Chapter 16
Cellular Movement: Motility and Contractility

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Two eukaryotic motility systems

1. Interactions between motor proteins and microtubules
   - E.g., *fast axonal transport* in neurons, or the sliding of MTs in *cilia* and *flagella*

2. Interactions between actin and members of the *myosin* motor proteins
   - E.g., muscle contraction
Intracellular Microtubule-Based Movement: Kinesin and Dynein

- MTs provide a rigid set of tracks for transport of a variety of organelles and vesicles

- Traffic toward the minus ends of MTs is considered “inbound”; toward the plus end is “outbound”

- *Microtubule-associated motor proteins* walk along the MTs and provide the force needed for movement
MT Motor Proteins Move Organelles Along Microtubules During Axonal Transport

• Proteins and neurotransmitters produced in the cell body must be transported to the nerve ending.

• This process, **fast axonal transport**, involves movement of vesicles and organelles along MTs.

• Organelles can be observed moving along filaments through axoplasm (cytoplasm of axons) at rates of about 2 μm/sec.
Two proteins responsible for fast axonal transport

- Kinesin I is involved in ATP-dependent transport toward the plus ends (away from the centrosome), called *anterograde axonal transport*

- Cytoplasmic dynein moves particles (*cargo*) in the opposite direction, called *retrograde axonal transport*
Figure 16-2

Vesicle

Kinesin

Microtubule

Direction of movement

ATP → ADP + P

Dynein

ADP + P → ATP

Vesicle
Video: Movement of Organelles in Vivo
Kinesin movement along MTs

• Kinesin movement looks like “walking” with the two globular head domains taking turns as the front foot

• Each kinesin molecule exhibits processivity

• It can move long distances along an MT before detaching from it by releasing bound ADP and acquiring a new ATP, so that the cycle repeats
Figure 16-3B

Stalk
Springlike linker region
Back “foot”

ATP
ADP + P_i

Front “foot” binds a new \( \beta \)-tubulin subunit

Front “foot”
Back “foot” will move to front

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Microtubule Motors Are Involved in Shaping the Endomembrane System and Vesicle Transport

• MT motors are important for dynamically shaping the complicated endomembrane system

• E.g., ER membrane extensions can be moved along MTs

• The vesicles to and from the Golgi complex are carried by MT motors on microtubule tracks
Microtubule-Based Motility: Cilia and Flagella

- Microtubules are required for movements of cilia and flagella, the motile appendages of eukaryotic cells

- The two appendages share a common structural basis
Figure 16-6A, B

(a) Cilia on a mammalian tracheal cell

(b) Beating of a cillum
Video: Flagellum Movement in Swimming Sperm
Cilia and Flagella Consist of an Axoneme Connected to a Basal Body

- Cilia and flagella share a common structure, the **axoneme**

- It is connected to a **basal body** and surrounded by an extension of the cell membrane

- Between the axoneme and basal body is a **transition zone** in which the MTs take on the pattern characteristic of the axoneme
Structure of cilia and flagella

• The basal body looks like a centriole, with 9 sets of tubular structures around the circumference

• Each set is a *triplet* with three MTs that share common walls

• Axonemes have a characteristic “9+2” pattern, with 9 *outer doublets* and 2 MTs in the center, the central pair
Figure 16-7

(a) Cilia

Central pair
Plasma membrane
Outer doublet
9+2 arrangement
Outer doublets
Central pair
Radial spoke

(b) Cross section through axoneme

(c) Cross section through transition zone Triplets

(d) Cross section through basal body

Basal plate

0.1 μm
Activity: Cilia and Flagella
Microtubule Sliding Within the Axoneme Causes Cilia and Flagella to Bend

- The **sliding-microtubule model** suggests that sliding of MTs relative to each other is converted into localized bending because the doublets are connected to the central pair and to each other.

- Therefore, they cannot easily slide past each other.

