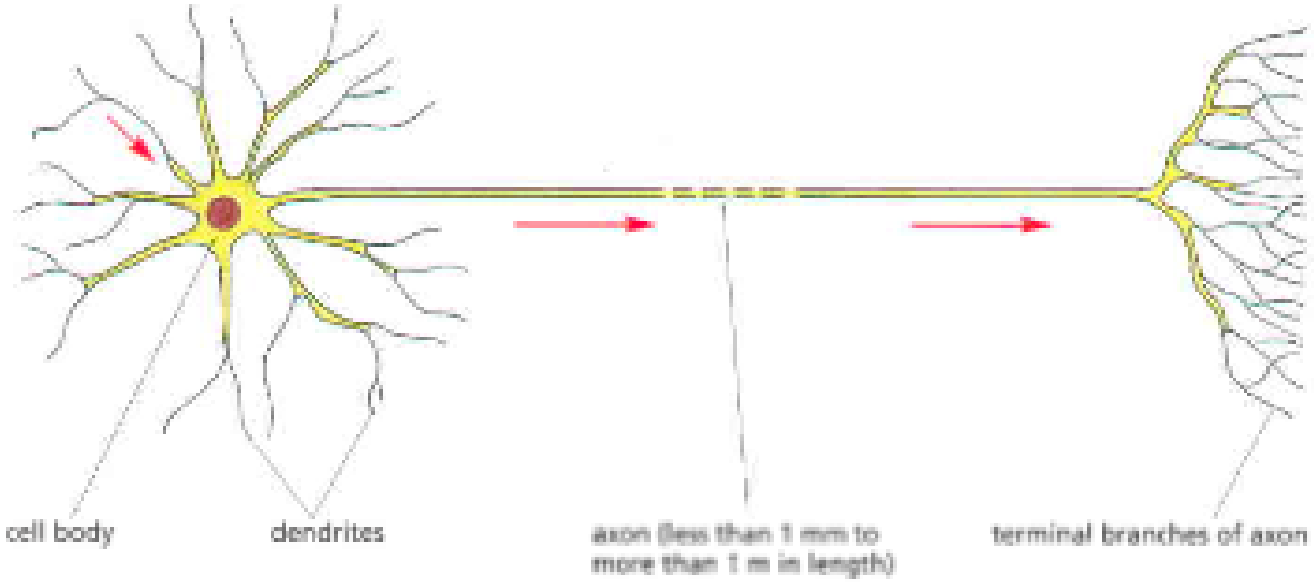


Figure 11–28 A typical vertebrate neuron. The arrows indicate the direction in which signals are conveyed. The single axon conducts signals away from the cell body, while the multiple dendrites (and the cell body) receive signals from the axons of other neurons. The nerve terminals end on the dendrites or cell body of other neurons or on other cell types, such as muscle or gland cells.

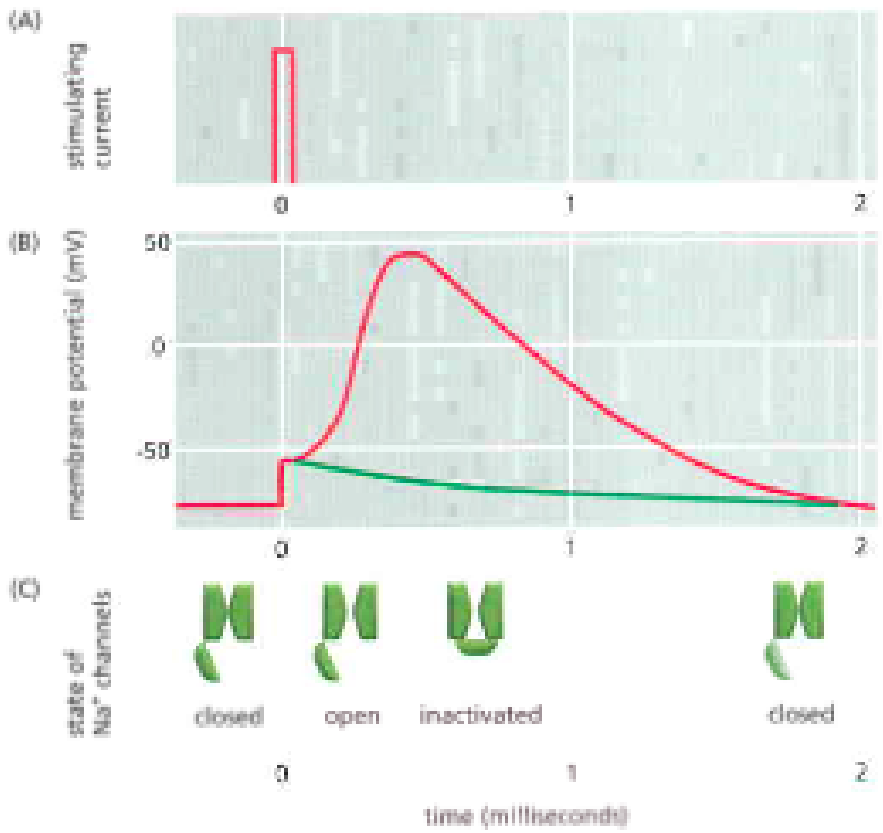


Figure 11–29 An action potential. <CGAG> (A) An action potential is triggered by a brief pulse of current, which (B) partially depolarizes the membrane, as shown in the plot of membrane potential versus time. The green curve shows how the membrane potential would have simply relaxed back to the resting value after the initial depolarizing stimulus if there had been no voltage-gated Na^+ channels in the membrane; this relatively slow return of the membrane potential to its initial value of −70 mV in the absence of open Na^+ channels occurs because of the efflux of K^+ through voltage-gated K^+ channels, which open in response to membrane depolarization and drive the membrane back toward the K^+ equilibrium potential. The red curve shows the course of the action potential that is caused by the opening and subsequent inactivation of voltage-gated Na^+ channels, whose state is shown in (C). The membrane cannot fire a second action potential until the Na^+ channels have returned to the closed conformation; until then, the membrane is refractory to stimulation.

