

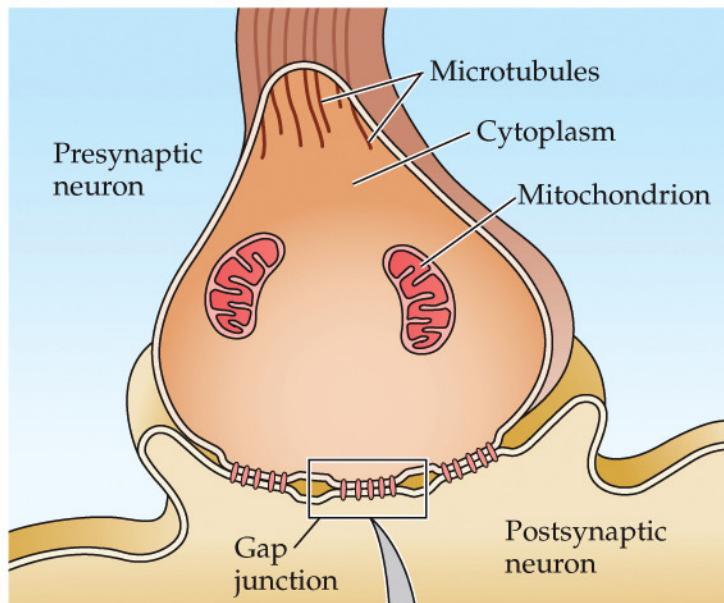
BMD ENG 301 Quantitative Systems Physiology (Nervous System)

Lecture 10: Synaptic Transmission
2022_v2

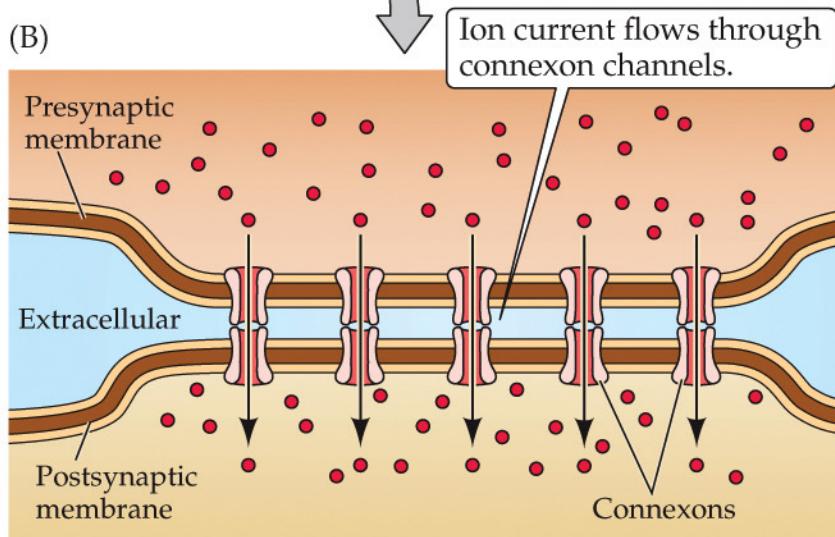
Professor Malcolm A. MacIver

Electrical and chemical synapses differ fundamentally in their transmission mechanisms

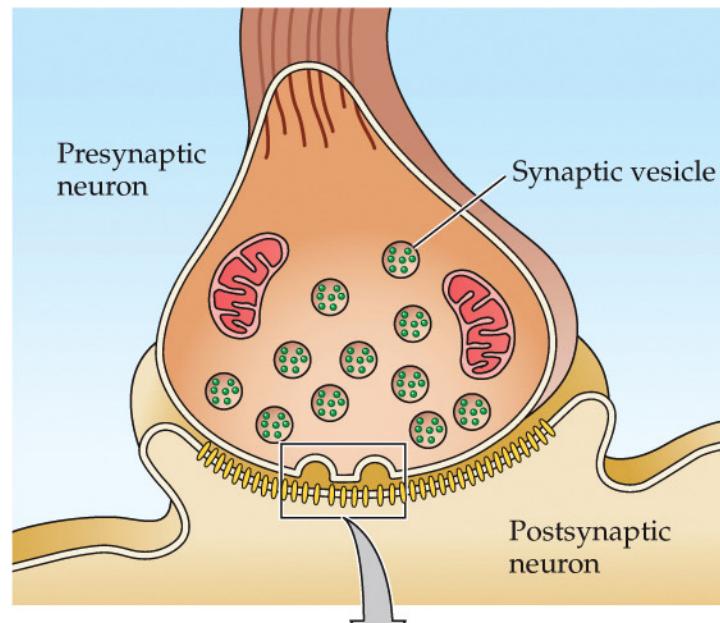
(A) Electrical synapse



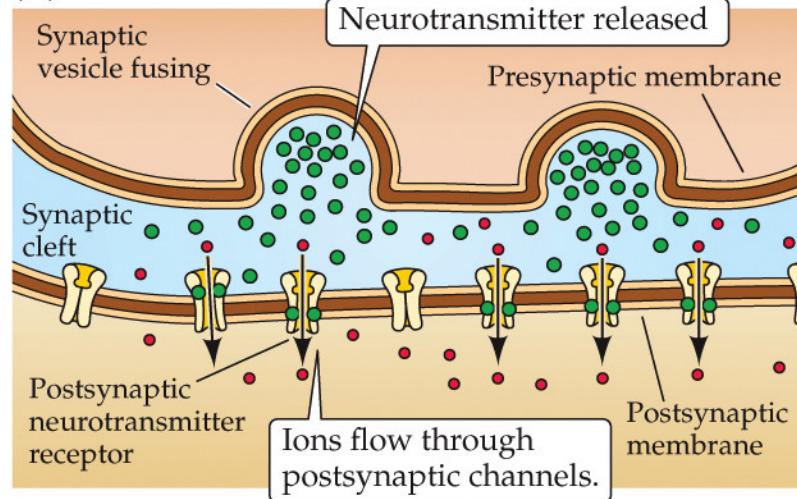
(B)



(C) Chemical synapse



(D)

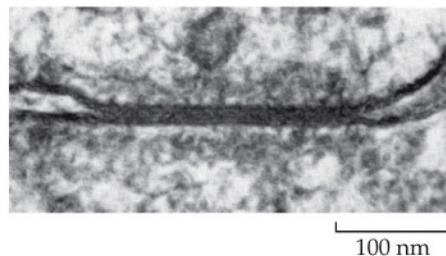


Structure of electrical synapses

(A)

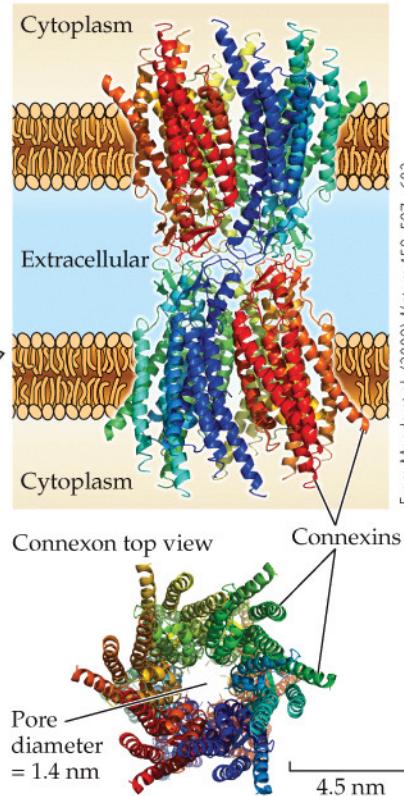


(B)



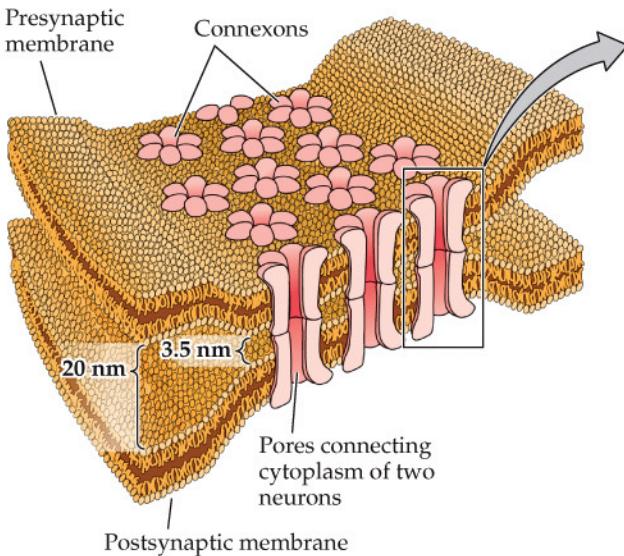
From Sorelo et al. (1974)
J. Neurophysiol. 37: 541–559.

(D) Connexon side view



From Maeda et al. (2009) *Nature* 458: 597–602.