- The resulting bending takes the form of a wave.
Actin-Based Cell Movement: The Myosins

- Movements of molecules and other cellular components also occur along another system in the cell—the actin cytoskeleton
Myosins Are a Large Family of Actin-Based Motors with Diverse Roles in Cell Motility

- **Myosins** are ATP-dependent motors that exert force on actin filaments

- Currently there are 24 known classes of myosins

- All have at least one polypeptide chain called the *heavy chain*, with a globular head group attached to a tail of varying length
Figure 16-9

Myosin II

- Head
- Neck
- Tail
- Light chains
- Two heavy-chain tails coiled around each other
- Actin binding domain

Myosin I

Myosin V

Myosin VI
Myosin functions

- Myosins function in a wide range of cellular events, including
  - Muscle contraction
  - Cell movement
  - Phagocytosis
  - Vesicle transport
Many Myosins Move Along Actin Filaments in Short Steps

- Myosin II is an efficient motor that “walks” along actin like kinesin walks along microtubules.

- Both have two heads that walk along a protein filament, and both use ATP hydrolysis to change their shape.

- However, there are important differences.
Kinesins vs. myosin

• Kinesins operate alone or in small numbers to transport vesicles over large differences

• A single myosin II molecule slides an actin filament about 12–15 nm per power stroke

• Myosin II molecules move short distances but operate in large arrays, in some cases billions of motors working together to mediate muscle contraction
Filament-Based Movement in Muscle

• Muscle contraction is the most familiar example of mechanical work mediated by intracellular filaments

• Much of what is known about contractile processes is based on studies involving skeletal muscle
Figure 16-13

(a) Organization of myosin molecules into a thick filament

(b) Portion of a thick filament
Troponin and tropomyosin

• Troponin is composed of three polypeptides: $TnT$, $TnC$, and $TnI$

• One troponin complex associates with each tropomyosin

• Together they constitute a calcium-sensitive switch that activates contraction in striated muscle
Figure 16-14

- Tropomyosin
  - 38.5 nm
  - Troponin complex
    - TnI
    - TnC
    - TnT
  - Monomers of G-actin
- Helical strand of F-actin

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Organization of Muscle Filament Proteins

- The actin in thin filaments is oriented so that all the plus ends are anchored at Z lines
- Myosin II moves toward the plus ends, so the thick filaments move toward the Z lines during contraction
- Structural proteins contribute to the architecture of muscle cells
Structural proteins associated with thin filaments

- $\alpha$-actinin keeps actin filaments bundled into parallel arrays
- \textit{CapZ} maintains the attachment of the plus ends to the Z line and caps the actin in the filaments
- \textit{Tropomodulin} binds the minus ends of the filaments to maintain stability and \textit{nebulin} stabilizes the thin filament organization
Structural proteins associated with thick filaments

- *Myomesin* is present at the H zone and bundles the myosin molecules

- *Titin* attaches the thick filaments to the Z lines and keeps thick filaments in correct position relative to thin filaments during contraction
Figure 16-16A

(a) Sliding filament model
(b) Length-tension diagram
Figure 16-17
Figure 16-19

(a) Low calcium concentration
(b) High calcium concentration

Thin filament
- TnI
- TnC
- Myosin-binding site
- Tropomyosin
- Myosin head

Thick filament

Ca^{2+}

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SR Function in Calcium Release and Uptake

- The SR has two functional components
  - The *medial element* that contains calcium ATPase pumps
  - The *terminal cisternae* contain a high concentration of ATP-dependent Ca\(^{2+}\) pumps that can produce very high calcium concentrations in the lumen of the SR
Figure 16-21

1. An action potential moves down the axon of the neuron until it reaches the neuromuscular junction, where synapses exist between the neuron and the muscle cell.

2. Depolarization of the terminals of the axon causes the release of neurotransmitters, which bind acetylcholine receptors on the surface of the muscle cell, initiating depolarization of the muscle cell.