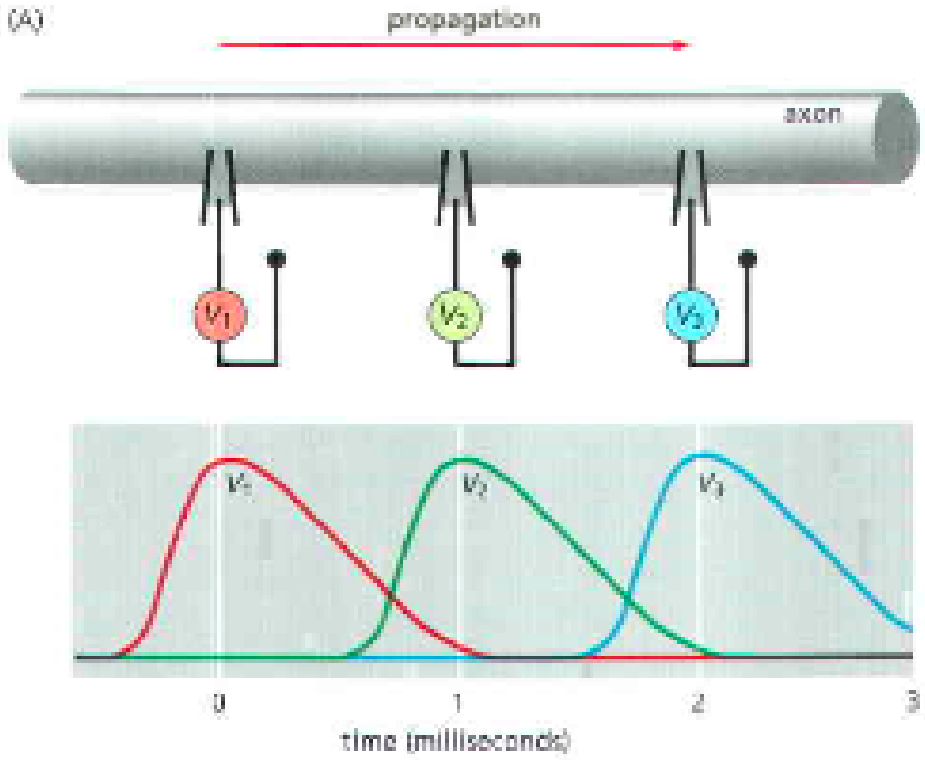
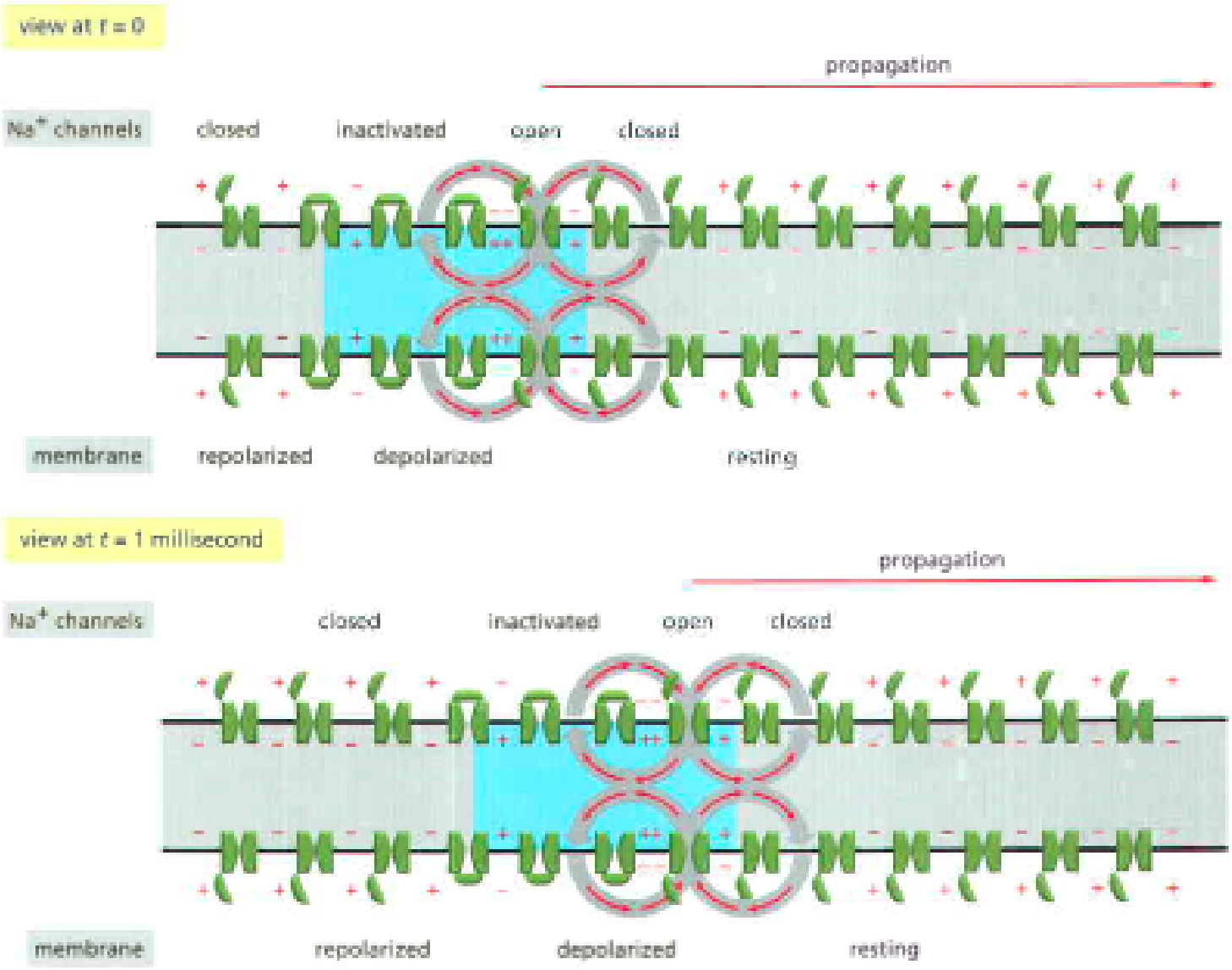


Figure 11–30 The propagation of an action potential along an axon. (A) The voltages that would be recorded from a set of intracellular electrodes placed at intervals along the axon. (B) The changes in the Na^+ channels and the current flows (*orange arrows*) that give rise to the travelling disturbance of the membrane potential. The region of the axon with a depolarized membrane is shaded in *blue*. Note that an action potential can only travel away from the site of depolarization, because Na^+-channel inactivation prevents the depolarization from spreading backward.

