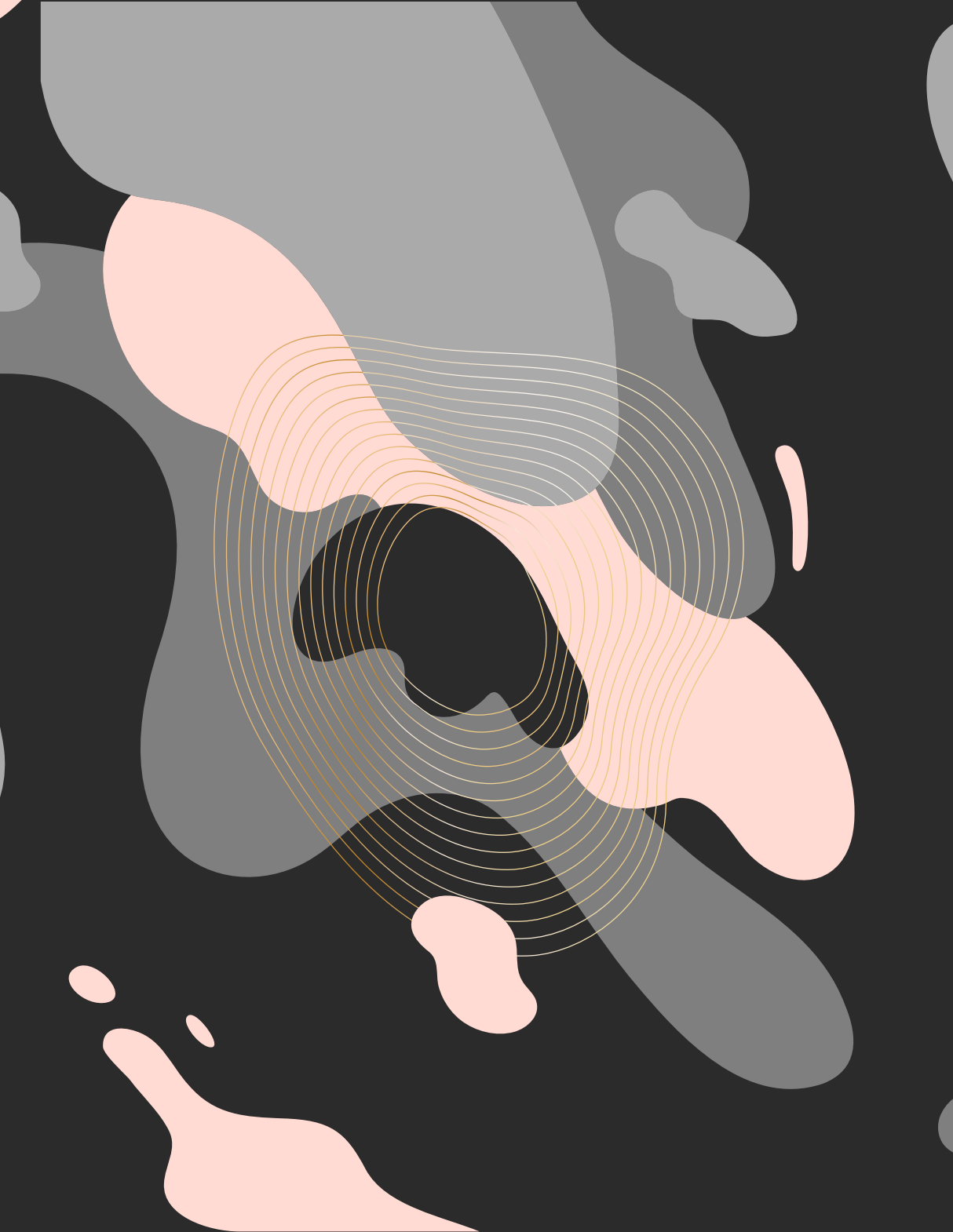


Cell Motility & Molecular Motors

motor proteins + cytoskeleton $\xrightarrow[\text{hydrolysis}]{\text{ATP}}$ cellular movements

microtubules

* **Kinesins**:
  - 2 globular heads binding ATP, utilized in the movement, stalk & tail (bind cargo) → light chain
  - transporting from centre to periphery (+)
  - mitotic spindle (chromosome separation)
  - human walking

* **dyneins**: (Kartagener Syndrome)
  - 2 globular heads binding ATP, utilized in the movement, stalk (bind cargo) ← Dynactin complex binds cargo to dynein → 7 domains
  - transporting from periphery to centre (−)
  - mitotic spindle, flagella & cilia
  - drunken sailor