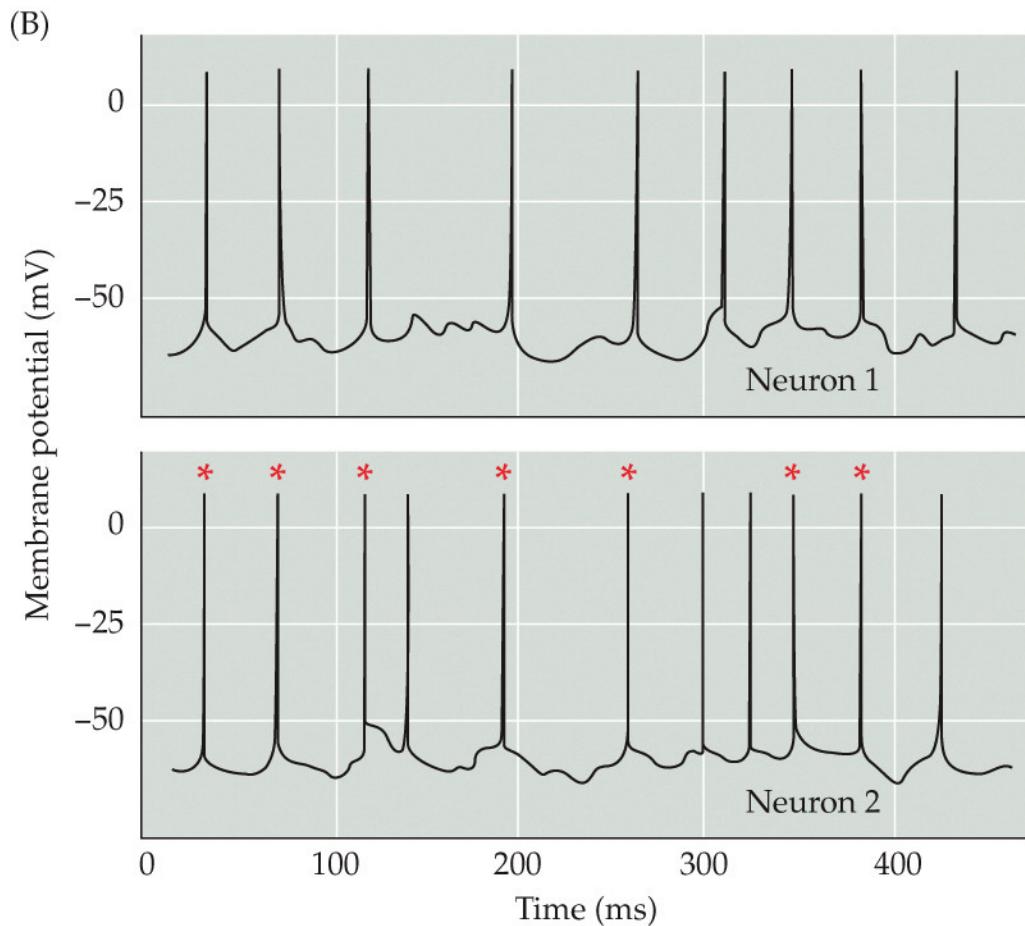
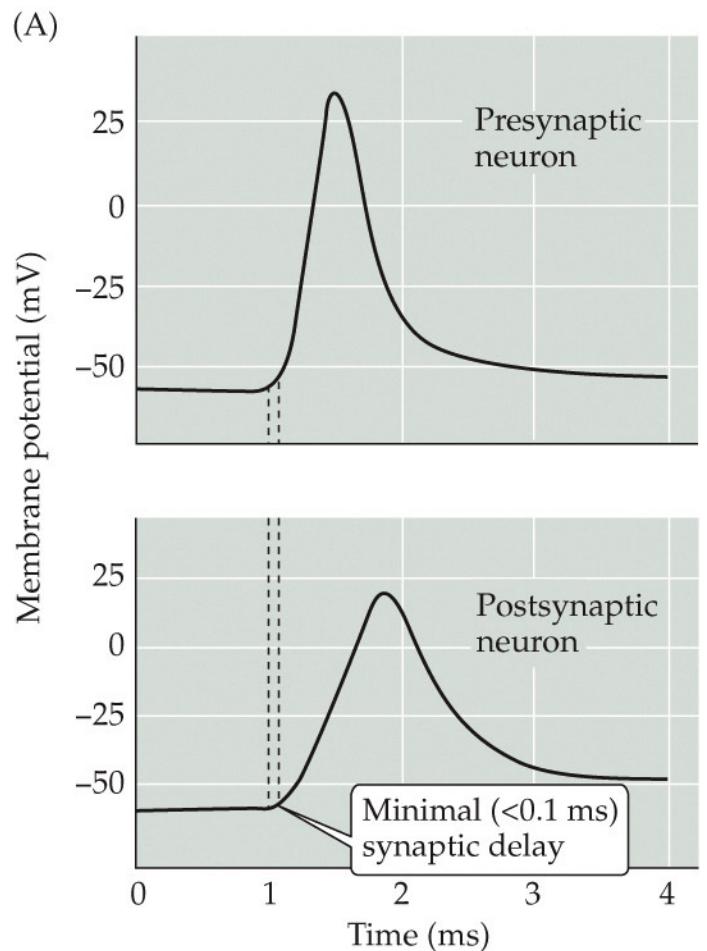
(C)



NEUROSCIENCE 6e, Figure 5.2

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Function of gap junctions at electrical synapses

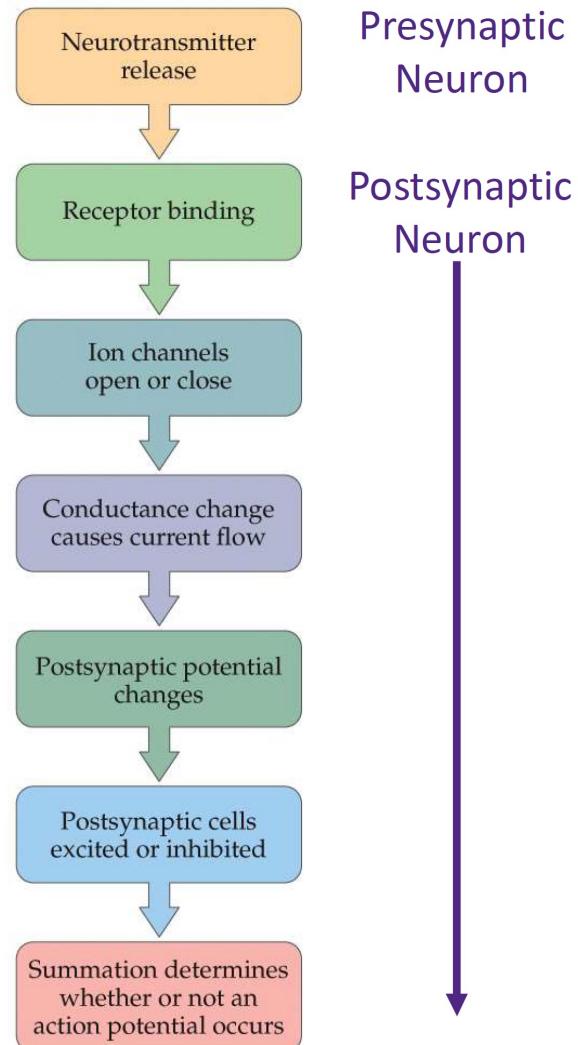
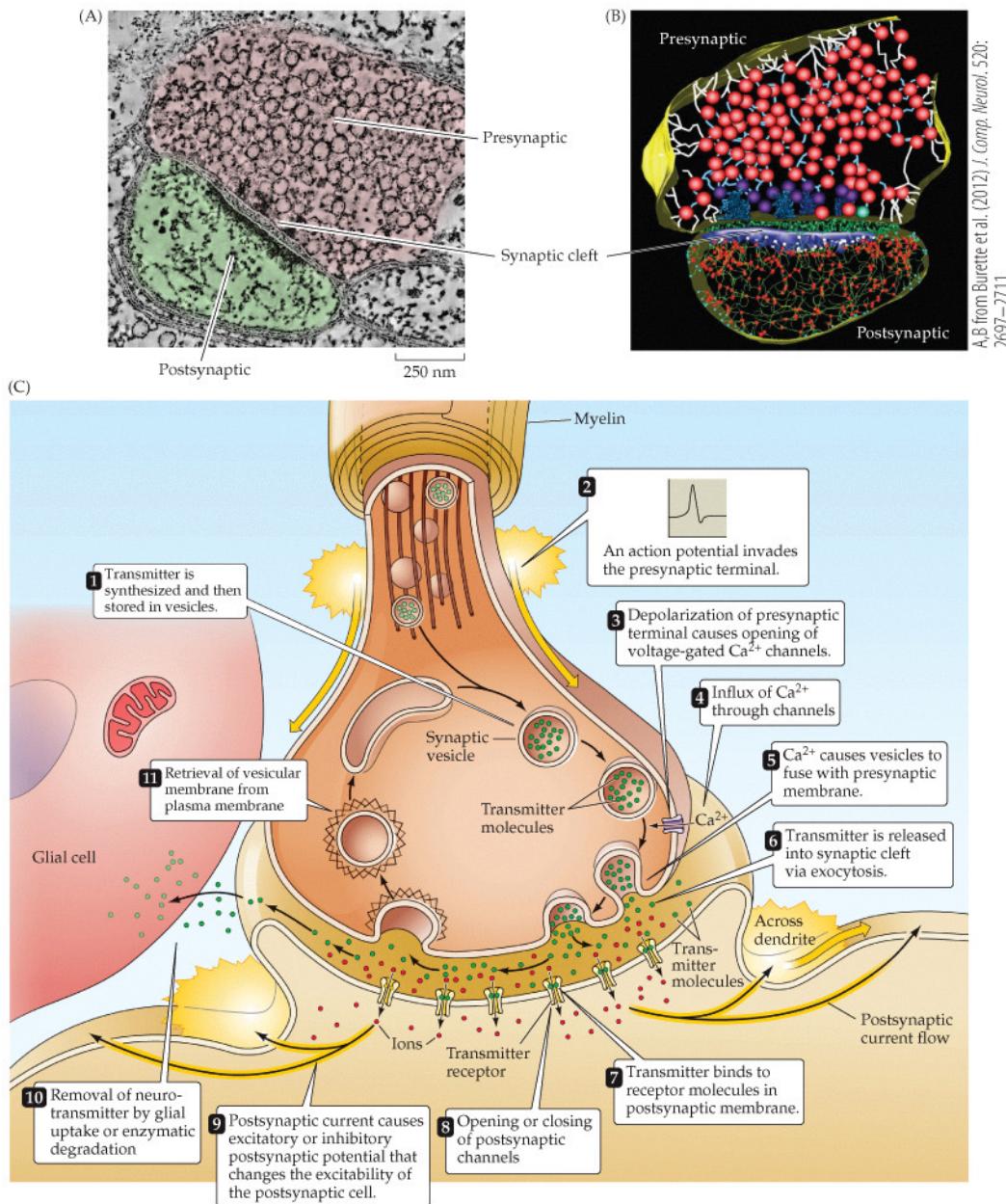


A after Furshpan and Potter (1959) *J. Physiol. (Lond.)* 145: 289–324. B after Beierlein and Connors (2000) *Nature Neurosci.* 3: 904–910.