(B)


view at t = 0
propagation
Na+ channels
closed
inactivated
open
closed
membrane
repolarized
depolarized
resting
view at t = 1 millisecond
propagation
Na+ channels
closed
inactivated
open
closed
membrane
repolarized
depolarized
resting

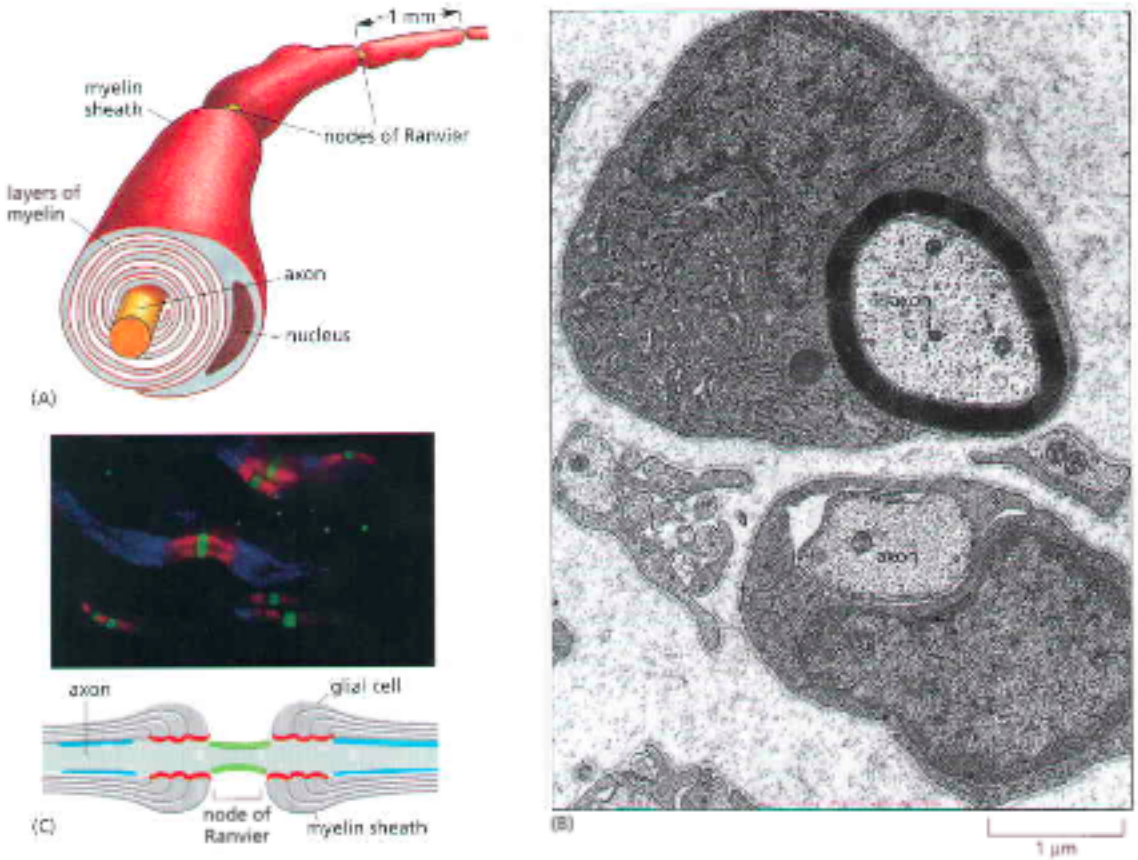


Figure 11–32 Myelination. (A) A myelinated axon from a peripheral nerve. Each Schwann cell wraps its plasma membrane concentrically around the axon to form a segment of myelin sheath about 1 mm long. For clarity, the membrane layers of the myelin in this drawing are shown less compacted than they are in reality (see part B). (B) An electron micrograph of a section from a nerve in the leg of a young rat. Two Schwann cells can be seen: one near the bottom is just beginning to myelinate its axon; the one above it has formed an almost mature myelin sheath. (C) Fluorescence micrograph and diagram of individual myelinated axons teased apart in a nerve. Three different proteins are detected by staining with antibodies. Voltage-gated Na^+ channels (stained in *green*) are concentrated in the axonal membrane at the nodes of Ranvier. An extracellular protein (called *Caspr*, stained in *red*) marks the end of each myelin sheath. Caspr assembles at the junctions where the glial cell plasma membrane tightly abuts the axon to provide the electrical seal. Voltage-gated K^+ channels (stained in *blue*) localize to regions in the axon plasma membrane that are close to the nodes. (B, from Cedric S. Raine, in Myelin [P. Morell, ed.]. New York: Plenum, 1976; C, from M.N. Rasband and P. Shrager, *J. Physiol.* 525:63–73, 2000. With permission from Blackwell Publishing.)

