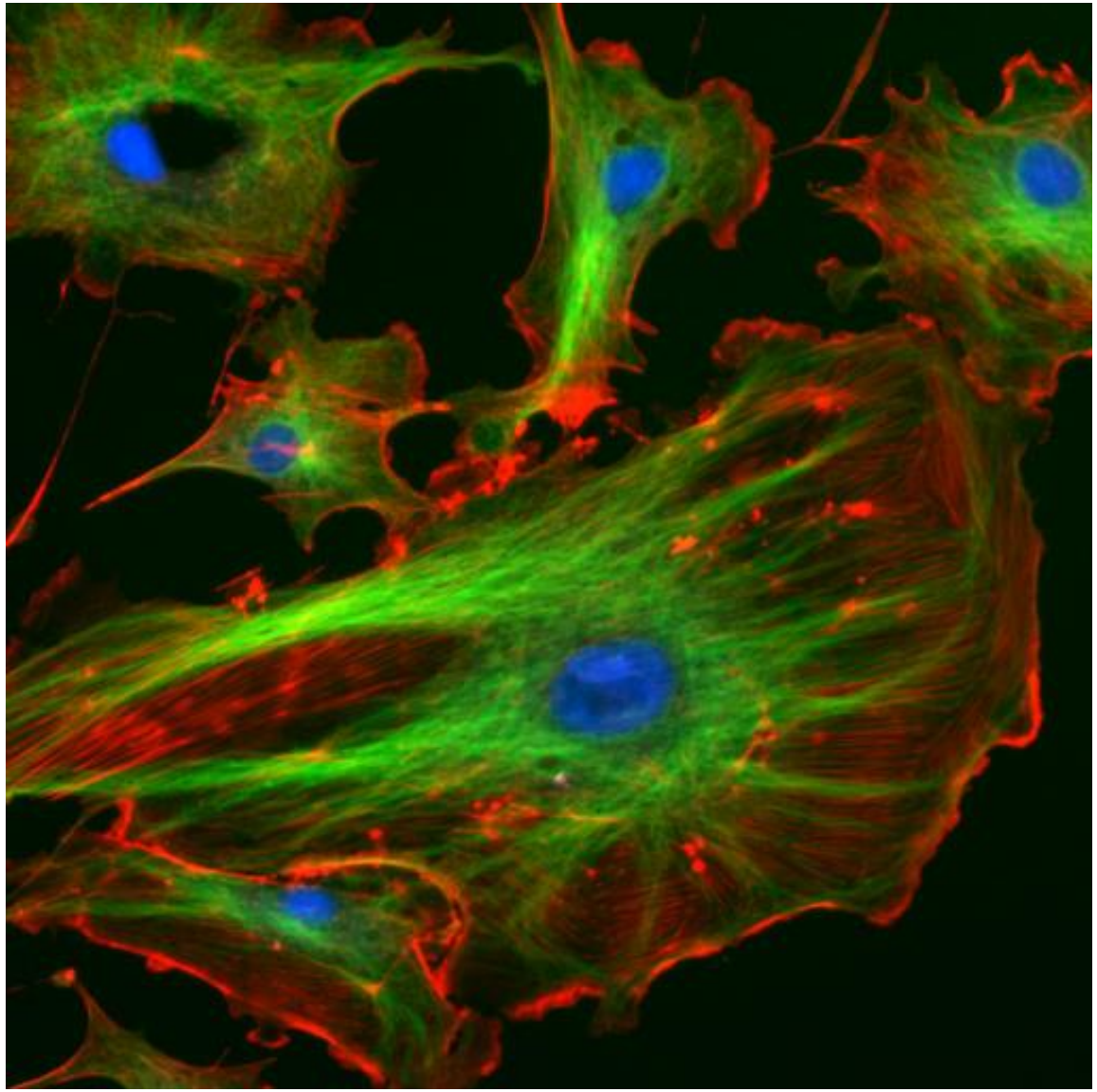

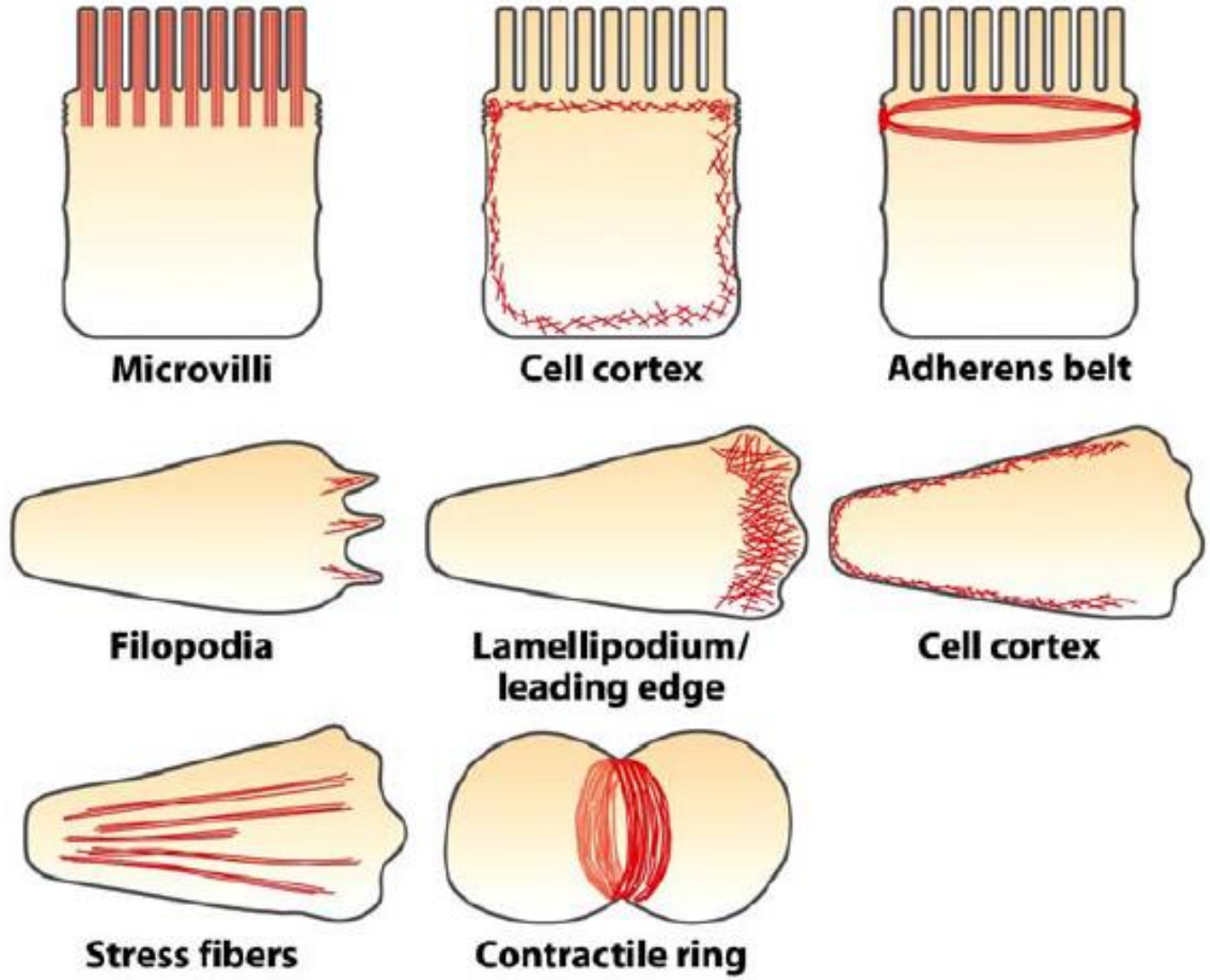

Figure 17-4a
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The in vitro polymerization of G-actin proceeds in three sequential phases

