The 'molecular motors' are **kinesin** and **dynein.**	The 'molecular motor' is myosin.
Form the spindle, which moves the chromosomes in mitosis.	When a cell divides, it is pinched into two by a constricting band of microfilaments.
Transport secretory granules, vesicles, and mitochondria from one part of the cell to another.	Abundant at the *desmosomes* and *zonulae adherentes* (intercellular junctions).
	Abundant in *lamellipodia,* and in the core of intestinal microvilli.
	Microfilaments (actin) in skeletal muscle bring about contraction.

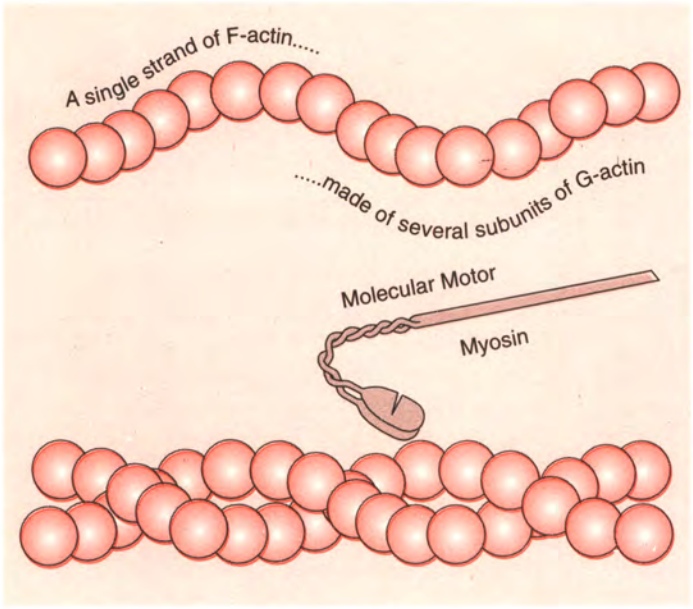

Fig. 2.2

What are the other types of filaments found in the cell?

Intermediate filaments have a diameter (8 – 10 nm) that is between (i.e., intermediate to) that of microtubule and microfilament. They are more abundant than either microtubule or microfilament. They are made of **cytokeratin**. Unlike microtubule or microfilaments, these proteins are very stable and remain mostly polymerized. They serve as the 'bones' of the cell, giving structural strength to the cell. For example, the nucleus sits in a cage made of intermediate filaments. In axons, the intermediate filaments are called **neurofilaments**. They maintain the axonal diameter.

What are the filamentous structures in the cell?

The filamentous structures include the centrioles, cilia and flagella. All are hollow cylindrical structures with microtubules running in their wall longitudinally.

Name the different types of intercellular junction.

The different types of intercellular junctions (Fig. 2.3) are: (i) zona occludens (or tight junction), (ii) zona adherens, (iii) desmosome (or macula adherens) and (iv) gap junctions.

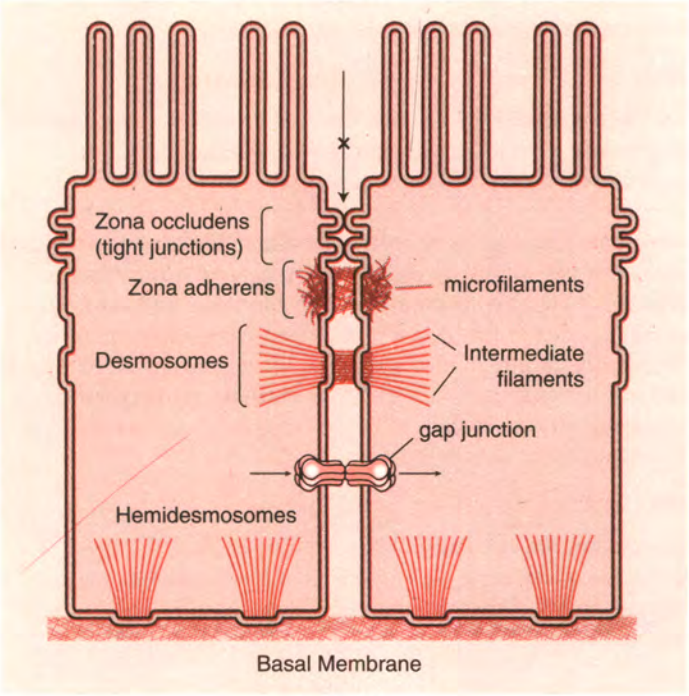

Fig. 2.3

8

Degeneration & Regeneration of Nerve & Muscle

What are the salient changes associated with nerve degeneration?