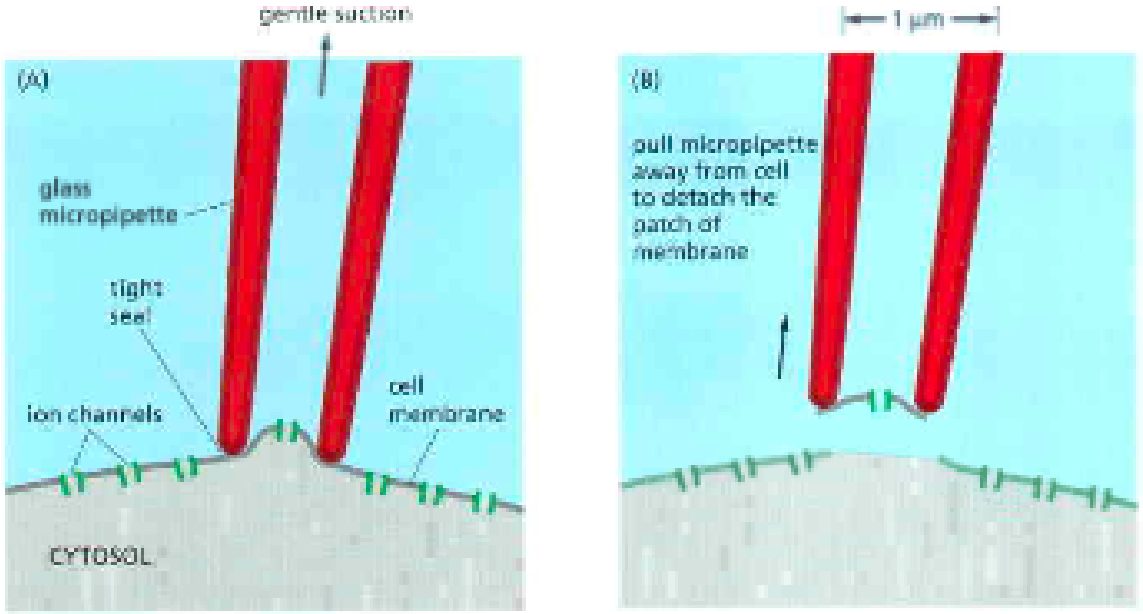
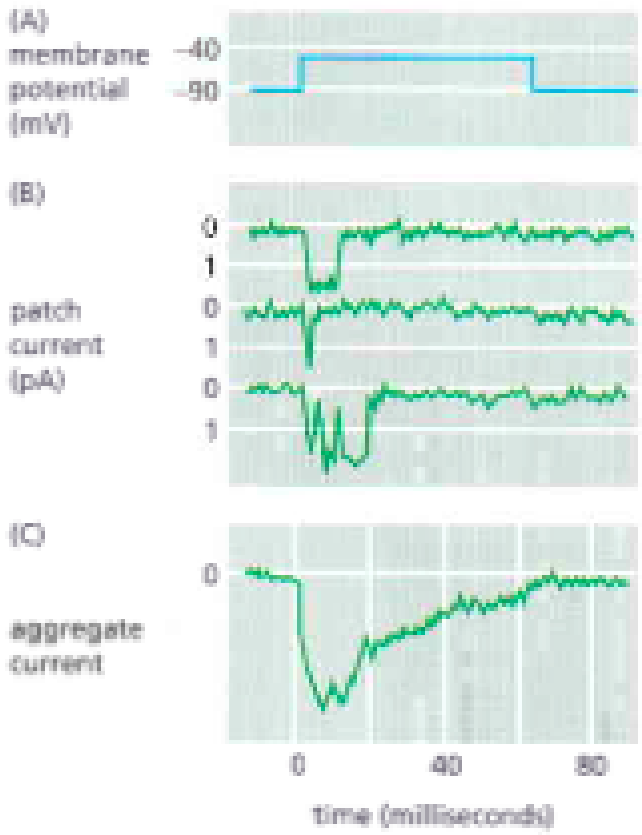
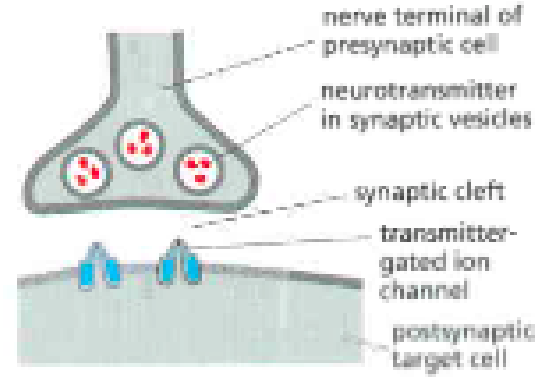


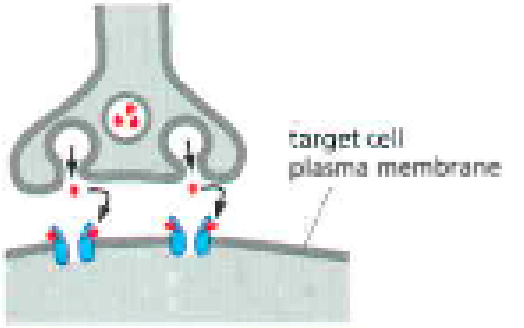
Figure 11–33 The technique of patch-clamp recording. Because of the extremely tight seal between the micropipette and the membrane, current can enter or leave the micropipette only by passing through the channels in the *patch* of membrane covering its tip. The term *clamp* is used because an electronic device is employed to maintain, or "clamp," the membrane potential at a set value while recording the ionic current through individual channels. The current through these channels can be recorded with the patch still attached to the rest of the cell, as in (A), or detached, as in (B). The advantage of the detached patch is that it is easy to alter the composition of the solution on either side of the membrane to test the effect of various solutes on channel behavior. A detached patch can also be produced with the opposite orientation, so that the cytoplasmic surface of the membrane faces the inside of the pipette.

Figure 11–34 Patch-clamp measurements for a single voltage-gated Na^+ channel. A tiny patch of plasma membrane was detached from an embryonic rat muscle cell, as in Figure 11–33. (A) The membrane was depolarized by an abrupt shift of potential. (B) Three current records from three experiments performed on the same patch of membrane. Each major current step in (B) represents the opening and closing of a single channel. A comparison of the three records shows that, whereas the durations of channel opening and closing vary greatly, the rate at which current flows through an open channel is practically constant. The minor fluctuations in the current records arise largely from electrical noise in the recording apparatus. Current is measured in picoamperes (pA). By convention, the electrical potential on the outside of the cell is defined as zero. (C) The sum of the currents measured in 144 repetitions of the same experiment. This aggregate current is equivalent to the usual Na^+ current that would be observed flowing through a relatively large region of membrane containing 144 channels. A comparison of (B) and (C) reveals that the time course of the aggregate current reflects the probability that any individual channel will be in the open state; this probability decreases with time as the channels in the depolarized membrane adopt their inactivated conformation. (Data from J. Patlak and R. Horn, *J. Gen. Physiol.* 79:333–351, 1982. With permission from The Rockefeller University Press.)