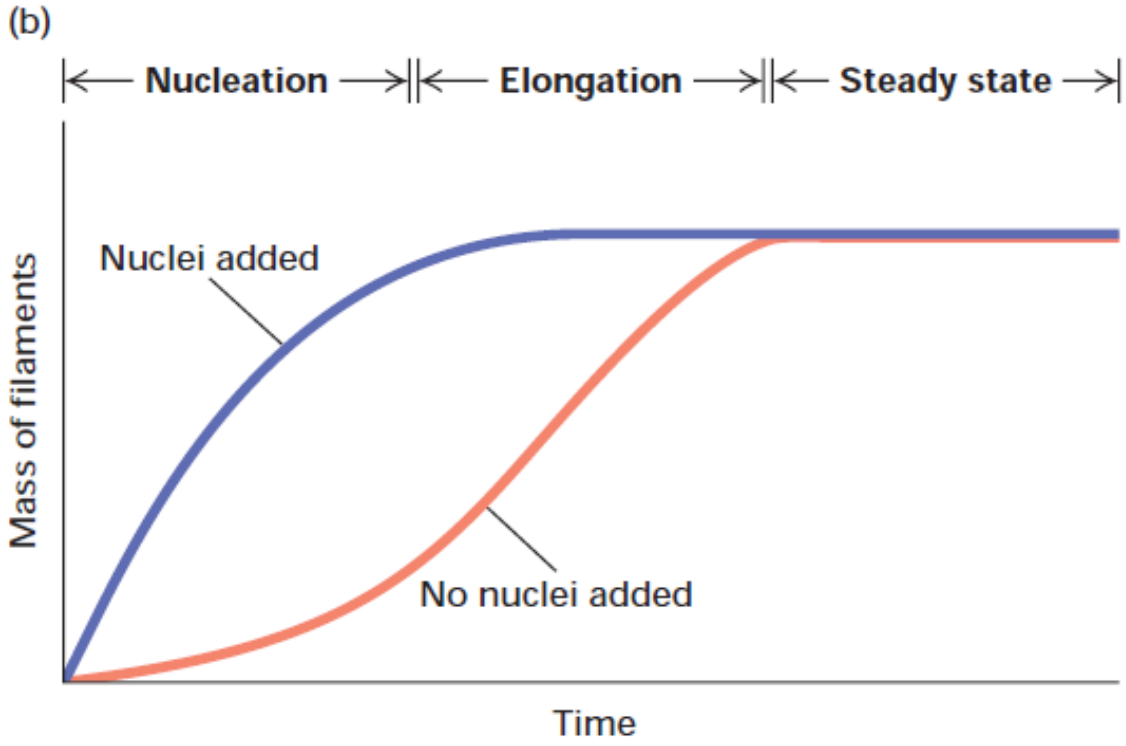
1. Nucleation phase –oligomer formation
2. Elongation phase –elongation of the fibril
3. Steady state phase – No net change in the mass of filament

After ATP–G-actin monomers are incorporated into a filament, the bound ATP is slowly hydrolyzed to ADP.

As a result of this hydrolysis, most of the filament consists of ADP–F-actin.

However, ATP hydrolysis is not essential for polymerization to take place, as evidenced by the ability of G-actin containing ADP or a nonhydrolyzable ATP analog to polymerize into filaments.

Barbed end or Plus end (Additions of ATP bound G actin)
Pointed end or Minus end (Removal of ADP bound G actin)