When an axon is crushed or severed, it results in degeneration of the neuron both distal (anterograde) and proximal (retrograde) to the site of injury.

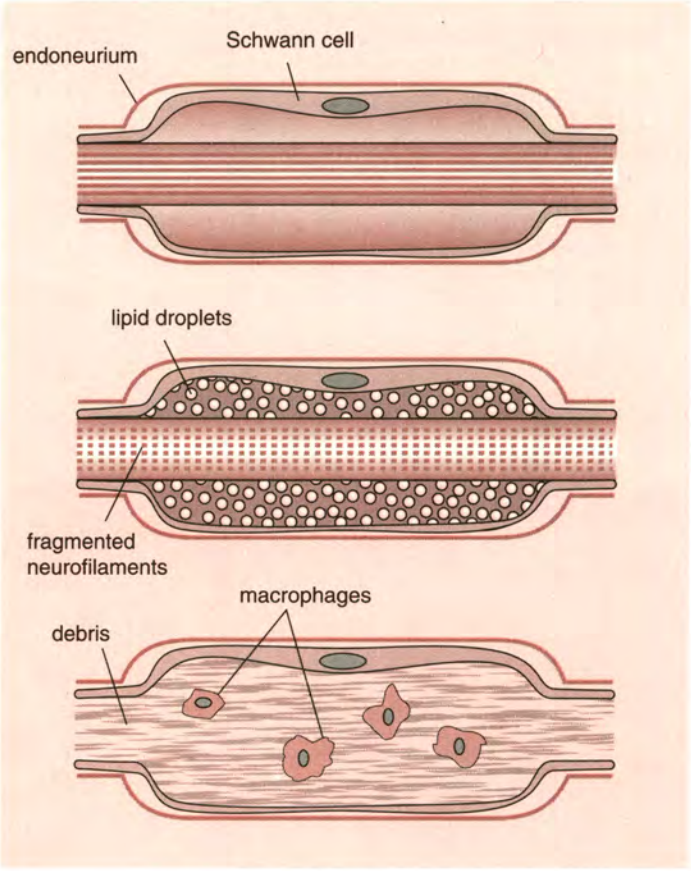

Fig. 8.1

Anterograde degenerative changes starts within 24 hours and is called **Wallerian degeneration**. The neurofilaments break up, and the axon breaks up into short lengths. *Within 10 days*, the myelin sheath breaks down into lipid droplets around the axon. *Within 30 days*, the myelin gets denatured chemically. *Within 3 months*, macrophages from the endoneurium invade the degenerating myelin sheath and axis cylinder and phagocytose the debris, leaving behind only the endoneurial tube (Fig. 8.1).

Retrograde degenerative changes affect the dendritic tree, the parent cell body and the part of the axon proximal to the lesion. Acute retrograde (**chromatolytic**) changes start after 24 hours

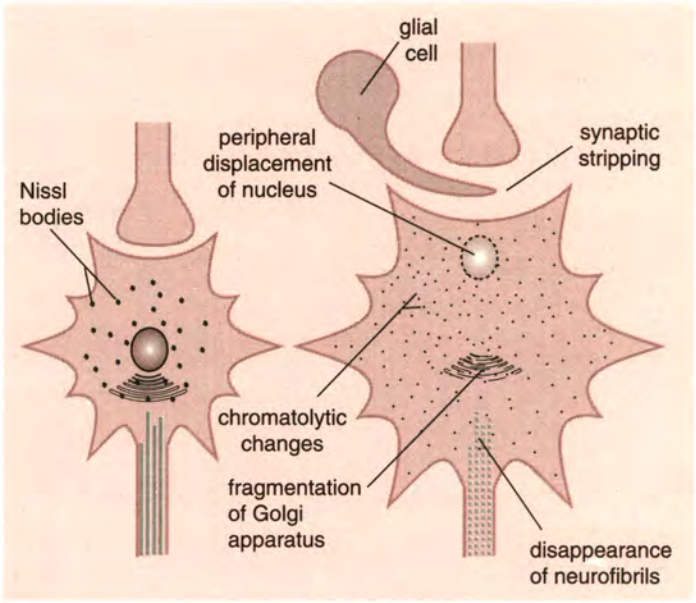

Fig. 8.2

and are characterized by the break up of the Nissl substance in the cell body (Fig. 8.2). Chronic retrograde atrophic response involves the atrophy of the nerve cell body with all its processes.

