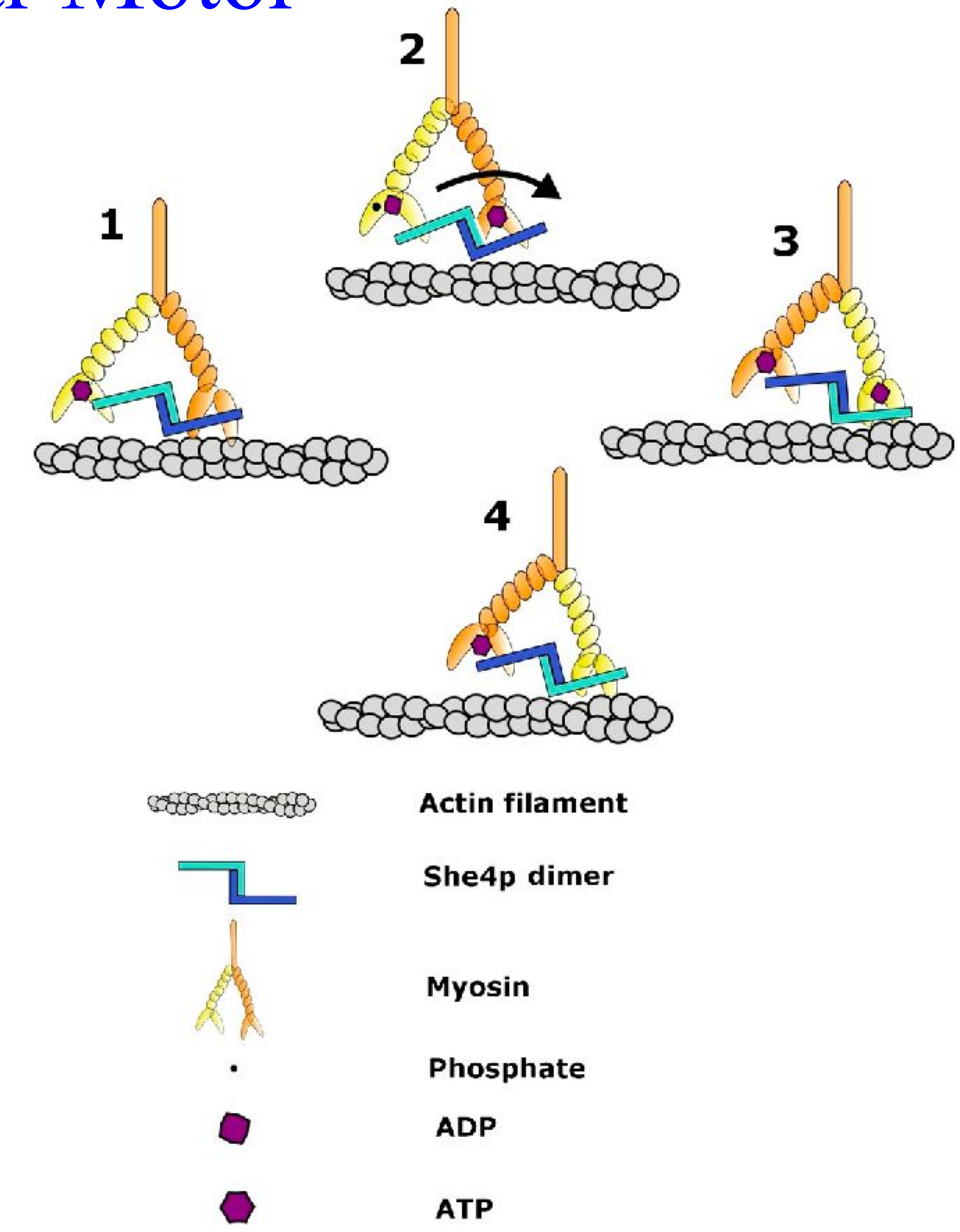
A-band: hexagonally arranged thick filaments (Myosin)

I-band: hexagonally arranged thin filaments (actin, troponin, tropomyosin)

Contraction: thick filaments slide or walk along thin filaments. Myosin heads binds to actin. ATP utilized leading to power stroke

Relaxation: Myosin head dissociate from thin filament.