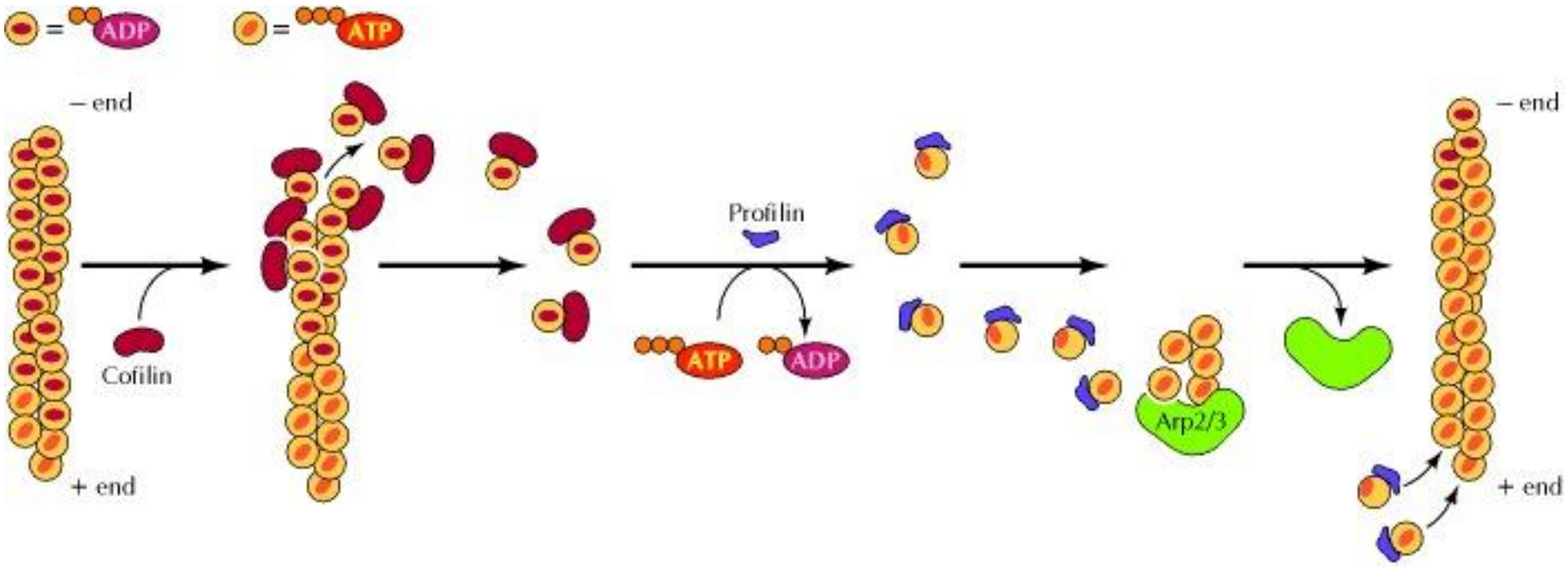
Time course of the in vitro polymerization reaction (pink curve) reveals the initial lag period.
If some actin filament fragments are added at the start of the reaction to act as nuclei, elongation proceeds immediately without any lag period (purple curve).

Treadmilling –rate of addition of G actin monomers at +end is similar to dissociation of G-actin at – end

4 ways how a cell controls actin polymer length

1. Altering rate of nucleation
2. Altering rate of + end assembly
3. Altering rate of – end dissociation
4. Overall filament stability

- Arp2/3 –Branching of filaments
- Profilin –helps in better binding of G-actin at + end (rate of addition increases with dissociation at – end remaining the same, and hence length increases)
- Capz- Blocks incoming G-actin at the + end
- Tropomodulin – binds at the – end and alters the dissociation at the – end
- Tropomyosin – binds to the sides of the actin filament and stabilizes it



So far we've talked about the structural role of the microfilaments.

They also have a transport role, serving as sort of a set of train tracks for ATP-powered motor proteins to move along.