What are the salient changes associated with nerve regeneration?

Nerve regeneration begins about 20 days after nerve section and is complete in 3 months. The Schwann cells at the site of injury multiply and grow at the rate of up to 1 mm per day, forming a solid cord of elongated cells (**band of Bungner**) within the endoneurial tube (Fig. 8.3). The plasmalemma of the Schwann cells and adjacent basal lamina separate creating an annular compartment between the Schwann cells and the endoneurium. Up to 100 axonal sprouts, each containing a neurofibril in it, grow out in all directions from the proximal axon. Some of them grow into the distal annular compartment. The daily rate of growth is up to 3—4 mm in the peripheral stump. Eventually all but one axonal sprout degenerate. The surviving fibril enlarges to fill the distal tube. The Schwann cells in the Band of Bungner form myelin sheath around the reinnervating axonal sprout. The sheath begins to develop in about 15 days and is completed in one year. The Nissl substance and Golgi apparatus gradually reappear. The cell regains its normal size and the nucleus returns to its central position.

According to Seddon's classification, nerve injuries are of three types: (i) **neuropraxia**, which occurs due to minor nerve stretch

11

Ion Channels & their Role in Action Potential

What is sodium channel inactivation?

When the membrane depolarizes, there is an increase in both Na^+ and K^+ permeability due to the opening of Na^+ and K^+ channels respectively. The K^+ channels remain open as long as the membrane remains depolarized. However, the Na^+ channels start closing down spontaneously after a few milliseconds (Fig. 11.1) *even if the membrane remains depolarized.* This process is called **Na^+ channel inactivation**. They recover from inactivation only after the membrane returns to the normal resting potential. Na^+ channel inactivation has two important consequences: the **refractory period** and **membrane accommodation**.

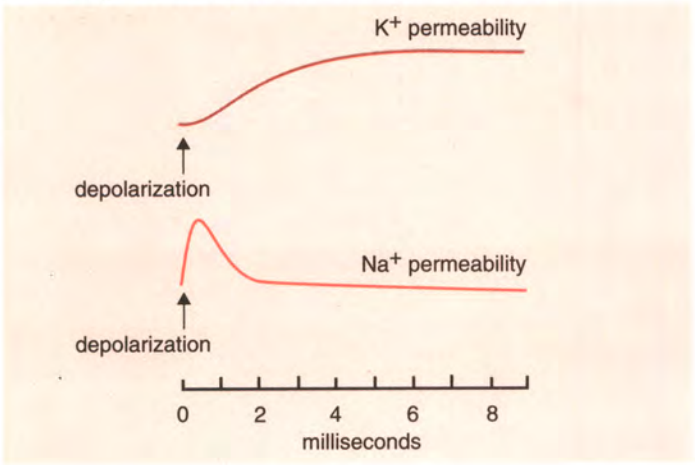

Fig. 11.1

What is the mechanism of Na^+ channel inactivation?

Na^+ channels are guarded by two gates: the **activation (m) gate** and the **inactivation (h) gate**. *During depolarization*, the activation gate opens quickly, followed *slowly* by the closure of inactivation gate. This results in a brief interval during which the channel remains open. *During repolarization*, the activation gate closes first followed by the opening of the inactivation gate, so that the channel remains obliterated (Fig. 11.2).

Why do K^+ channels have a stabilizing effect on membrane potential?