NEUROSCIENCE 6e, Figure 5.3

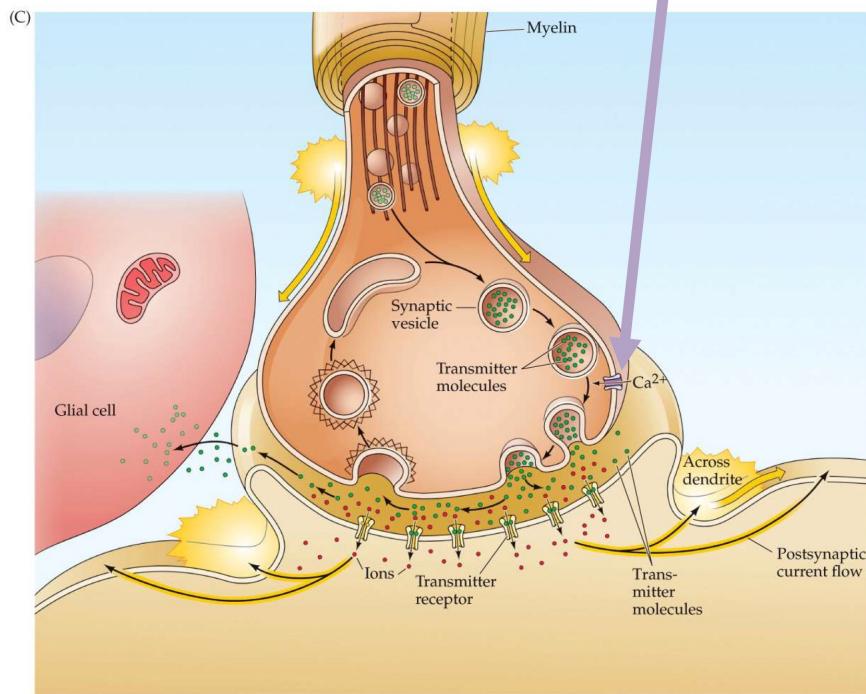
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Structure and function of chemical synapses



NEUROSCIENCE 6e, Figure 5.21
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2. Influx of Ca^{2+} ions triggers vesicle release of neurotransmitters



NEUROSCIENCE 6e, Figure 5.4 (Part 3)
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Voltage-gated calcium channels open upon depolarization from the action potential

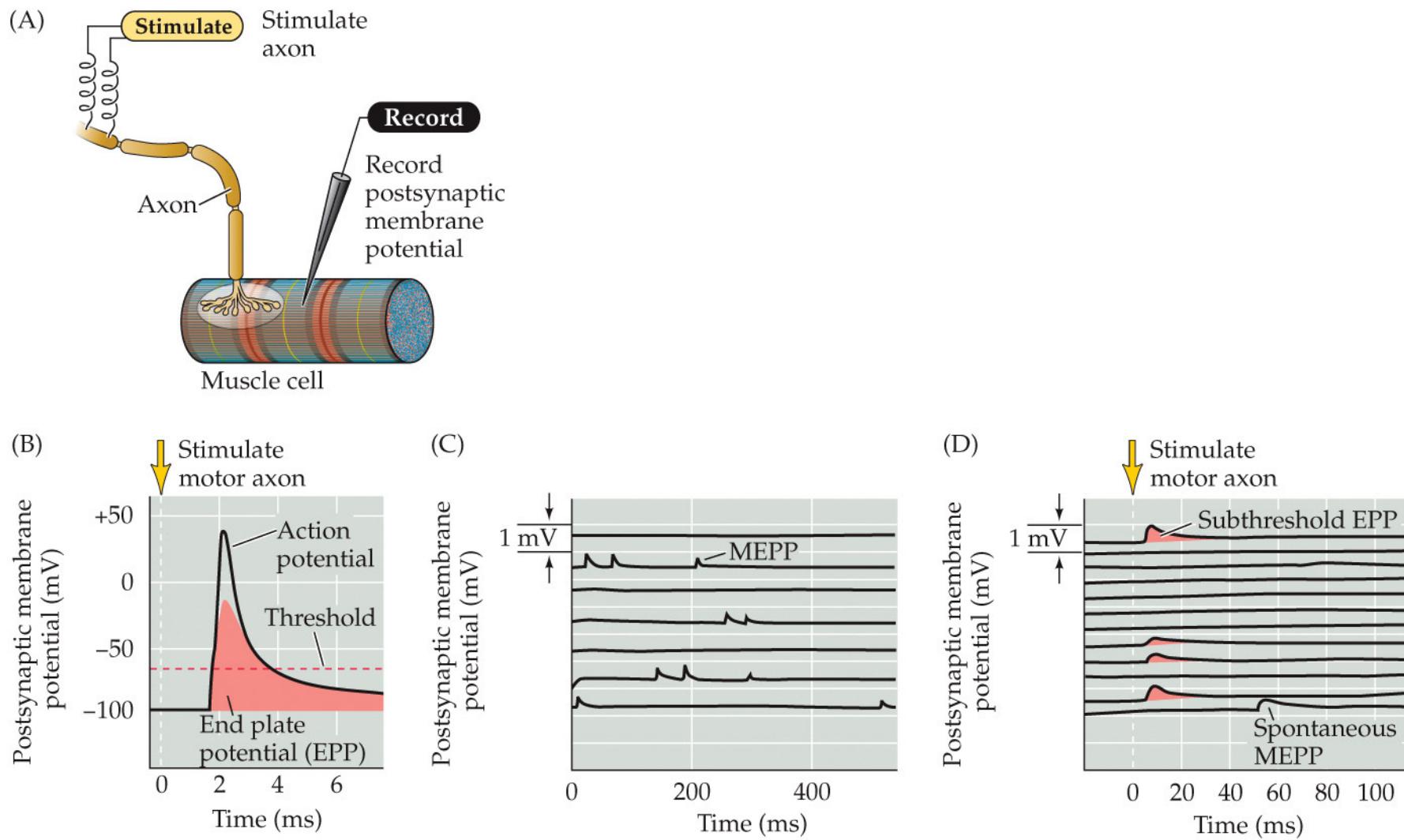
TABLE 2.1 ■ Extracellular and Intracellular Ion Concentrations

Ion	Concentration (mM)	
	Intracellular	Extracellular
Squid neuron		
Potassium (K^+)	400	20
Sodium (Na^+)	50	440
Chloride (Cl^-)	40-150	560
Calcium (Ca^{2+})	0.0001	10
Mammalian neuron		
Potassium (K^+)	140	5
Sodium (Na^+)	5-15	145
Chloride (Cl^-)	4-30	110
Calcium (Ca^{2+})	0.0001	1-2

NEUROSCIENCE 6e, Table 2.1
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Ca^{2+} is a critical intracellular signaling molecule!

Synaptic transmission at the neuromuscular junction

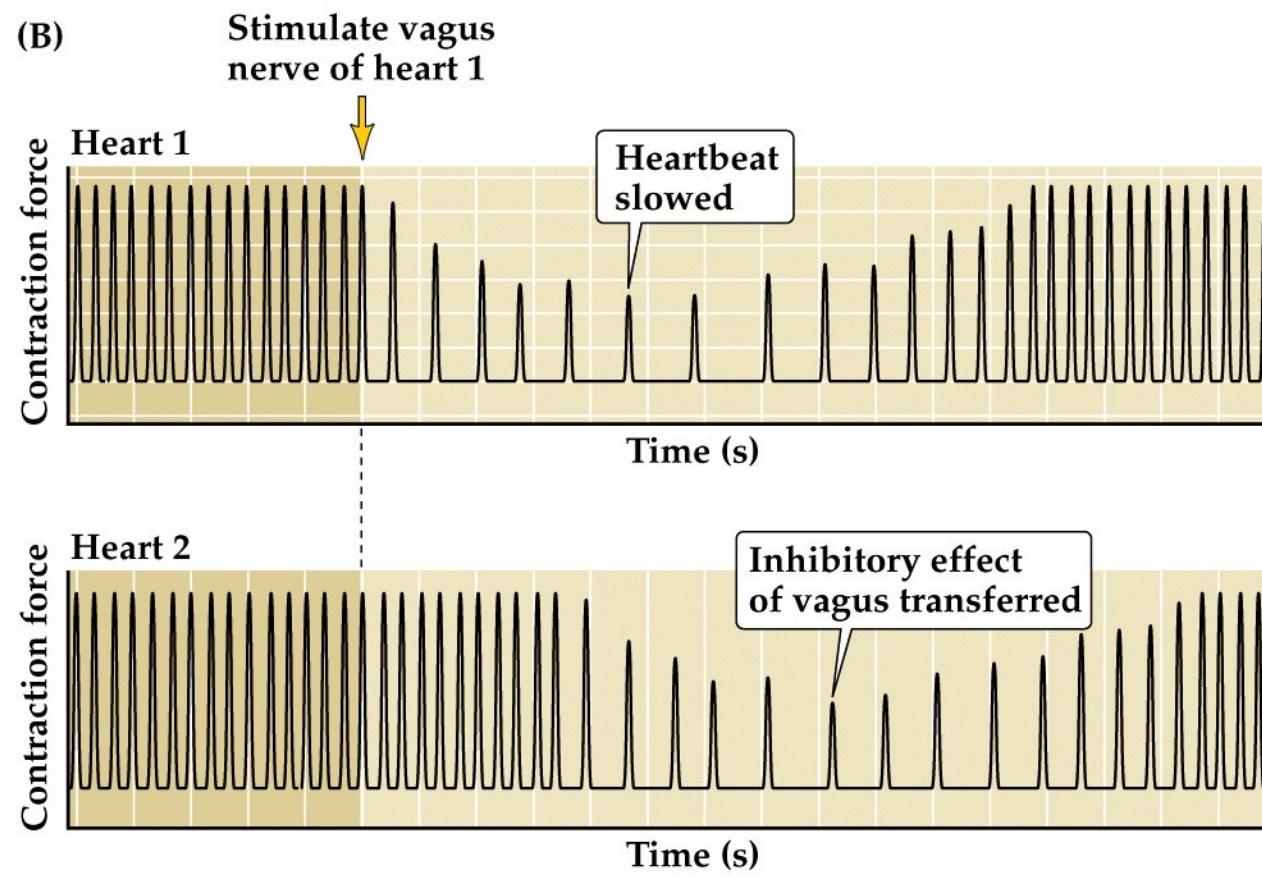
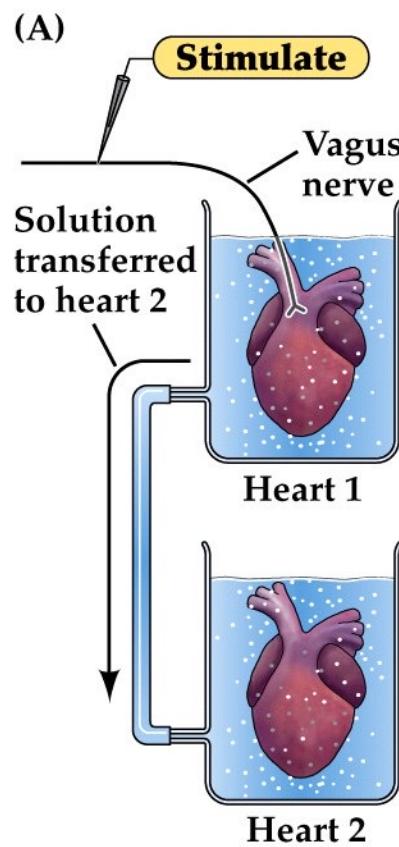


After Fatt and Katz (1952) *J. Physiol. (Lond.)* 117: 109–127.