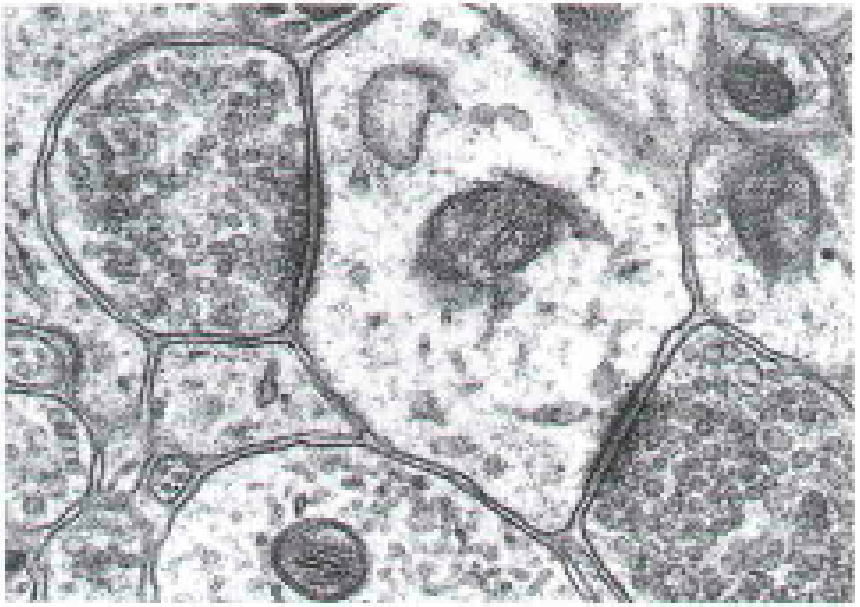


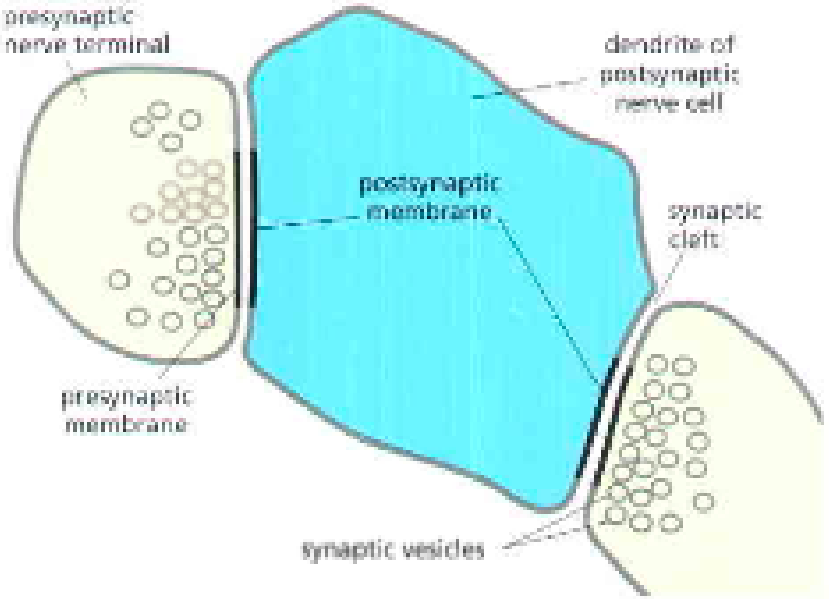
RESTING CHEMICAL SYNAPSE



ACTIVE CHEMICAL SYNAPSE

(A)





(B)

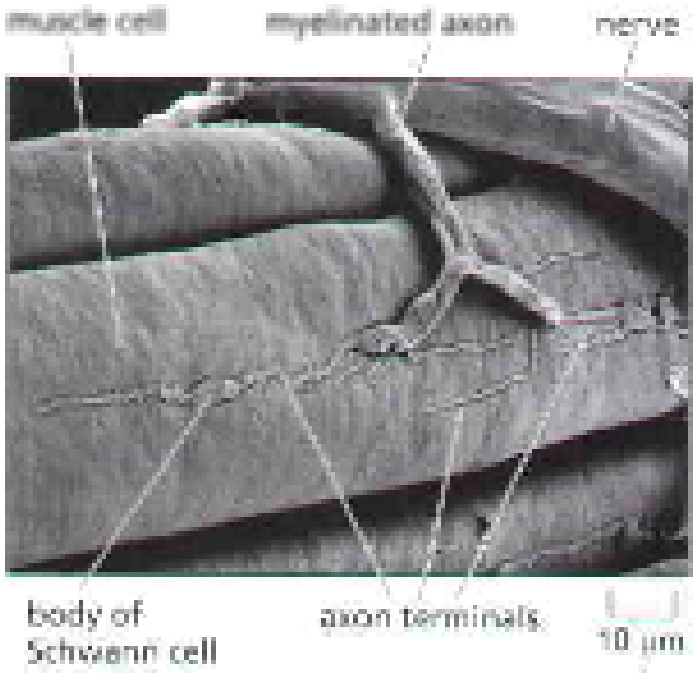


Figure 11–36 A low-magnification scanning electron micrograph of a neuromuscular junction in a frog. The termination of a single axon on a skeletal muscle cell is shown. (From J. Desaki and Y. Uehara, *J. Neurocytol.* 10:101–110, 1981. With permission from Kluwer Academic Publishers.)

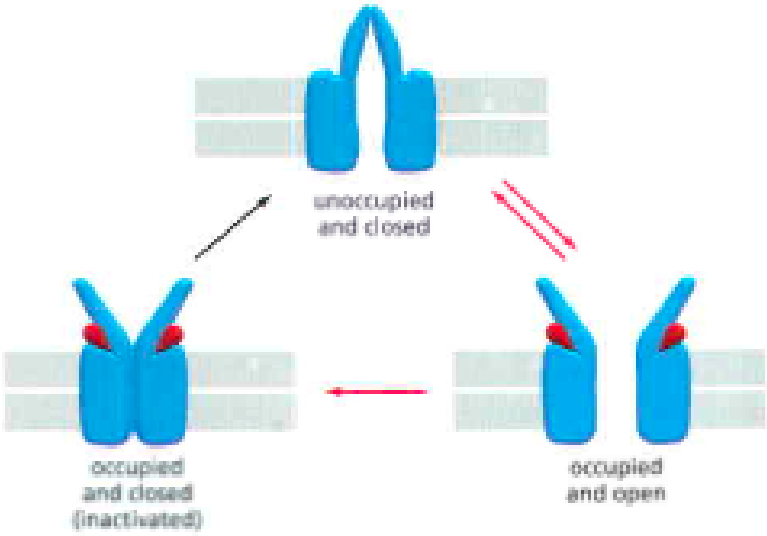


Figure 11–37 Three conformations of the acetylcholine receptor. The binding of two acetylcholine molecules opens this transmitter-gated ion channel. It then maintains a high probability of being open until the acetylcholine has been hydrolyzed. In the persistent presence of acetylcholine, however, the channel inactivates (desensitizes). Normally, the acetylcholine is rapidly hydrolyzed and the channel closes within about 1 millisecond, well before significant desensitization occurs. Desensitization would occur after about 20 milliseconds in the continued presence of acetylcholine.