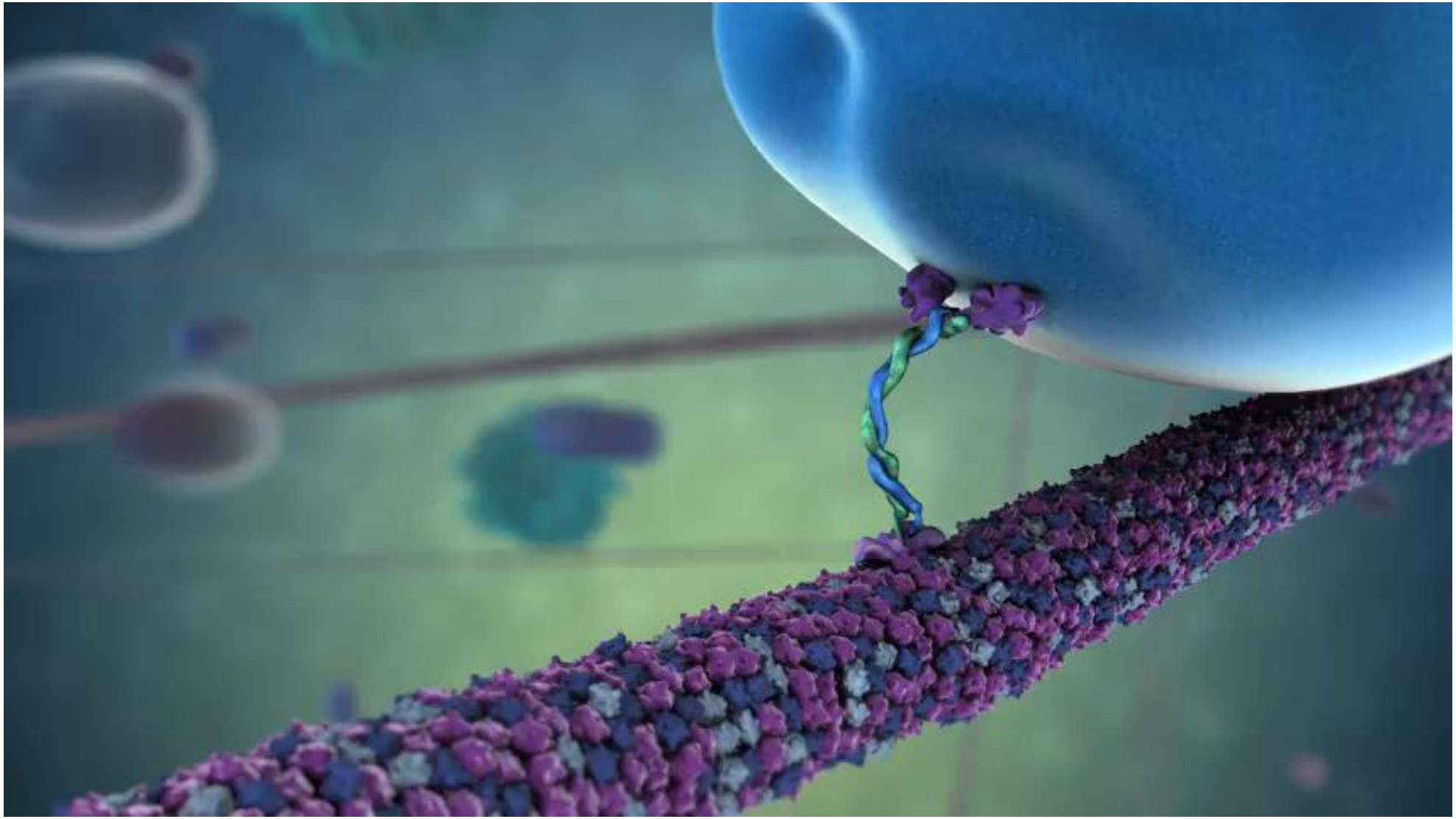
Myosin is the main motor protein that operates on microfilaments.

It has a 'head' which both binds actin and binds ATP, a 'neck' which acts as a lever – its length determines the stride at which myosin walks – and a 'tail' which binds cargo to be transported.

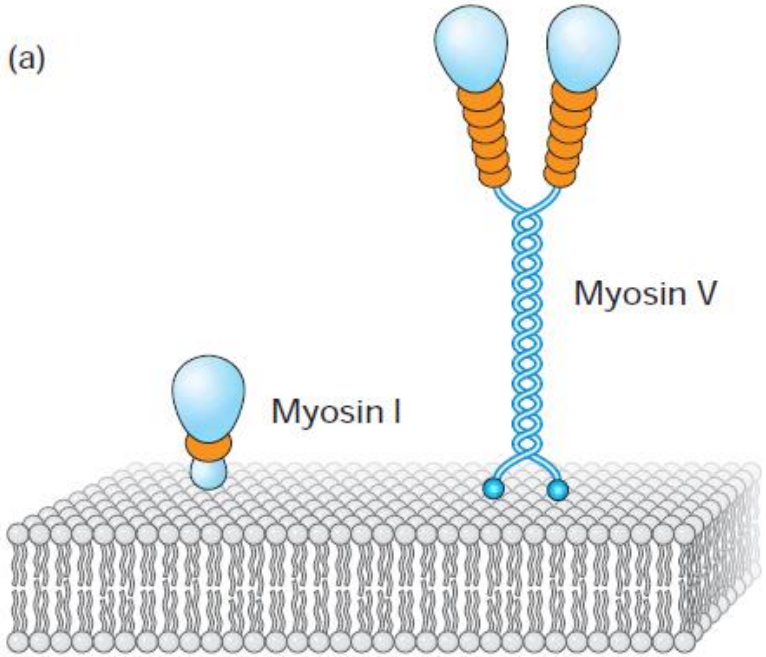
The tail is highly variable, as its sequence determines what cargo will be bound.