NEUROSCIENCE 6e, Figure 5.5

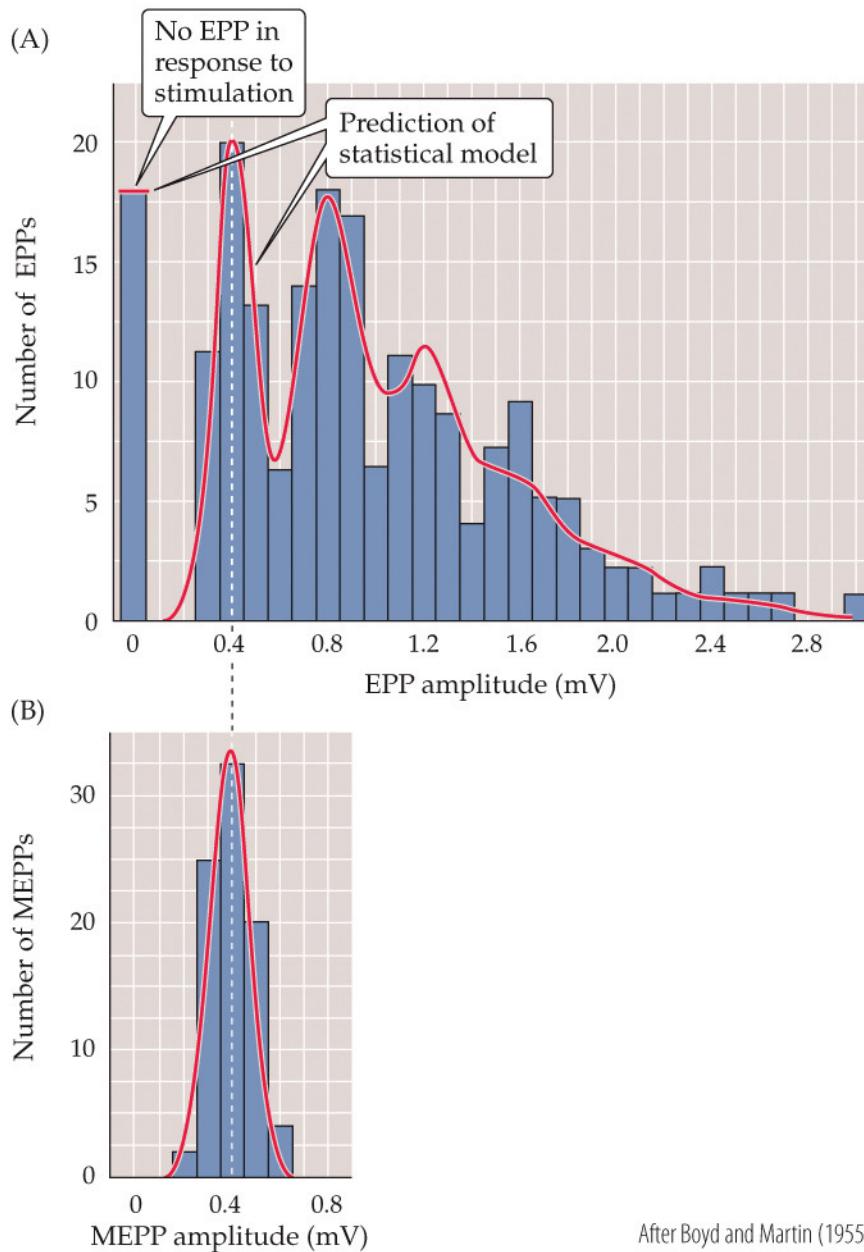
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Figure 5.4 Loewi's experiment demonstrated chemical neurotransmission



NEUROSCIENCE 5e, Figure 5.4
© 2012 Sinauer Associates, Inc.

Quantized distribution of EPP amplitudes evoked in a low-Ca²⁺ solution



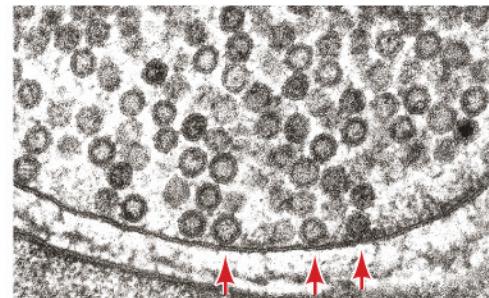
After Boyd and Martin (1955).

Relationship between synaptic vesicle exocytosis and quantal transmitter release

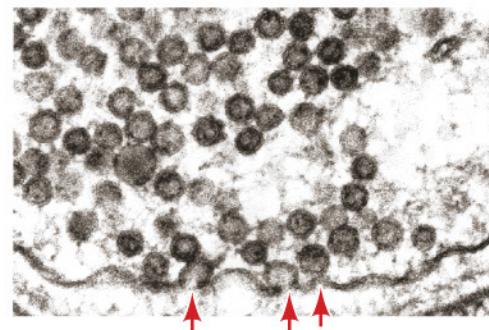
(A)



(B)

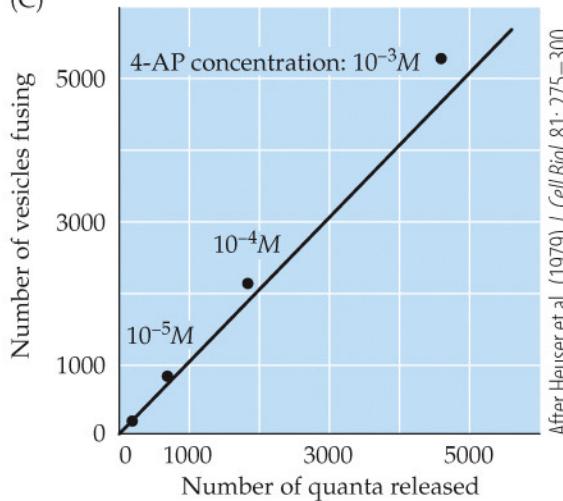


Stimulated



Courtesy of J. Heuser.

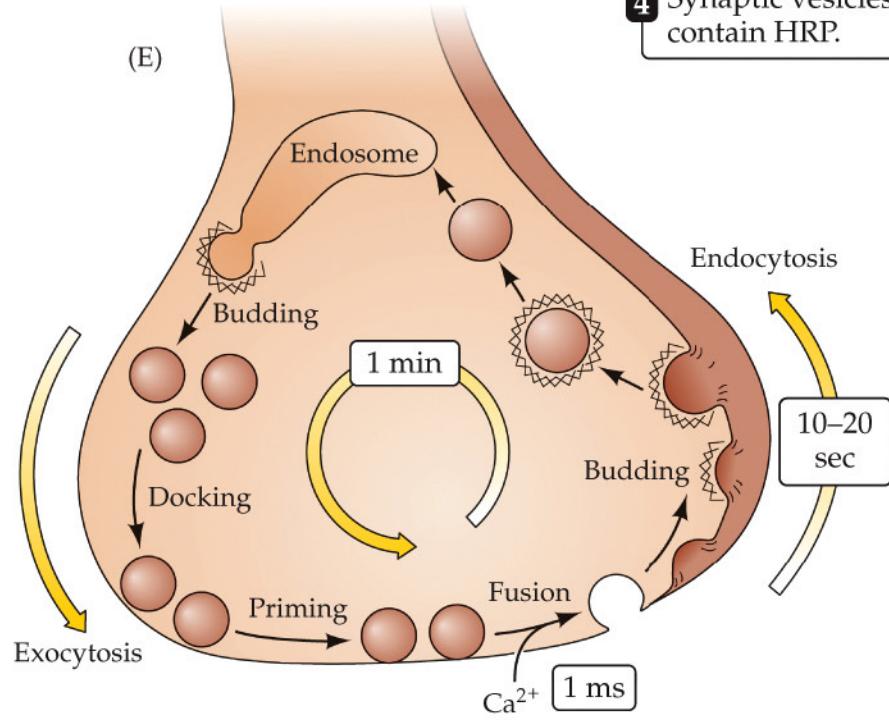
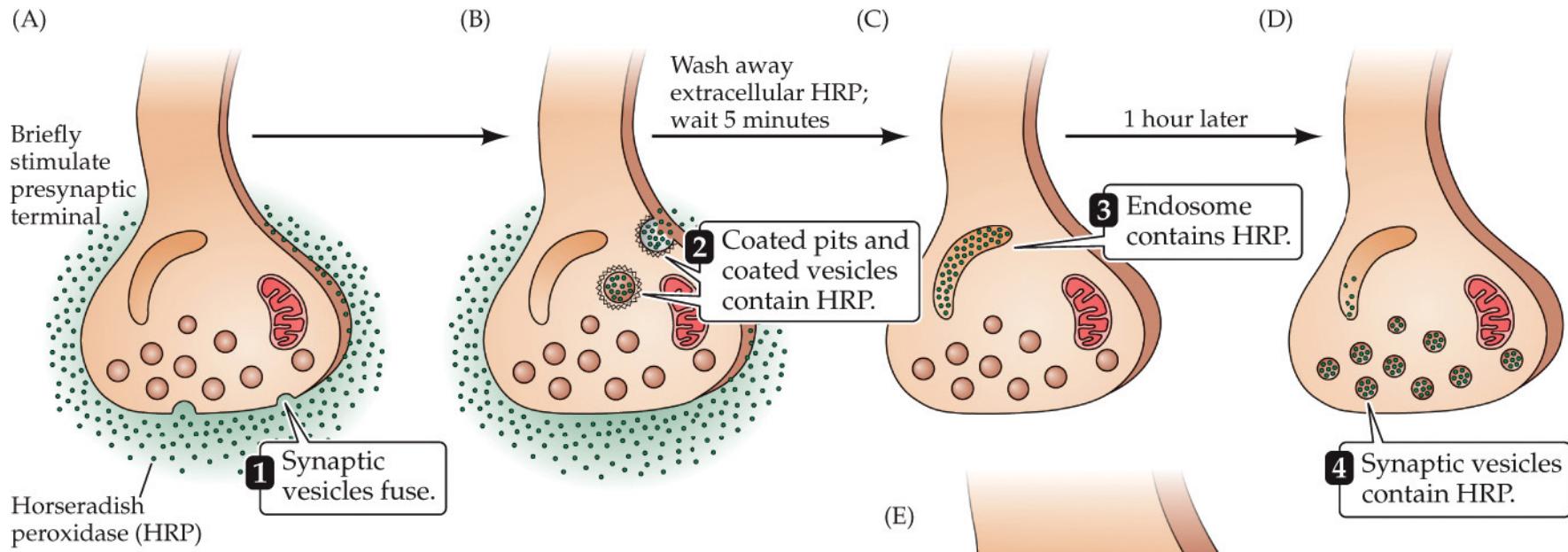
(C)