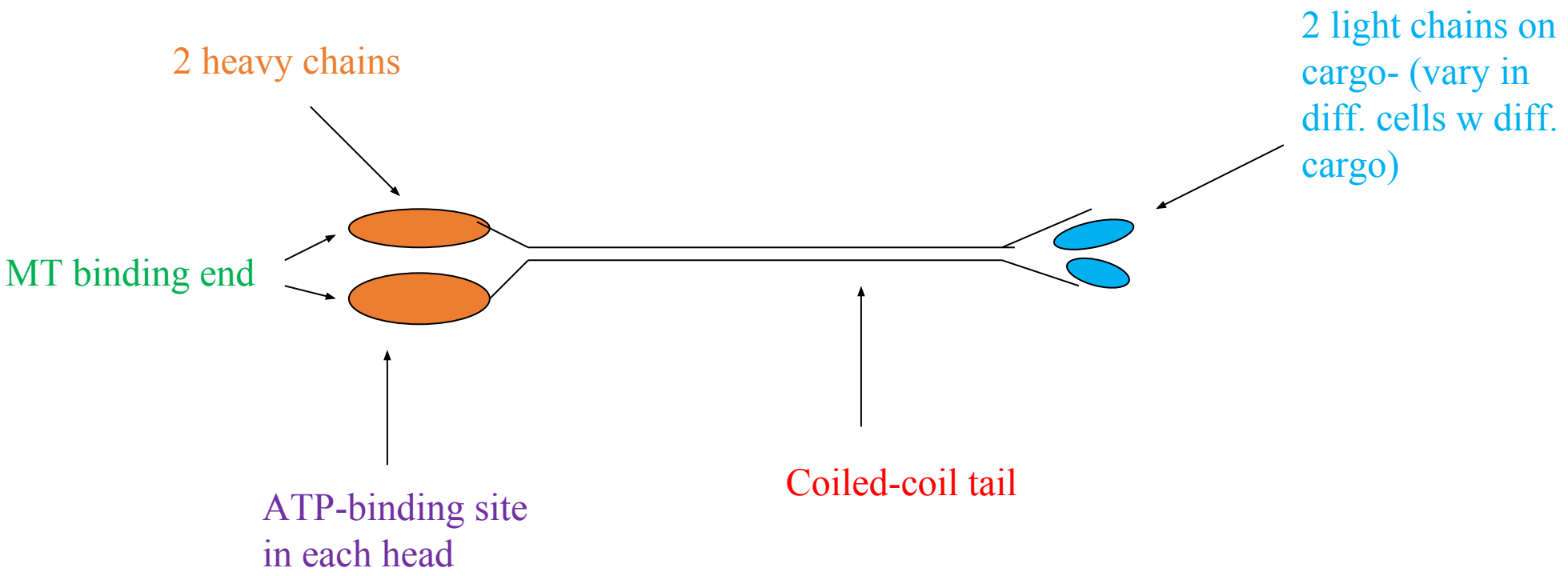
The coiled chain is perpendicular to the microtubules