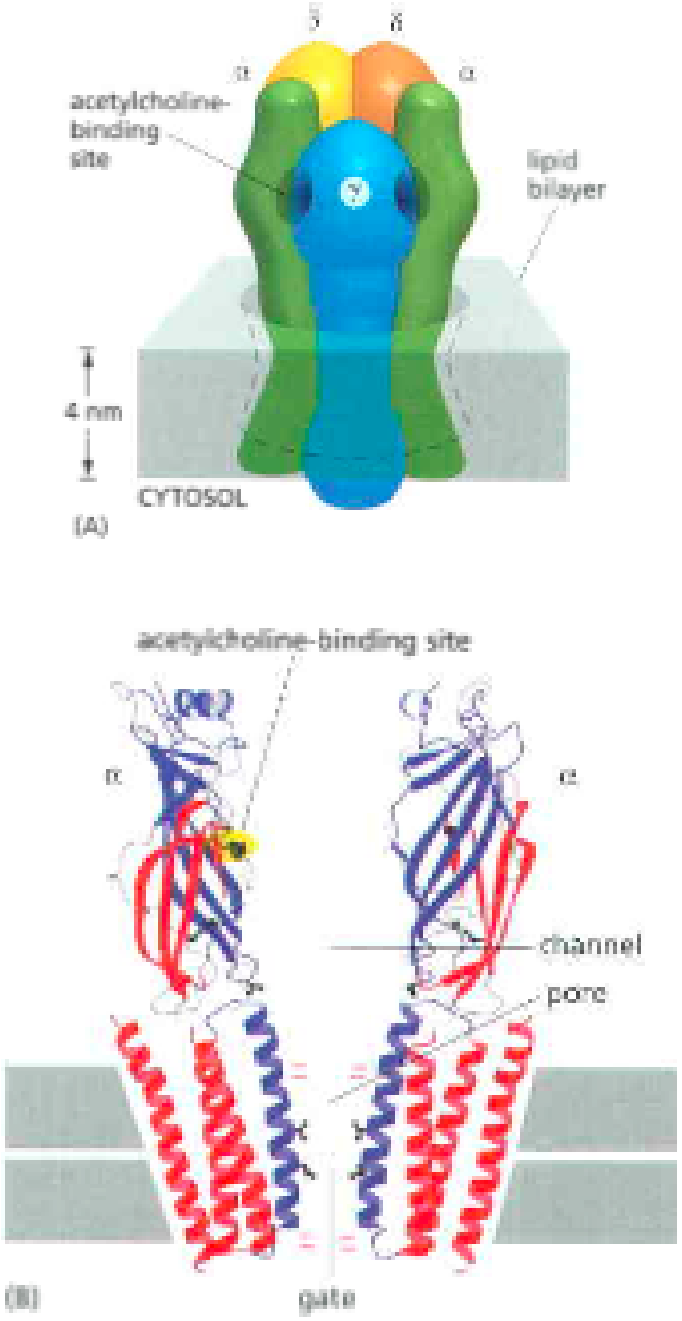
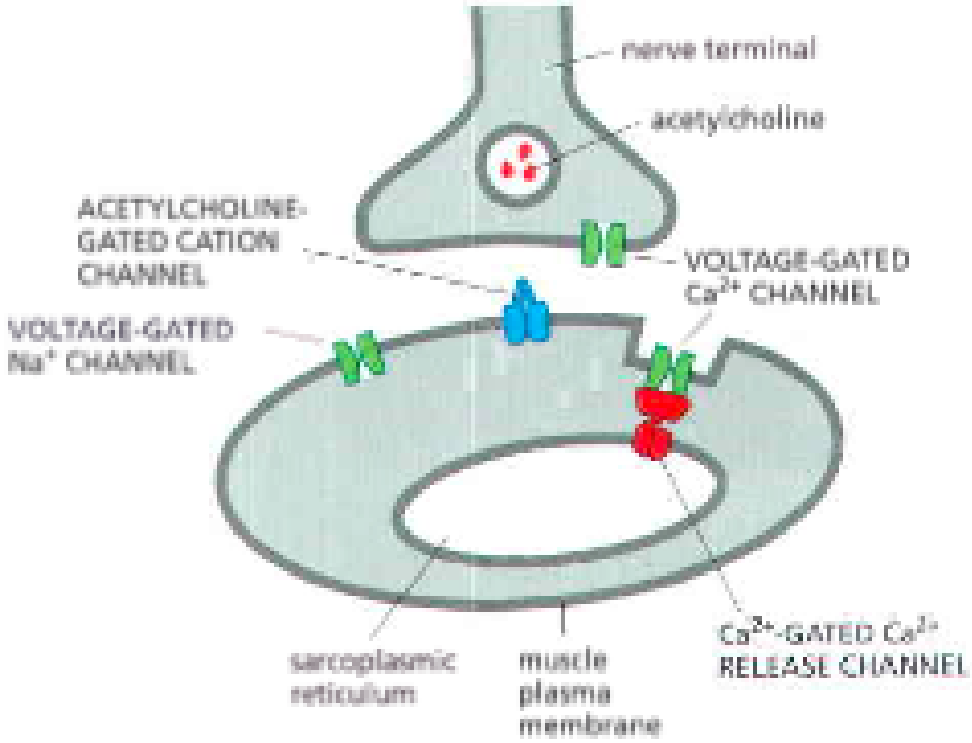
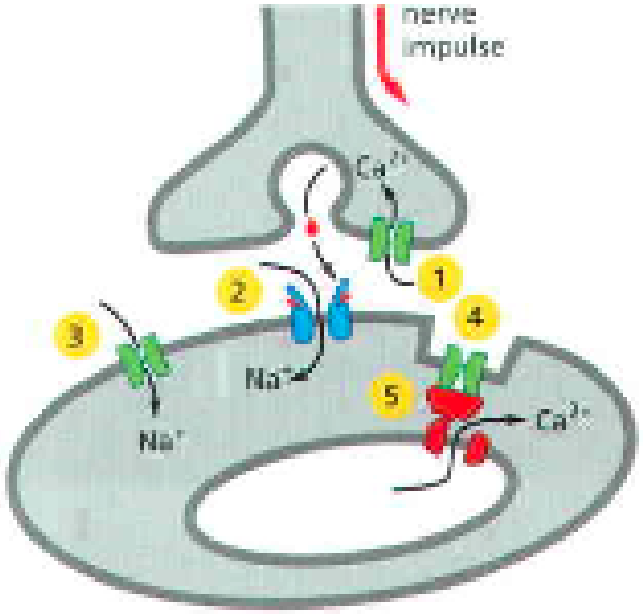