NEUROSCIENCE 6e, Figure 5.7

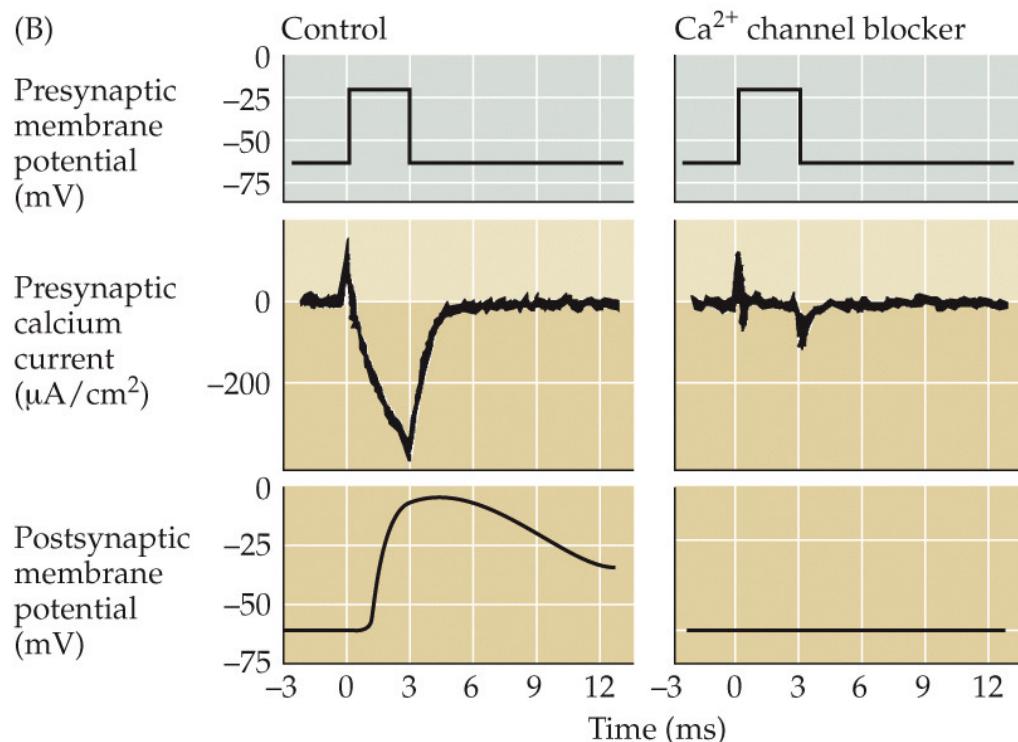
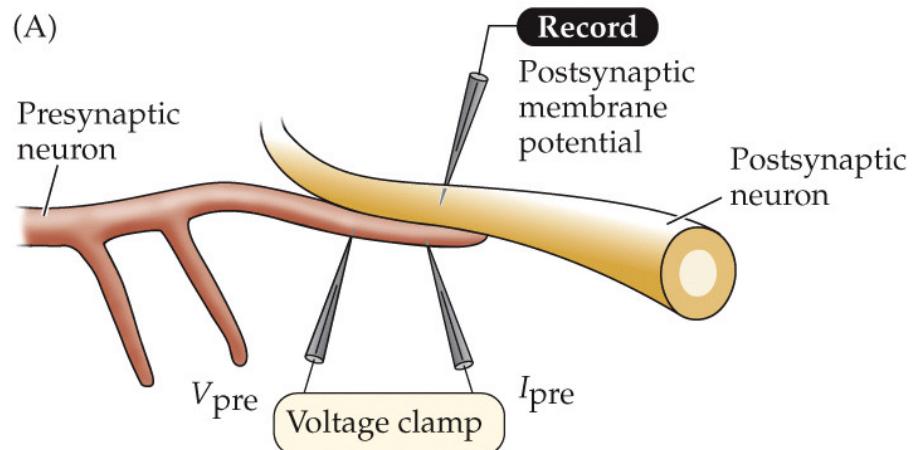
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Local recycling of synaptic vesicles in presynaptic terminals



After Heuser and Reese (1973).

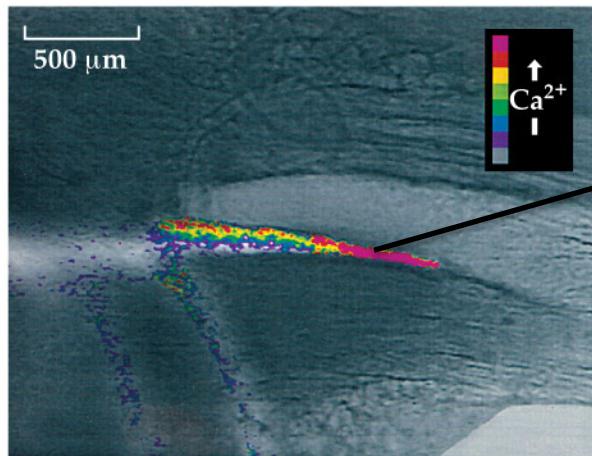
Entry of Ca^{2+} through presynaptic voltage-gated calcium channels causes transmitter release



After Augustine and Eckert (1984). *J. Physiol.* 346: 257–271.

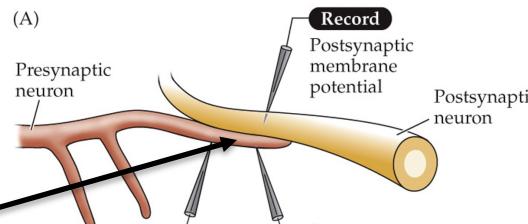
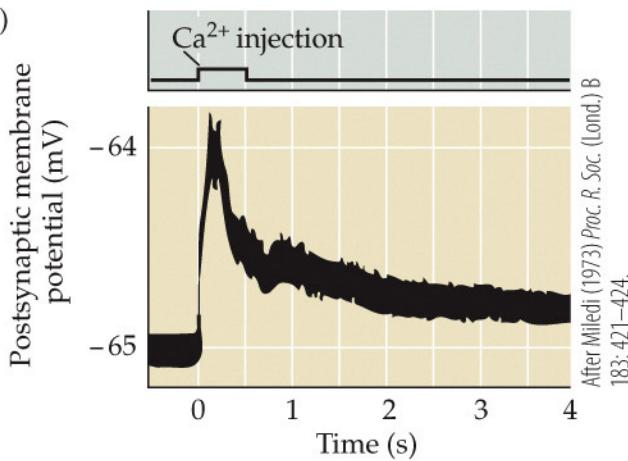
Evidence that a rise in presynaptic Ca^{2+} concentration triggers transmitter release from presynaptic terminals

(A)

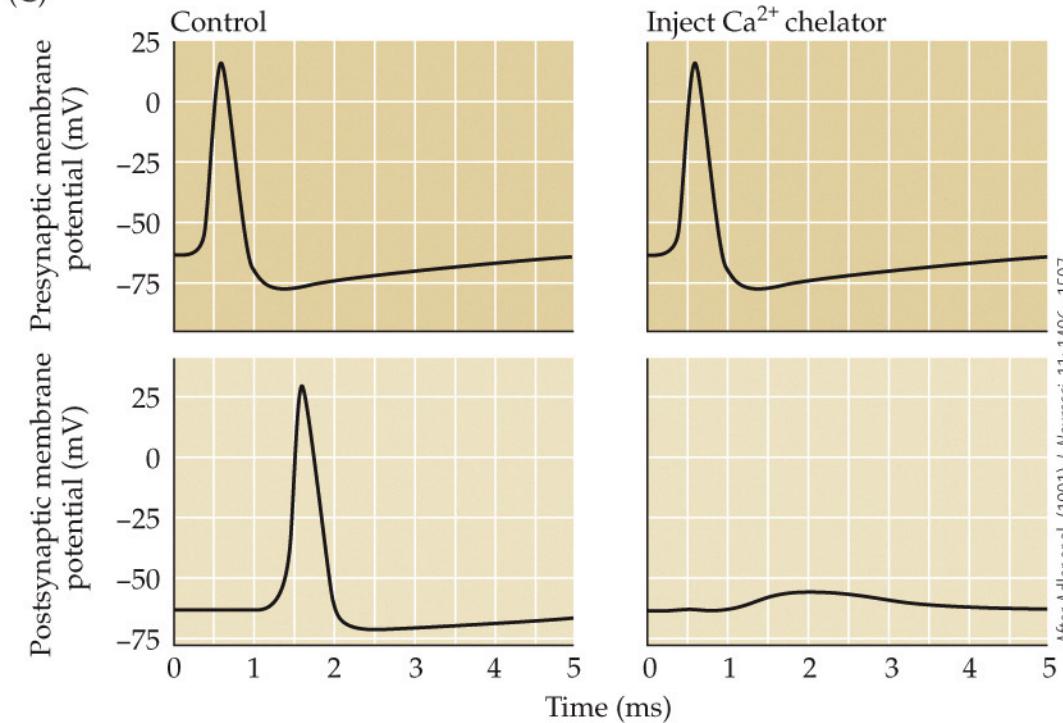


From Smith et al. (1993) *J. Physiol. (Lond.)* 472: 573–593.