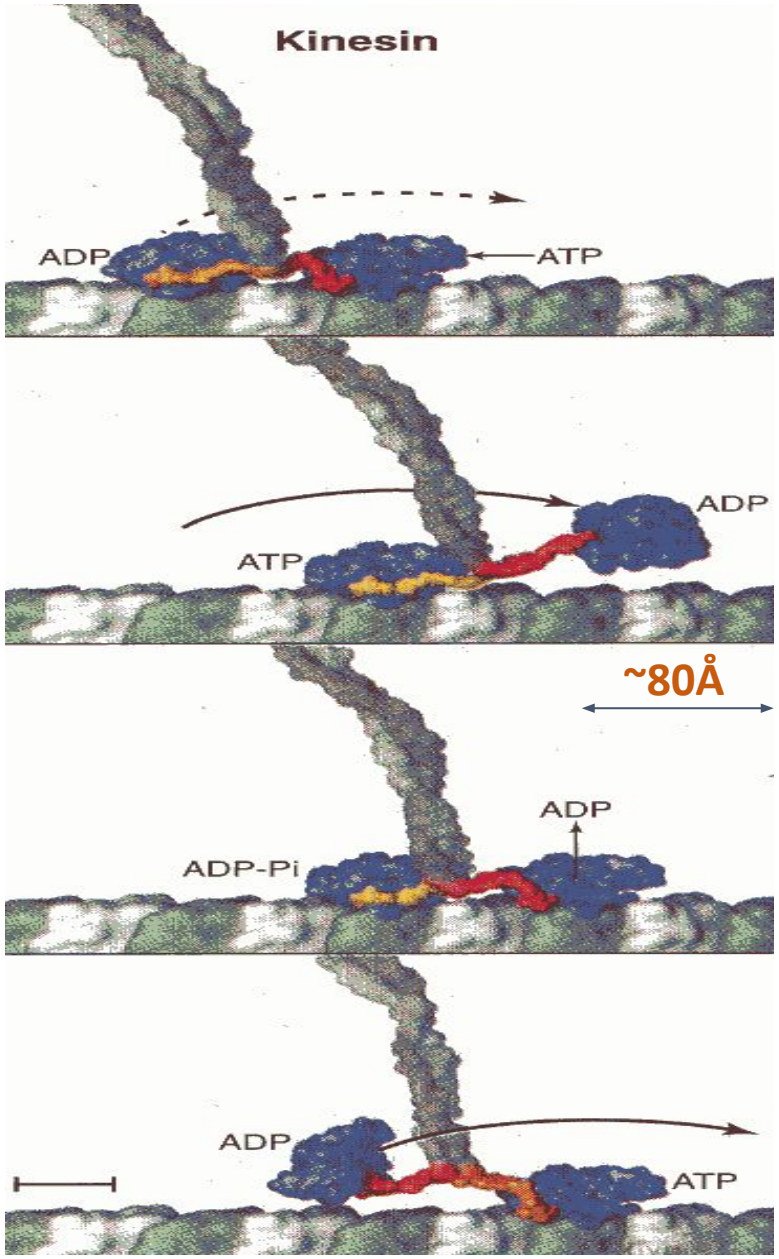


Kinesin linear Motors

Kinesin is a large protein with 4 polypeptide chains

Like myosin it has 2 light and 2 heavy chains, each with a globular head domain and long a-helical tail.



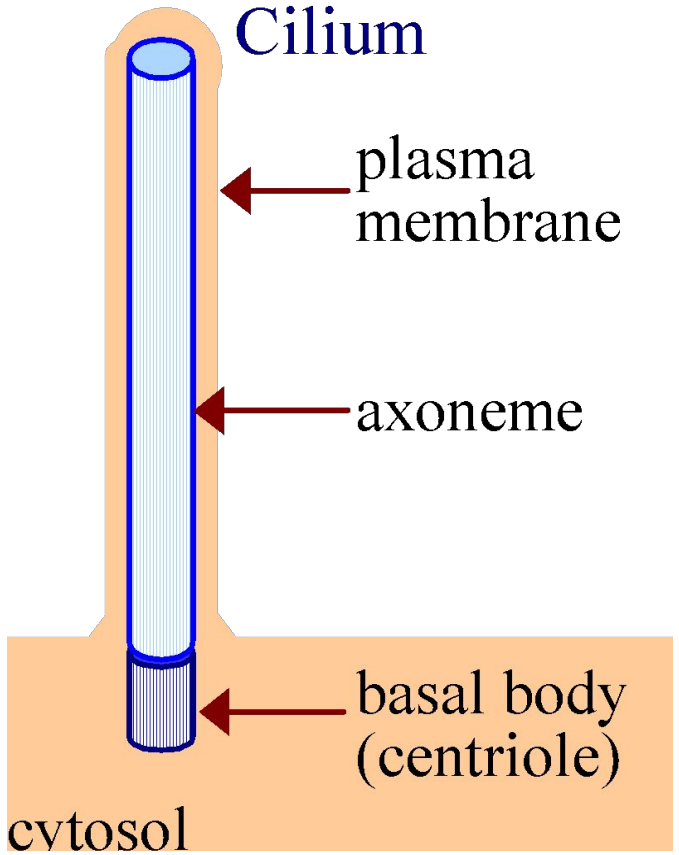


Kinesin linear Motors

- Kinesin “walks” along the microtubule (MT) protofilament, stepping from one tubulin subunit to the next.
- Moves from Minus end to Plus end.
- Unidirectional motion is produced by a pronounced conformational change in kinesin’s “neck linker.”