Figure 11–38 A model for the structure of the acetylcholine receptor. (A) Five homologous subunits (α, α, β, γ, δ) combine to form a transmembrane aqueous pore. The pore is lined by a ring of five transmembrane α helices, one contributed by each subunit. In its closed conformation, the pore is thought to be occluded by the hydrophobic side chains of five leucines, one from each α helix, which form a gate near the middle of the lipid bilayer. The negatively charged side chains at either end of the pore ensure that only positively charged ions pass through the channel. (B) Both of the α subunits contribute to an acetylcholine-binding site nestled between adjoining subunits; when acetylcholine binds to both sites, the channel undergoes a conformational change that opens the gate, possibly by rotating the helices containing the occluding leucines to move outward. In the structural drawing (*right*), the parts of the channel that move in response to AChR binding to open the pore are colored in *blue*. (Adapted from N. Unwin, *Cell* 72[Suppl.]:31–41, 1993. With permission from Elsevier.)

RESTING NEUROMUSCULAR JUNCTION

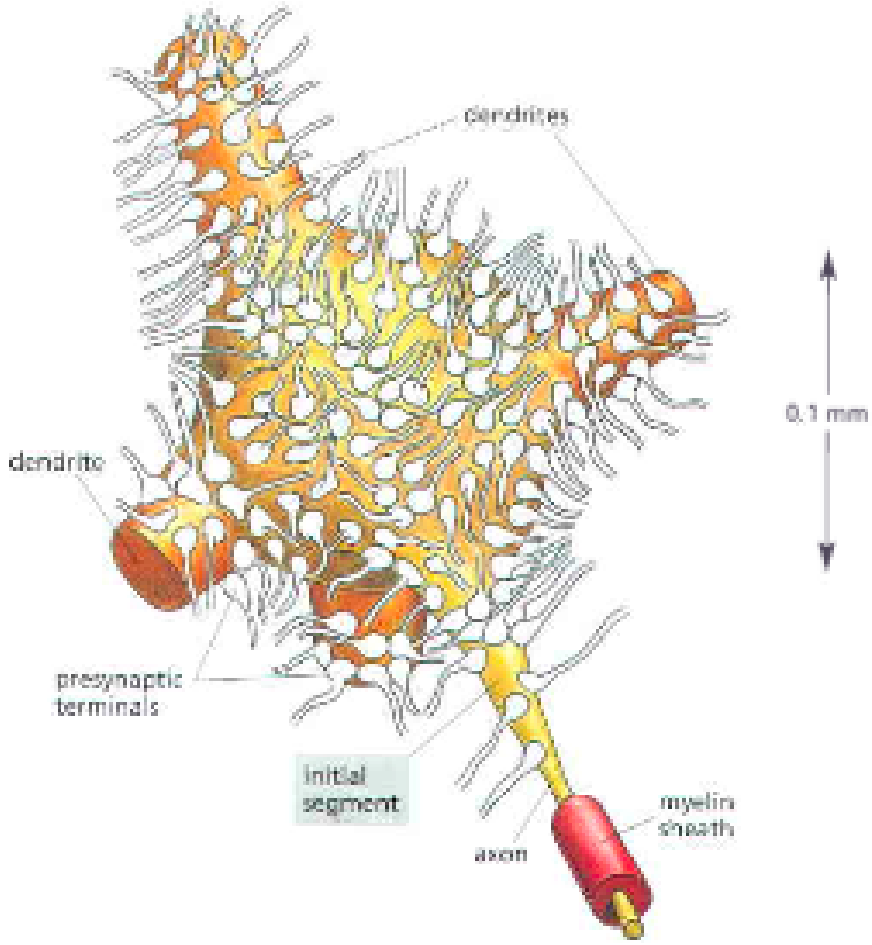


ACTIVATED NEUROMUSCULAR JUNCTION

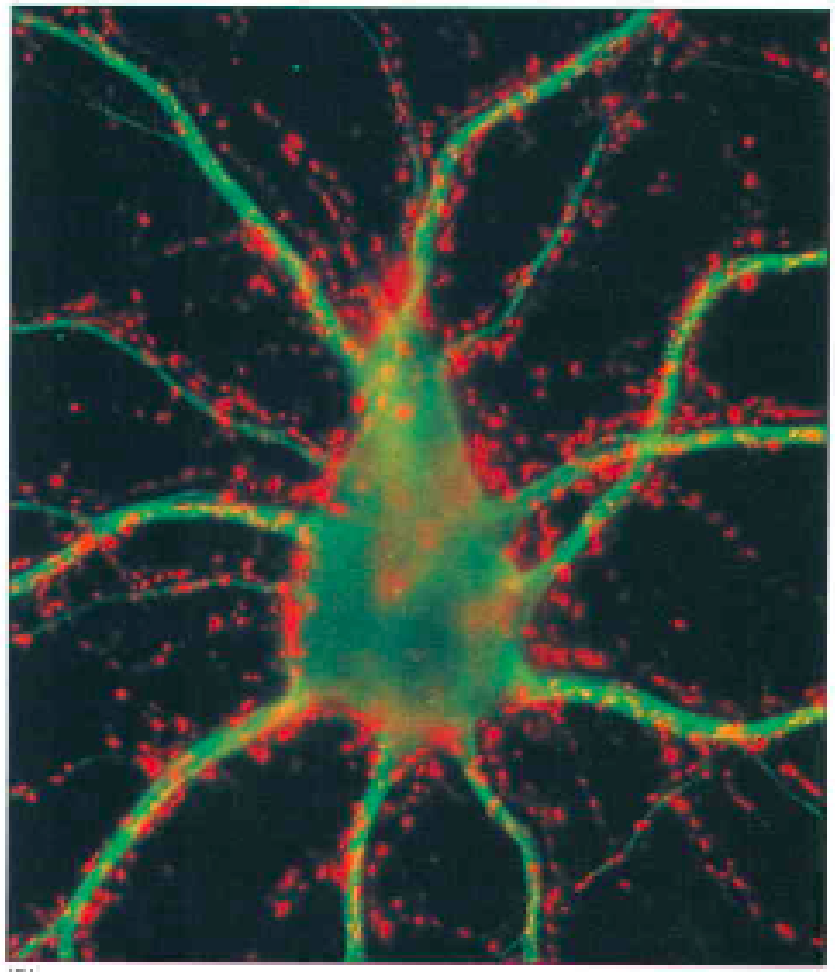


1. The process is initiated when the nerve impulse reaches the nerve terminal and depolarizes the plasma membrane of the terminal. The depolarization transiently opens voltage-gated Ca^{2+} channels in this membrane. As the Ca^{2+} concentration outside cells is more than 1000 times greater than the free Ca^{2+} concentration inside, Ca^{2+} flows into the nerve terminal. The increase in Ca^{2+} concentration in the cytosol of the nerve terminal triggers the local release of acetylcholine into the synaptic cleft.