If the membrane potential depolarizes, K^+ channels open up in large numbers. The increase in K^+ permeability hyperpolarizes the membrane. (This can be verified from the Goldman Equation). The membrane potential is thereby restored to its original value. Conversely, if the membrane hyperpolarizes, a large number of K^+ channels closes down. The fall in K^+ permeability depolarizes the membrane and restores the membrane potential to its original value. Thus, *whenever there is a change in membrane potential,*

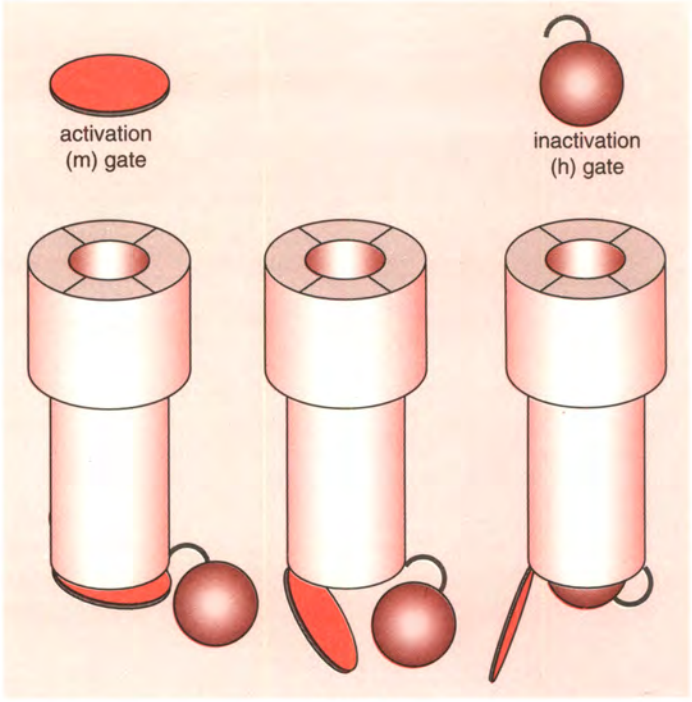

Fig. 11.2

the activated K^+ channels tend to restore the membrane potential to the original level. Hence, K^+ channels are said to have a **stabilizing (negative feedback) effect** on the membrane potential, i.e., they tend to prevent any change in membrane potential (Fig. 11.3).

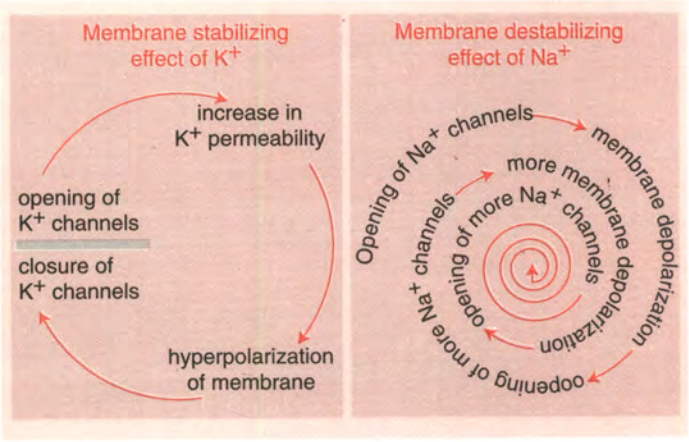

Fig. 11.3

14

Mechanism & Energetics of Muscle Contraction

Describe the steps of cross-bridge cycling.

The shortening of a muscle fiber occurs due to the *sliding of actin filaments on myosin filaments*. The repetitive events that bring about this shortening are called the **cross-bridge cycling** (Fig. 14.1). In brief, (i) ATP binds to myosin ATPase present on the myosin head and splits into ADP and P_i. The energy released activates the myosin head, which is now ready to bind to actin. (ii) The activated myosin head binds with the active sites of actin filaments forming *actomyosin*. Simultaneously, the myosin head flexes at its hinge (the **power stroke**). As a result, the actin filament slides on myosin filament, bringing the Z-disks closer and shortening the sarcomere. (iii) As the myosin head flexes, the ADP and Pi present on it are cast off, making way for a fresh molecule of ATP. When ATP binds to myosin ATPase, the myosin head detaches from actin, and the cross-bridge cycle is repeated all over again.