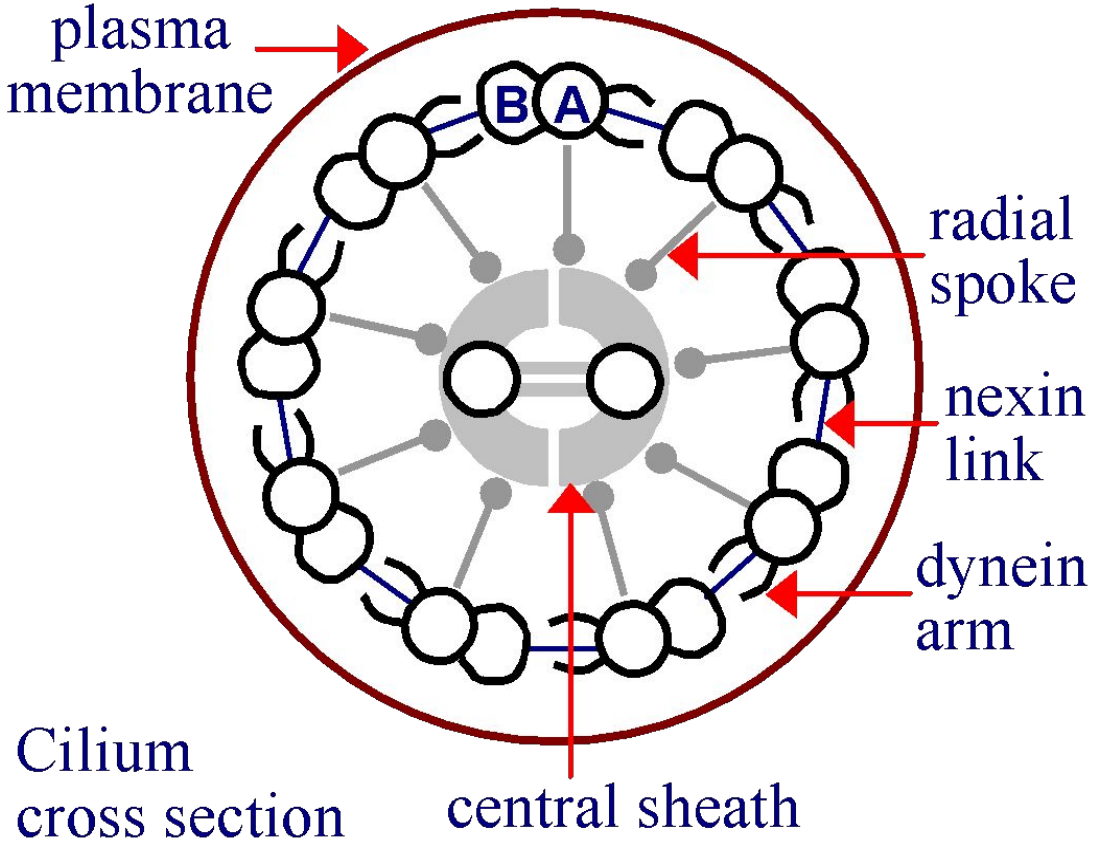
Dynein

- Cilia & flagella are bounded by the plasma membrane.
- A basal body, which is a single centriole cylinder, is at the base of each cilium or flagellum.
- Cilia & flagella have a core axoneme, a complex of microtubules and associated proteins.
- **Flagella** are usually **1 or 2** per cell. They tend to have a rotary or sinusoidal movement. They may have additional structures outside the core axoneme.
- **Cilia** are usually **many** per cell. They tend to have a whip-like movement.



Dynein

- An axoneme includes:
- Nine doublet microtubules around the periphery. The A tubule of each doublet has attached dynein arms.
- Two singlet central microtubules, surrounded by a sheath.



- Nexin links & radial spokes. These provide elastic connections between microtubule doublets and between the A tubule of each doublet and the central sheath.

Dyneins are a family of minus end directed MT motors. Largest and fastest molecular motors(14 mm/sec vs 2 mm/sec for kinesin)

Thank You