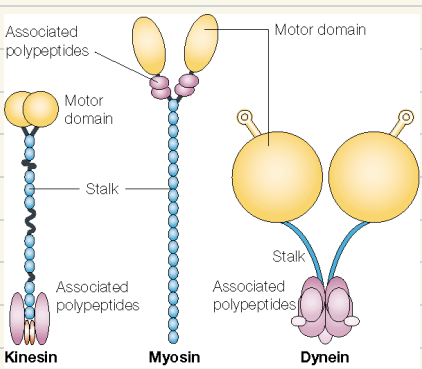
Primary Cilia Dyskinesia
- 50% of affected have ♥ on the right

actin filaments

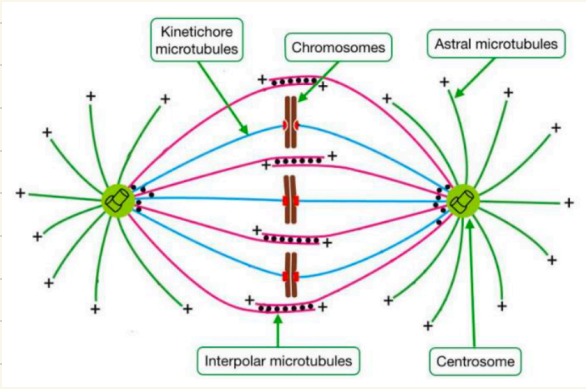
* **myosin**:
  - globular heads binding ATP, utilized in the movement, ~~stalk~~ & tail (binds cargo/other myosins)
  - transporting of vesicles to (+) of microfilaments

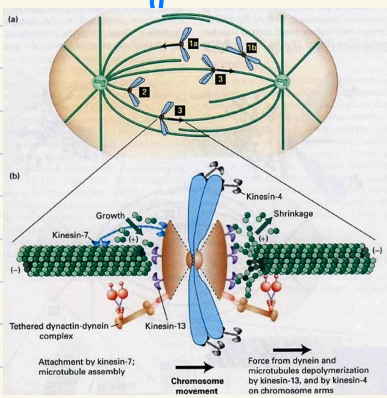
- Myosin I: in nearly all type cells
  - monomer (1 head + 1 tail)
  - vesicle transport within the cell

- Myosin II: in muscles
  - dimer (2 heads + 1 tail)
  - movement of entire cells i.e.
    - muscle contraction
    - contractile ring during cytokinesis
    - contractile bundles changing cell's shape



* **mitotic spindle**
  - Kinetochore - attachment sites on chromosomes
  - Polar - bind with polar microtubules of opposing centrosome & push them apart
  - astral - reach out into all sides from centrosome, anchoring them to surrounding structures

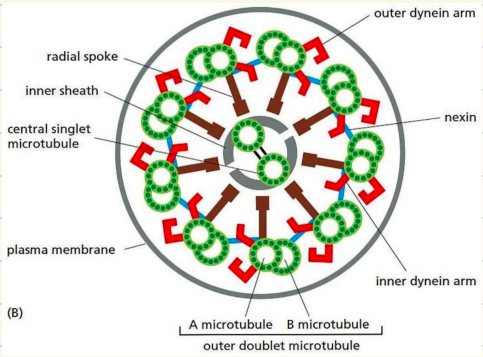


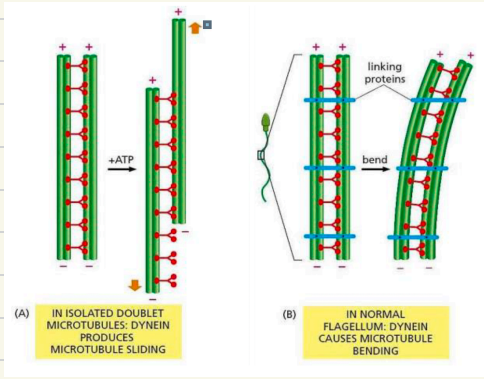


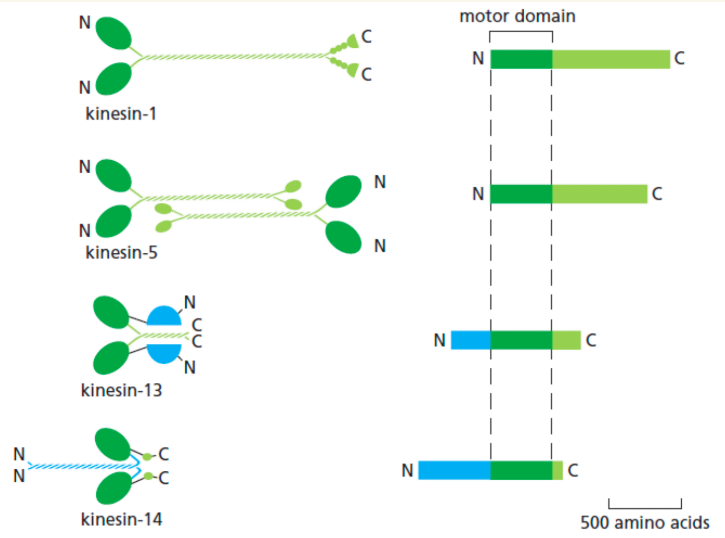
* **flagella & cilia**
  - Flagella - cellular movement
  - Cilia - manipulate/move cell's surroundings