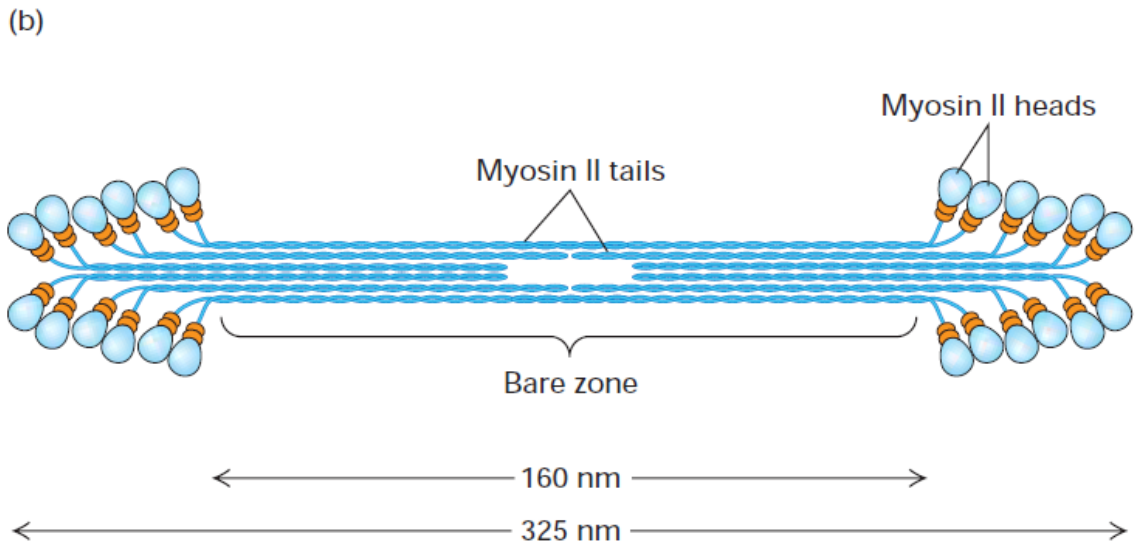
The head must burn one ATP molecule for every 'step' it takes.

Myosins are a huge family of proteins that come in 13 different classes.



A characteristic head, neck, and tail domain organization is found in all myosin heavy chains