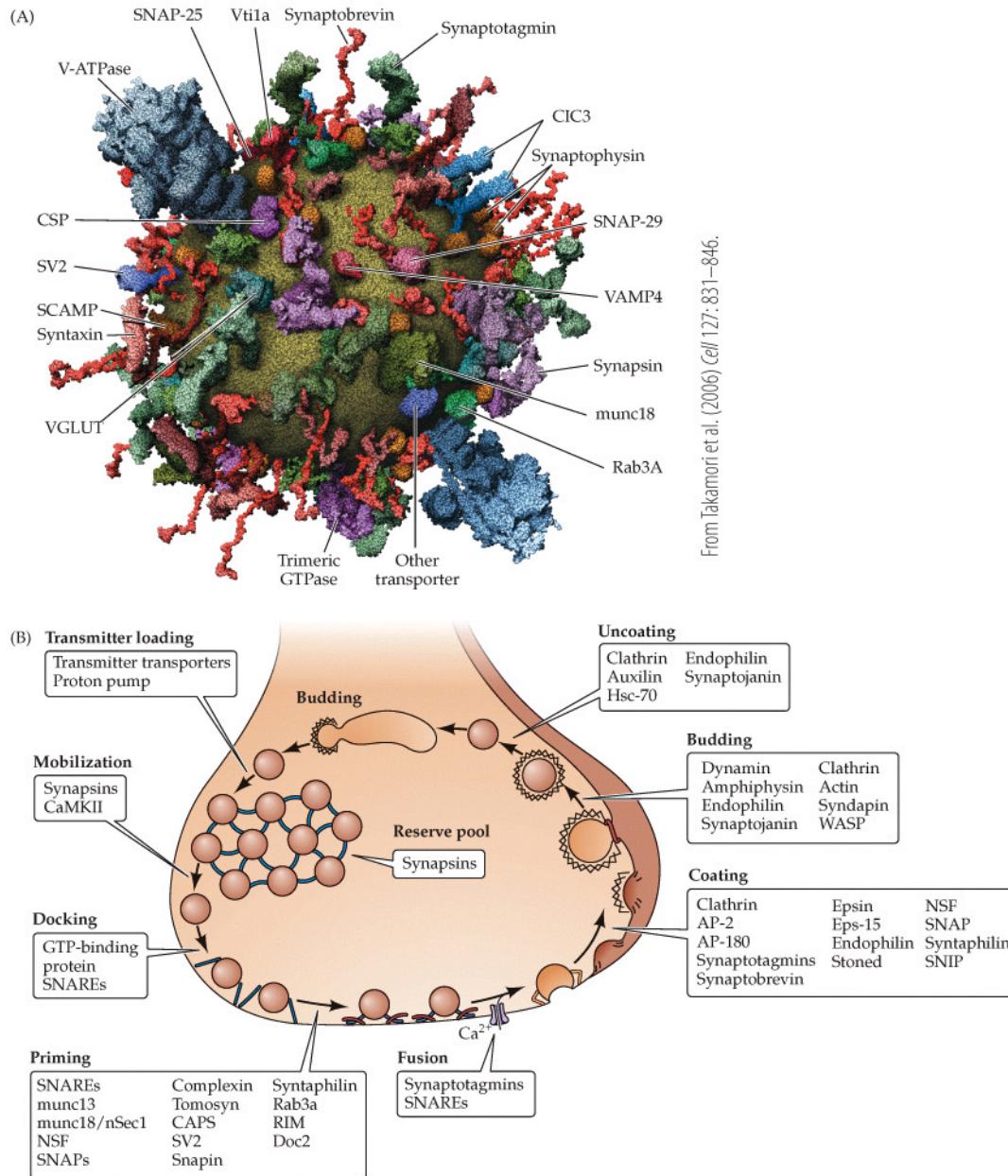
(B)



(C)

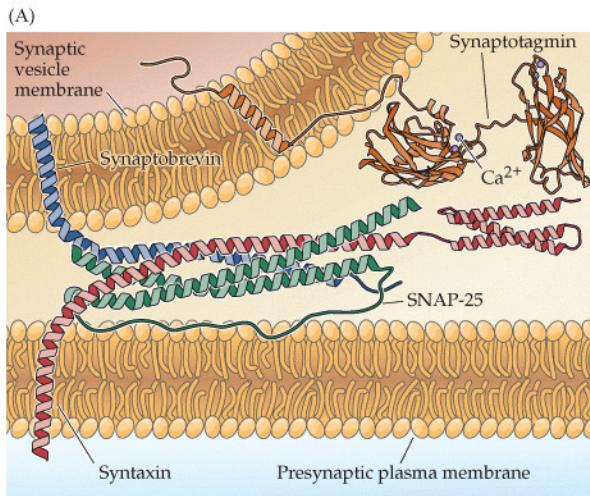


Presynaptic proteins and their roles in synaptic vesicle cycling



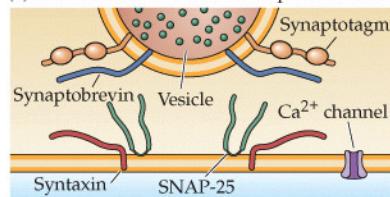
NEUROSCIENCE 6e, Figure 5.11
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Molecular mechanisms of exocytosis during neurotransmitter release

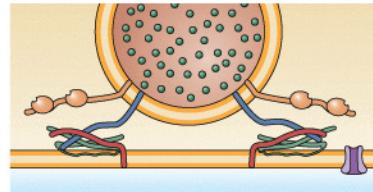


A from Sutton et al. (1998) *Nature* 395: 347–35. Also Madej et al. (2014) *Nucleic Acids Res.* D297–303. B after Zhou et al. (2015) *Nature* 525: 62–67.

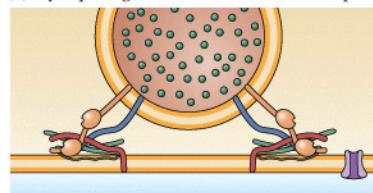
(B) (1) Free SNARES on vesicle and plasma membranes



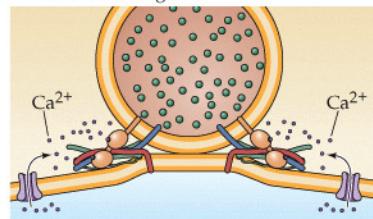
(2) SNARE complexes form as vesicle docks



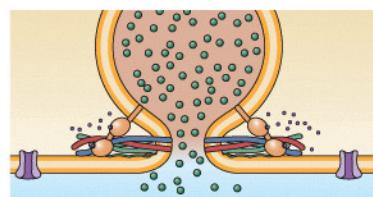
(3) Synaptotagmin binds to SNARE complex



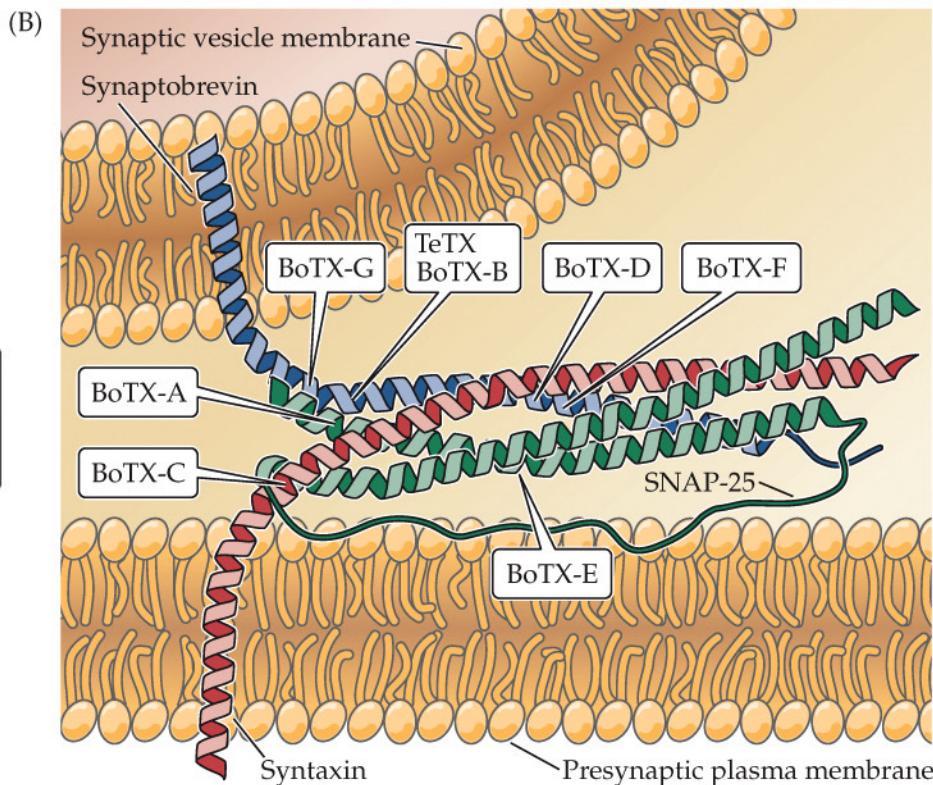
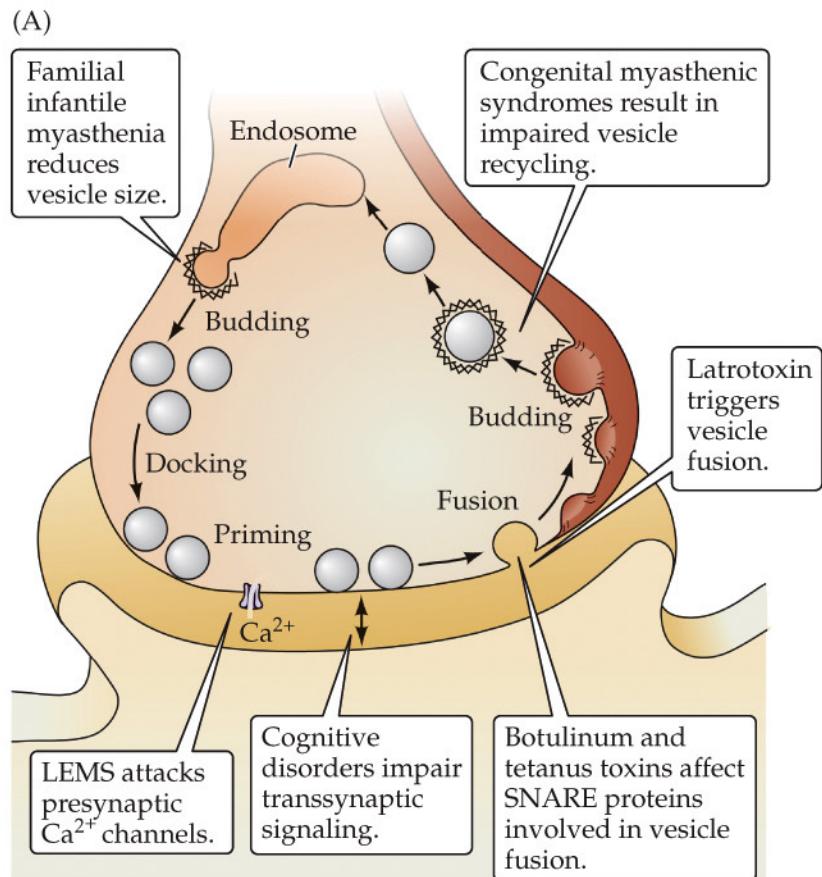
(4) Entering Ca^{2+} binds to synaptotagmin, leading to curvature of plasma membrane, which brings membranes together