2. The released acetylcholine binds to acetylcholine receptors in the muscle cell plasma membrane, transiently opening the cation channels associated with them. The resulting influx of Na^+ causes a local membrane depolarization.
3. The local depolarization of the muscle cell plasma membrane opens voltage-gated Na^+ channels in this membrane, allowing more Na^+ to enter, which further depolarizes the membrane. This, in turn, opens neighboring voltage-gated Na^+ channels and results in a self-propagating depolarization (an action potential) that spreads to involve the entire plasma membrane (see Figure 11–30).

4. The generalized depolarization of the muscle cell plasma membrane activates voltage-gated Ca^{2+} channels in specialized regions (the transverse [T] tubules—discussed in Chapter 16) of this membrane.
5. This, in turn, causes Ca^{2+}-gated *Ca^{2+} release channels* in an adjacent region of the sarcoplasmic reticulum (SR) membrane to open transiently and release the Ca^{2+} stored in the SR into the cytosol. The T-tubule and SR membranes are closely apposed with the two types of channels joined together in a specialized structure (see Figure 16–77). It is the sudden increase in the cytosolic Ca^{2+} concentration that causes the myofibrils in the muscle cell to contract.


dendrites
dendrite
presynaptic terminals
initial segment
myelin sheath
axon
0.1 mm

(A)



(B)

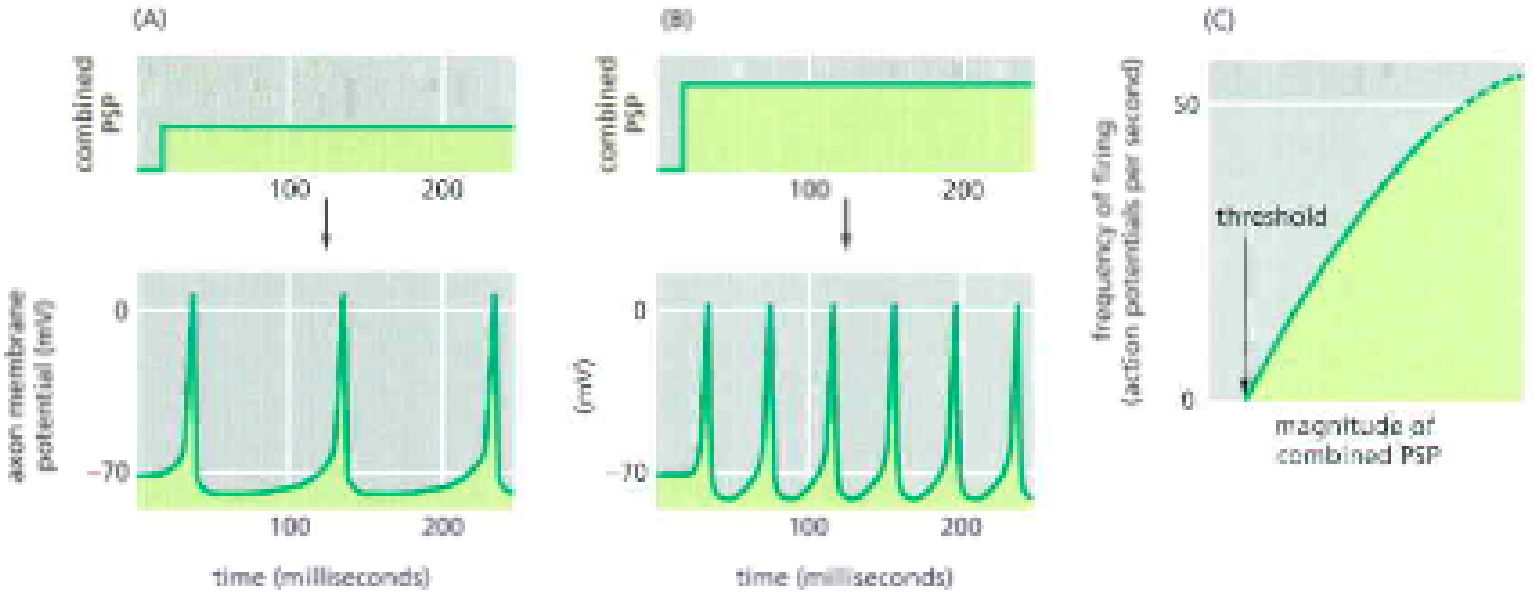


Figure 11–41 The magnitude of the combined postsynaptic potential (PSP) is reflected in the frequency of firing of action potentials. When successive action potentials arrive at the same synapse, each PSP produced adds to the preceding one to produce a larger combined PSP. A comparison of (A) and (B) shows how the firing frequency of an axon increases with an increase in the combined PSP, while (C) summarizes the general relationship.