3. The depolarization spreads into the interior via the T tubules, stimulating calcium release via ryanodine receptors in the terminal cisternae of the SR.
Smooth Muscle Is More Similar to Nonmuscle Cells than to Skeletal Muscle

• **Smooth muscle** is responsible for involuntary contractions in various tissues

• These contractions are relatively slow and of greater duration than in skeletal or cardiac muscle
The Structure of Smooth Muscle

- Smooth muscle cells are long and thin with pointed ends; there are no striations

- Instead of Z lines, smooth muscles have dense bodies, plaque-like structures

- Bundles of actin filaments are anchored to the dense bodies in a crisscross pattern; cross-bridges form in an irregular pattern
Figure 16-23

(a) Smooth muscle cells

(b) Contraction of smooth muscle cell
Regulation of Contraction in Smooth Muscle Cells

- When sarcoplasmic calcium concentration increases in smooth muscle (and nonmuscle) cells a set of events takes place

- This includes activation of **myosin light-chain kinase (MLCK)**, which then phosphorylates a regulatory light chain of myosin
Myosin light-chain phosphorylation

- Myosin light-chain phosphorylation leads to a conformational change in myosin, promoting its assembly into filaments

- It also activates the myosin so that it can interact with actin filaments to undergo the cross-bridge cycle
Actin-Based Motility in Nonmuscle Cells

- Actin and myosin have been discovered in nearly all eukaryotic cells
- They are known to play important roles in nonmuscle motility
Cell Migration via Lamellipodia Involves Cycles of Protrusion, Attachment, Translocation, and Detachment

- MFs are required for the movement of most cells in animals

- Cell crawling involves distinct events: extension of a protrusion, attachment to substrate, and generation of tension, which pulls the cell forward
Video: Lamellipodia in Cell Migration
Extending Protrusions

- To crawl, cells extend *protrusions* at their front, or *leading edge*

- A thin sheet of cytoplasm is a *lamellipodium* and a thin-pointed protrusion is a *filopodium*

- During normal *retrograde flow*, microfilaments move toward the rear of the protrusion as it extends
Retrograde flow

• Retrograde flow results from *actin assembly* at the growing tip of the protrusion and *rearward translocation* of filaments toward the base

• Arp2/3-dependent branching drives actin polymerization, particularly in lamellipodia

• Microtubules are also involved in the process
Figure 16-26

1. The leading edge extends via polymerization of actin at its tip.

2. New adhesions, anchored by actin, form on the undersurface of the lamellipodium.

3. The trailing edge (tail) of the cell detaches, and is drawn forward by contraction of the cell body.

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Integrins – transmembrane proteins needed for attachment

- Integrins on the outside of cells attach to extracellular matrix proteins

- Inside the cell integrins are connected to actin filaments via linker proteins

- The integrin-dependent attachments are called focal contacts
Translocation and Detachment

- Contraction at the rear of the cell squeezes the cell body forward and releases the attachments at the rear.

- Contraction, due to actin-myosin interactions, is under control of Rho, which activates nonmuscle myosin II at the rear of the cell.

- For movement to occur, new attachments must be balanced by loss of old ones.
Chemotaxis

- *Chemoattractants*: cells move toward a higher concentration of the diffusible molecules

- *Chemorepellants*: cells move toward a lower concentration of the diffusible molecules

- Binding of the molecules to cell surface receptors (G protein-linked receptors) leads to corresponding cytoskeletal changes
Amoeboid Movement Involves Cycles of Gelation and Solation of the Actin Cytoskeleton

• Amoebas and white blood cells exhibit a type of crawling called **amoeboid movement**, which is accompanied by protrusions of **pseudopodia**

• Gelation: as a pseudopod is extended, more material streams forward and congeals at the tip

• Solation: at the rear of the cell, cytosol changes to a more fluid state and streams forward
Amoeboid movement

- Gelsolin may be activated by calcium to convert the gel to a more fluid state

- Forward movement does not require squeezing from the rear; streaming can occur as long as the appropriate ions and other factors are present
Video: A Crawling Amoeba
Actin-Based Motors Move Components Within the Cytoplasm of Some Cells

- **Cytoplasmic streaming**: an actomyosin-dependent movement of cytoplasm in the cell

- Cytoplasmic streaming requires actin filaments

- In plants the process is called *cyclosis*; a dense set of aligned microfilaments is found near sites where cyclosis occurs