(5) Fusion of membranes leads to exocytotic release of neurotransmitter

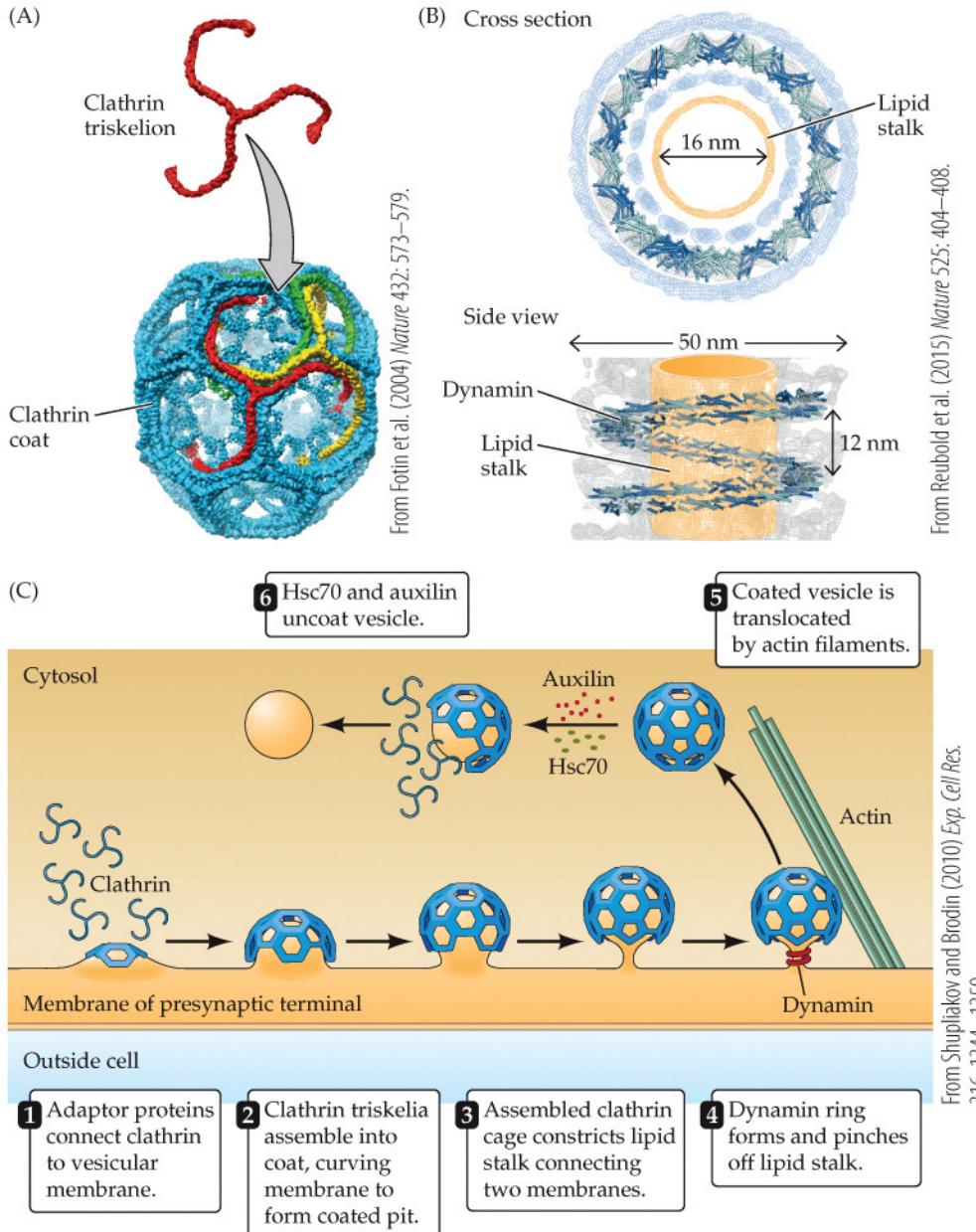


CLINICAL APPLICATIONS Disorders That Affect the Presynaptic Terminal



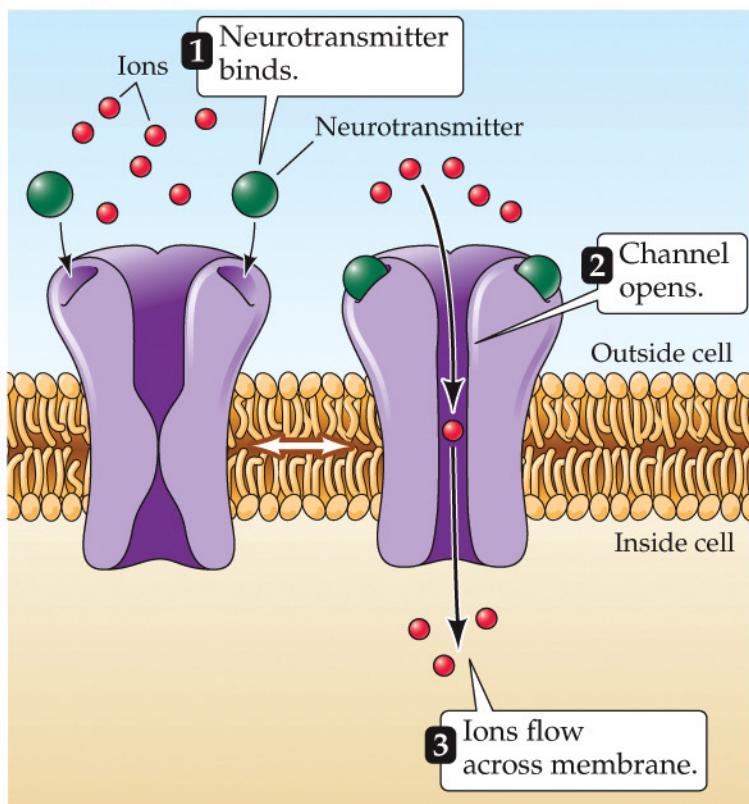
From Sutton et al. (1998) *Nature* 395:347–353.