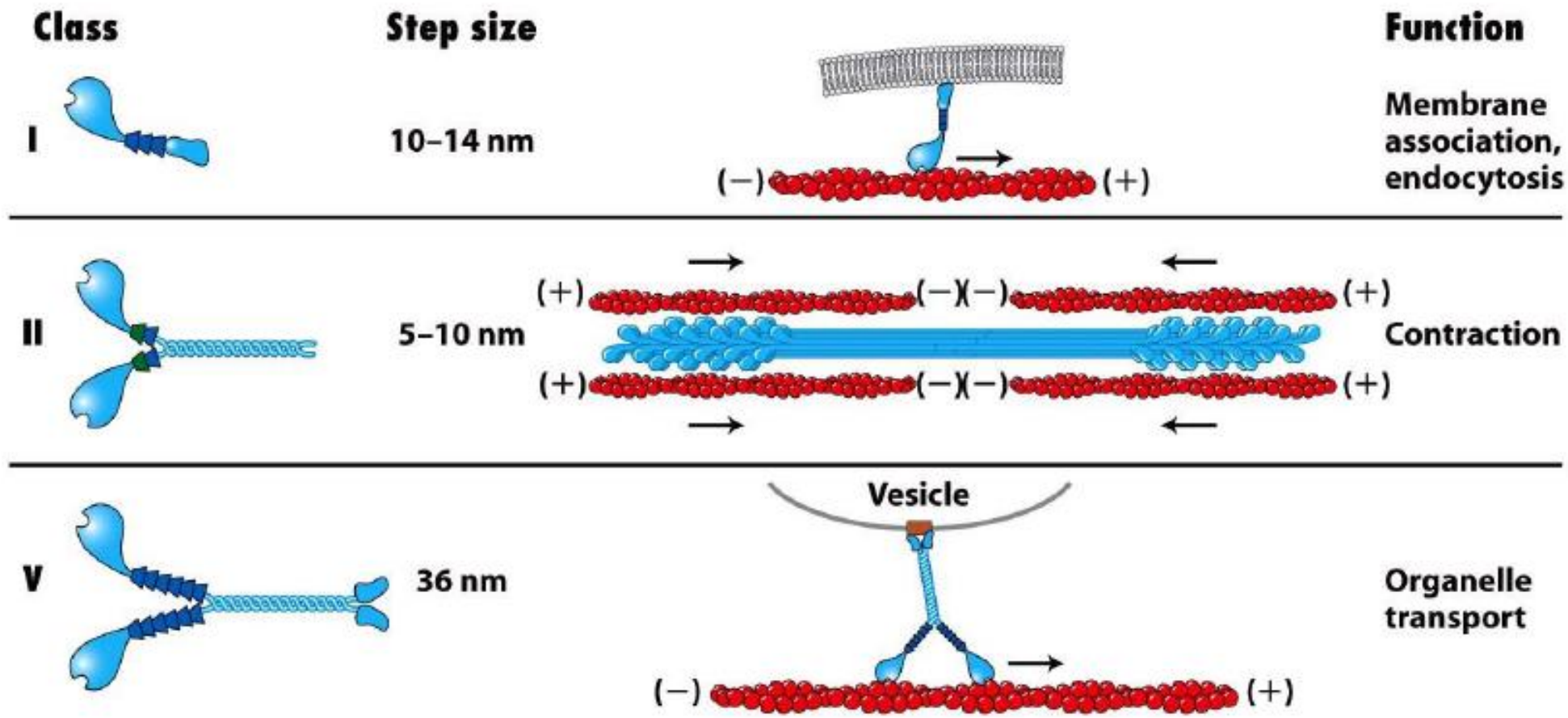


Figure 17-23
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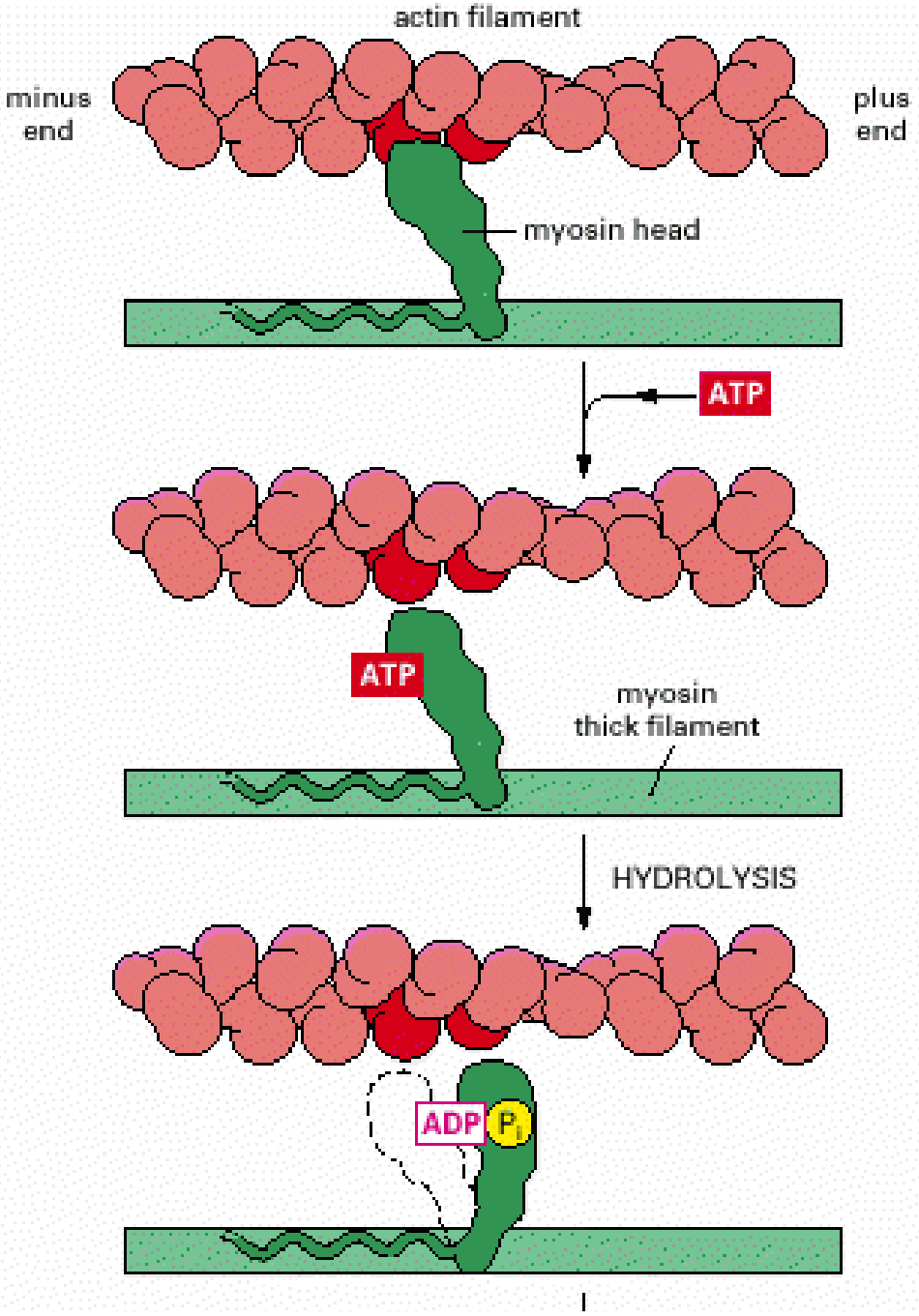
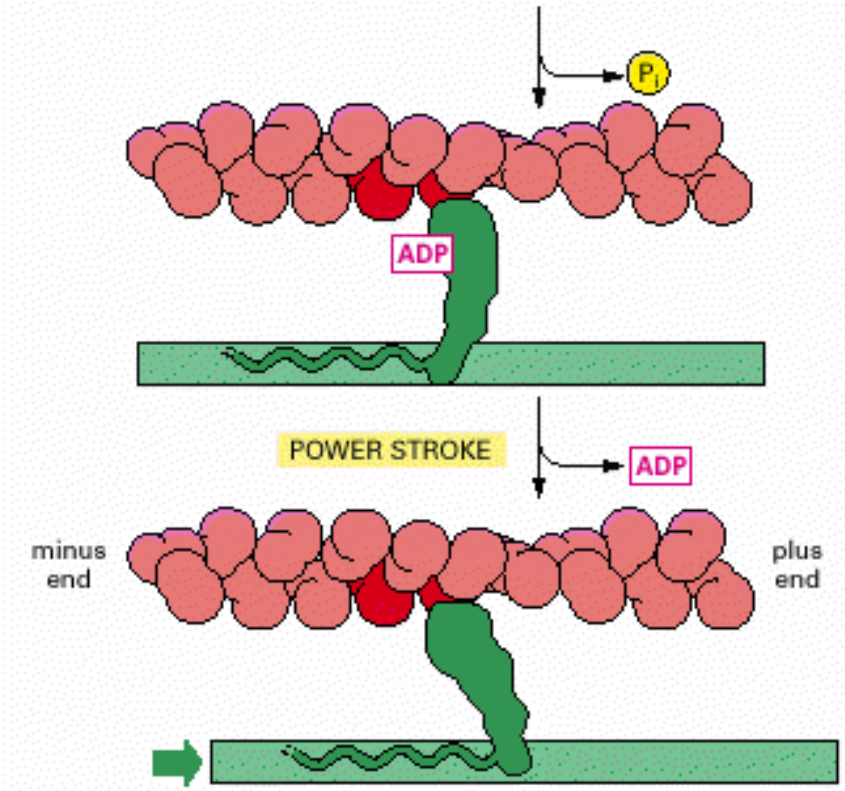


ATTACHED At the start of the cycle shown in this figure, a myosin head lacking a bound nucleotide is locked tightly onto an actin filament in a *rigor* configuration (so named because it is responsible for *rigor mortis*, the rigidity of death). In an actively contracting muscle, this state is very short-lived,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