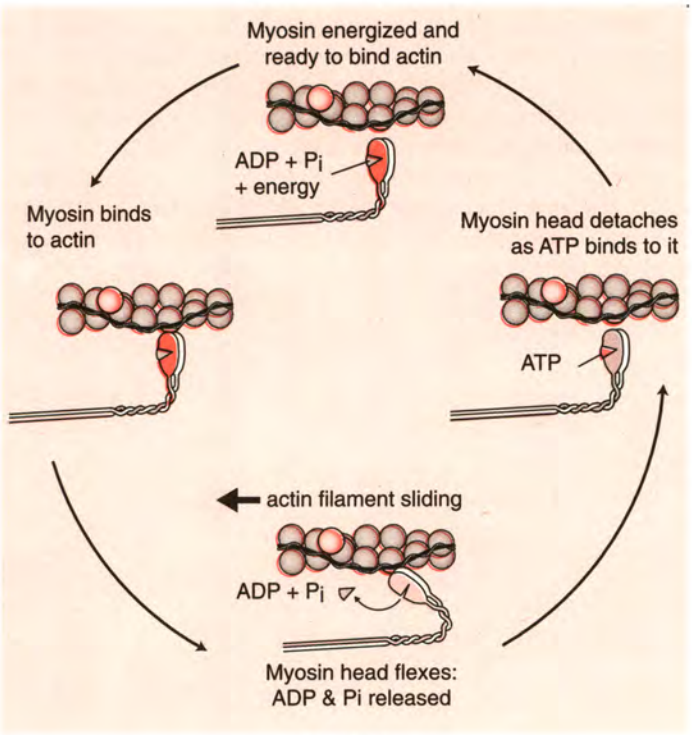

Fig. 14.1

What is the mechanism of excitation-contraction coupling in a skeletal muscle?

The term excitation *contraction coupling* refers to the events between the generation of sarcolemmal action potential and the outpouring of Ca^{2+} from L-tubule cisterns into the sarcoplasm. Although there is no continuity between the T-tubules and the L-tubules, yet, depolarization of the T-tubules results in an outpouring of Ca^{2+} from the L-tubules. The mechanism involves two membrane receptors: *dihydropyridine receptors (DHP)* and *ryanodine receptor (RYR) channels* (Fig. 14.2), that are mechanically interlocked.

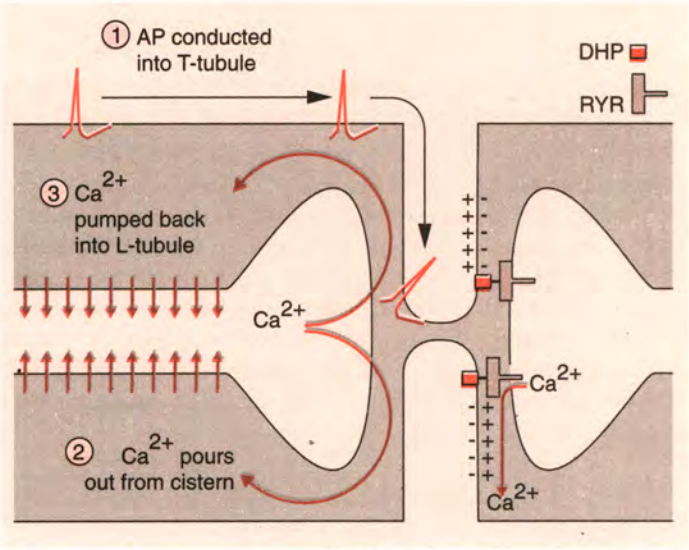

Fig. 14.2

What is the role of ATP in muscle contraction and relaxation?

ATP has three roles in muscle contraction and relaxation: (i) it provides the energy for the power stroke of myosin head; (ii) it brings about a dissociation of myosin head from actin filament; and (iii) it brings about muscle relaxation by pumping out Ca^{2+} from the sarcoplasm into the L-tubules.

Explain the mechanism of contraction remainder and rigor mortis.

When a muscle gets fatigued, its ATP content decreases. As a result, the *sarcoplasmic Ca^{2+} concentration remains elevated* even when the muscle is not depolarized. In the absence of ATP, therefore, the *active sites of actin remain uncovered* (due to high sarcoplasmic Ca^{2+}) and *bound to the myosin heads* (because ATP is also required for the dissociation of myosin heads from actin). The muscle therefore fails to relax completely and remains in a partially contracted state called **contraction remainder** (Fig. 15.5). For identical reasons (i.e. depletion of ATPs), the muscles become contracted and rigid after death, a state known as **rigor mortis**.