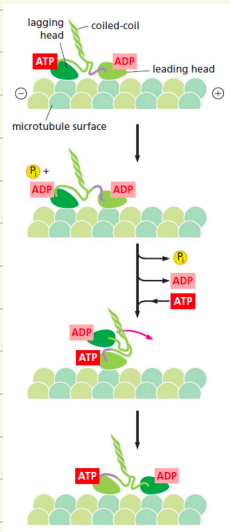
9 + 2 (axoneme):
↳ 9 peripheral doublets & 2 central singlets
- Pairs are connected by dynein
  1) Loosely connected : 1 microtubule moves relative to the other
  2) Tightly connected : both bend towards the same direction

→ (-) end of microtubules anchored in a basal body


outer dynein arm
radial spoke
inner sheath
central singlet microtubule
nexin
plasma membrane
inner dynein arm
(B)
A microtubule
B microtubule
outer doublet microtubule


+ATP
(A)
IN ISOLATED DOUBLET MICROTUBULES: DYNEIN PRODUCES MICROTUBULE SLIDING
linking proteins
bend
(B)
IN NORMAL FLAGELLUM: DYNEIN CAUSES MICROTUBULE BENDING





Cilia & flagella $(9+2)$ (d, s)

↳ attaches to -ve end of basal bodies

$(9+0)$

triplets

same as centrioles

move towards +ve end of cytoskeleton

Amoeboid movement

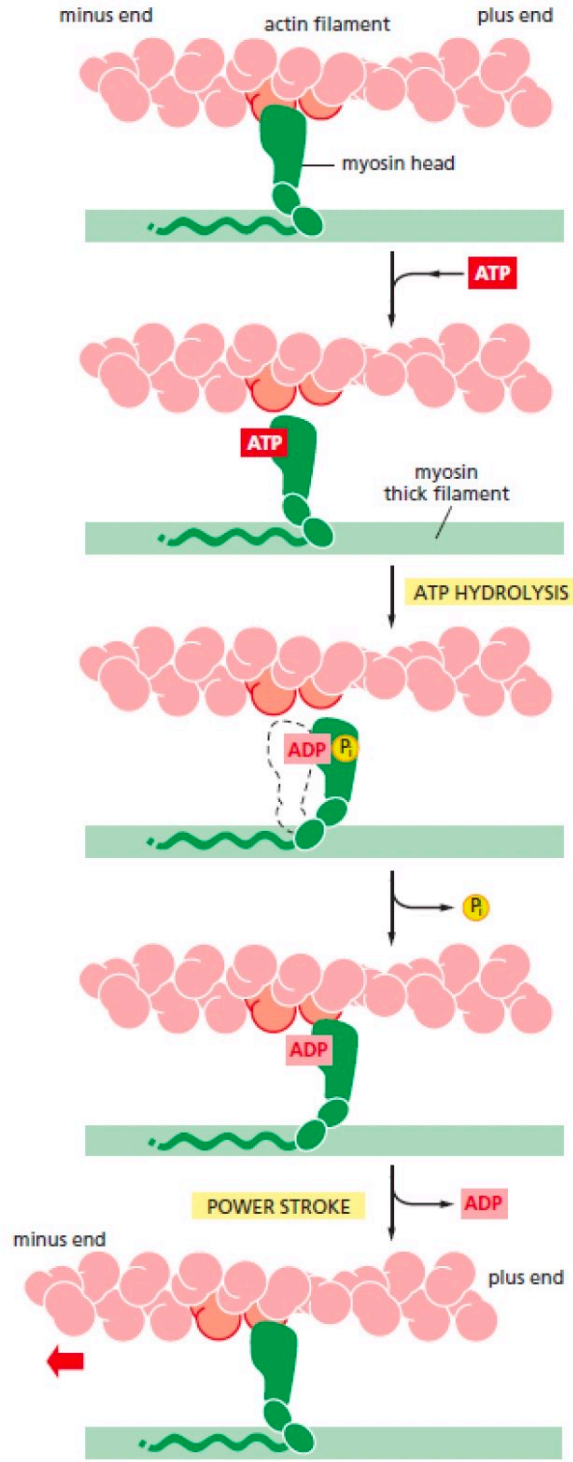
Actin, cell-ECM → focal adhesions, myosin II

(stable surface needed)

- Lamellipodia
- Filopodia → elongates (actin filaments) → attaches (focal adhesions) → contracts (myosin)
- Pseudopodia

Muscle Contraction

- Resting State: Myson-Actin weakly bound
- ATP binds to myosin head & hydrolyzes to ADP & P_i
- Myosin moves back gently & binds to different actin monomer weakly
- P_i is released & bond becomes stronger
- ADP is released, myosin moves forward, banging actin with it ∴ contraction



ATTACHED At the start of the cycle shown in this figure, a myosin head lacking a bound ATP or ADP is attached tightly to 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 to the myosin head.

RELEASED A molecule of ATP binds to the large cleft on the "back" of the myosin 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 actin 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 myosin head.

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 bound tightly to the actin filament in a rigor configuration. Note that the head has moved to a new position on the actin filament, which has slid to the left along the myosin filament.


myosin II
2 light chains
heavy chain