Molecular mechanisms of endocytosis following neurotransmitter release

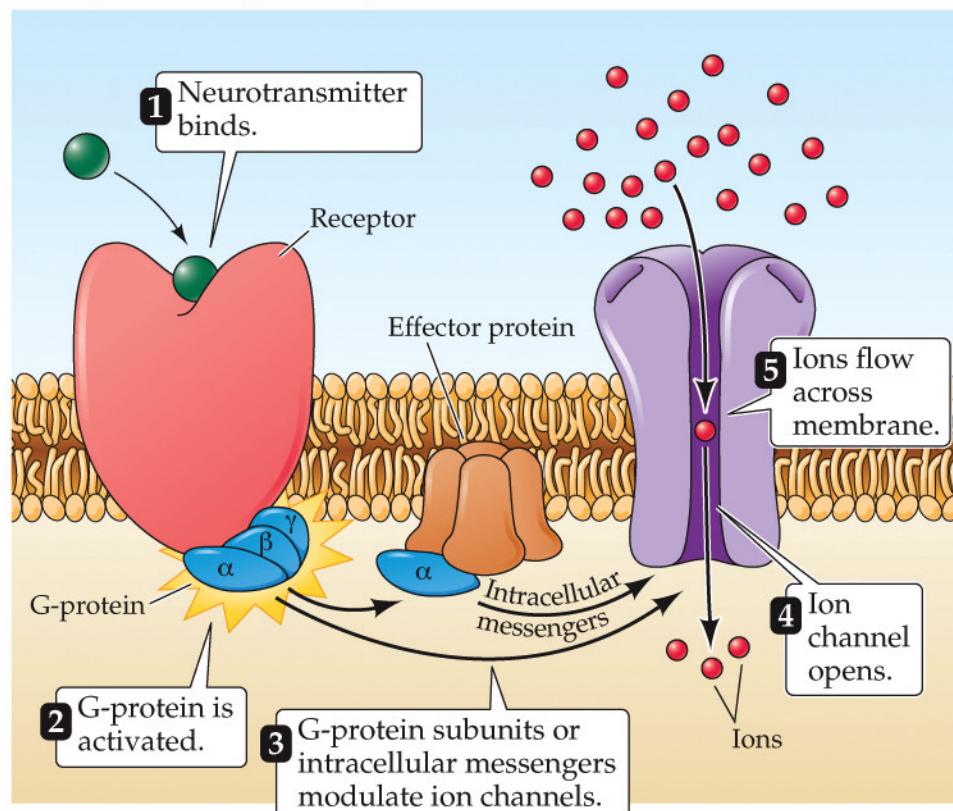


Two different types of neurotransmitter receptors

(A) Ligand-gated ion channels

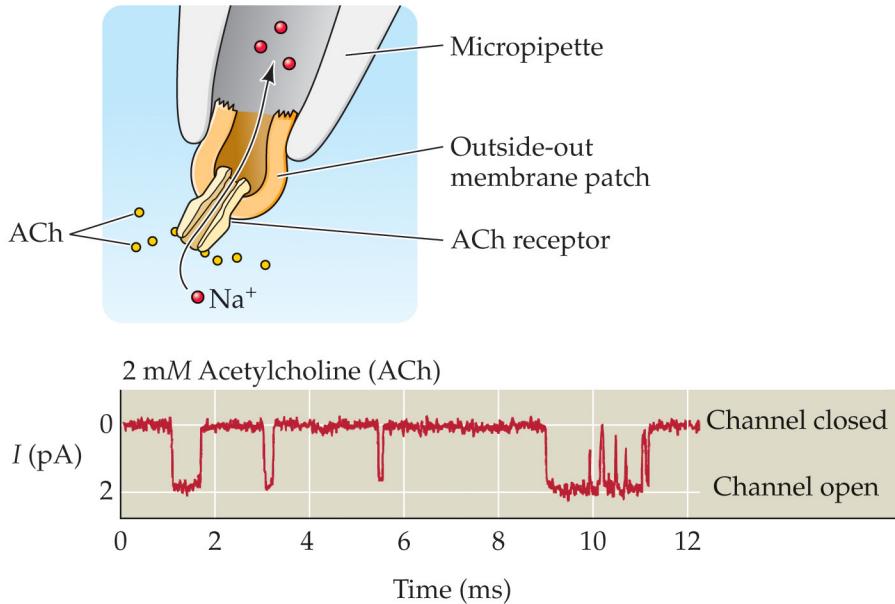


(B) G-protein-coupled receptors



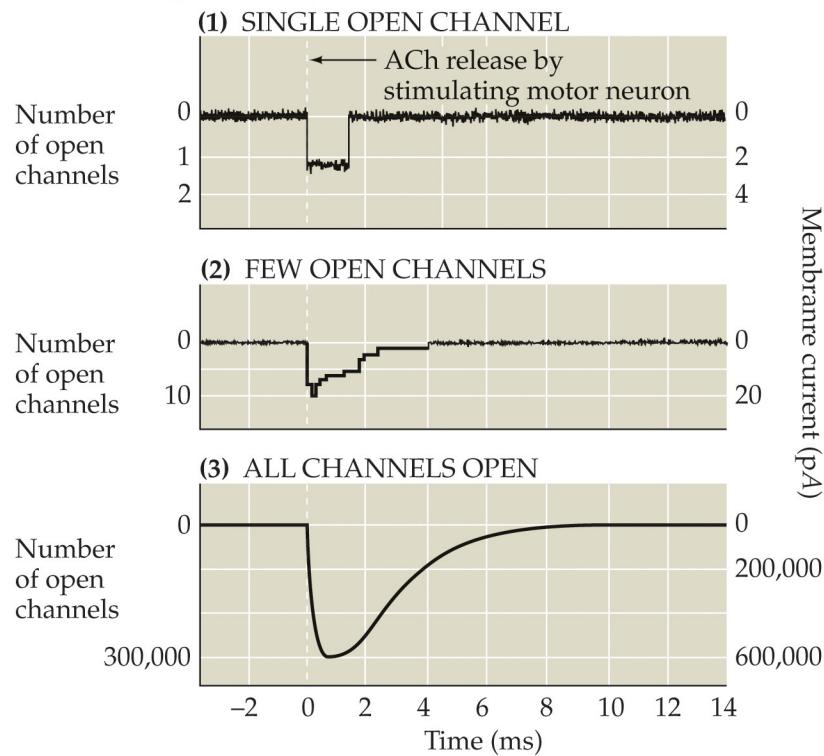
Activation of ACh receptors at neuromuscular synapses

(A) Patch clamp measurement of single ACh receptor current

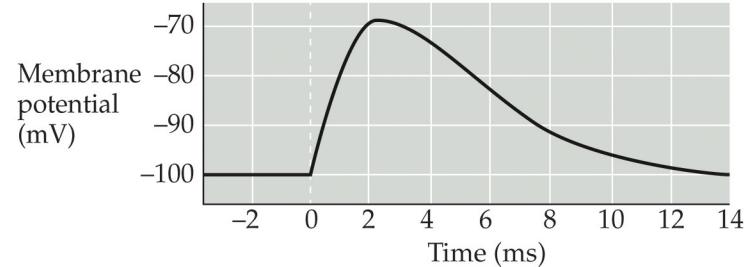


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(B) Currents produced by:

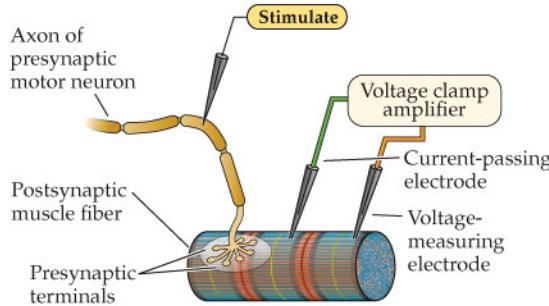


(C) Postsynaptic potential change (EPP) produced by EPC

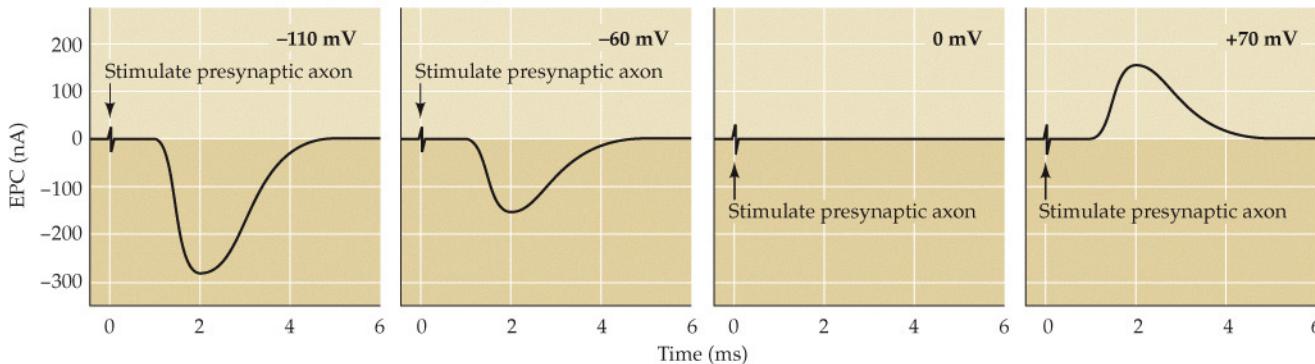


Influence of the postsynaptic membrane potential on end plate currents

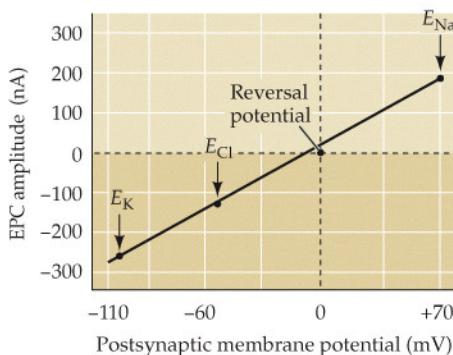
(A) Scheme for voltage clamping postsynaptic muscle fiber



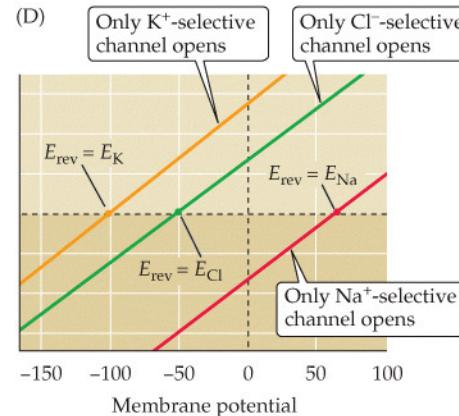
(B) Effect of membrane voltage on postsynaptic end plate currents (EPCs)



(C)



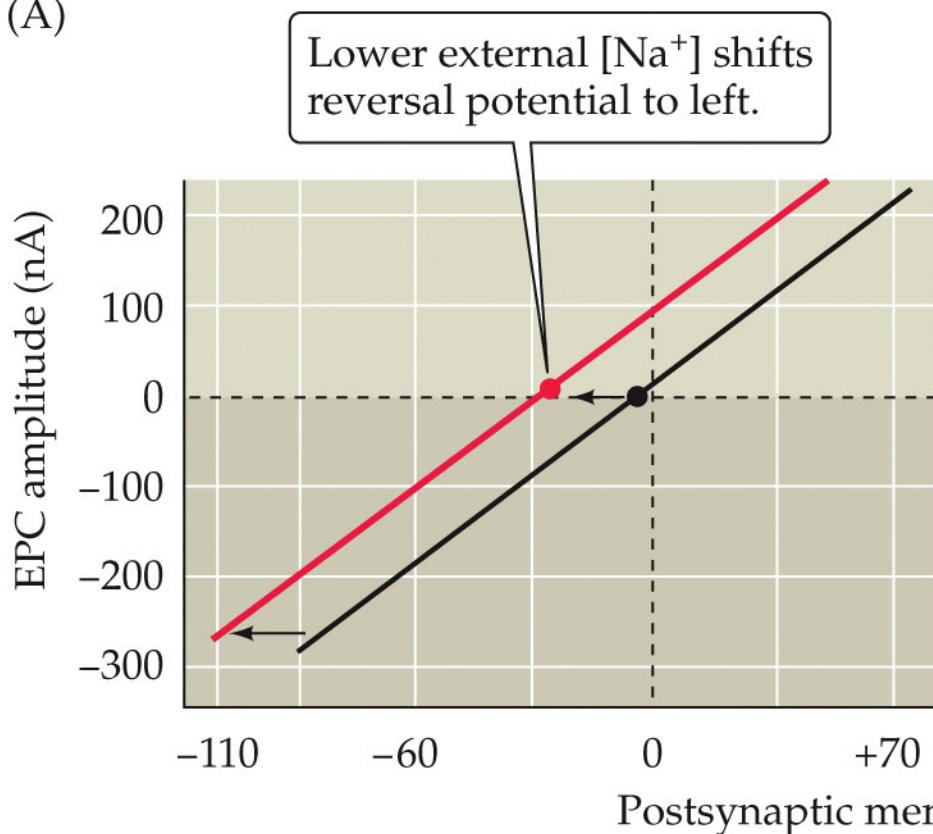
(D)



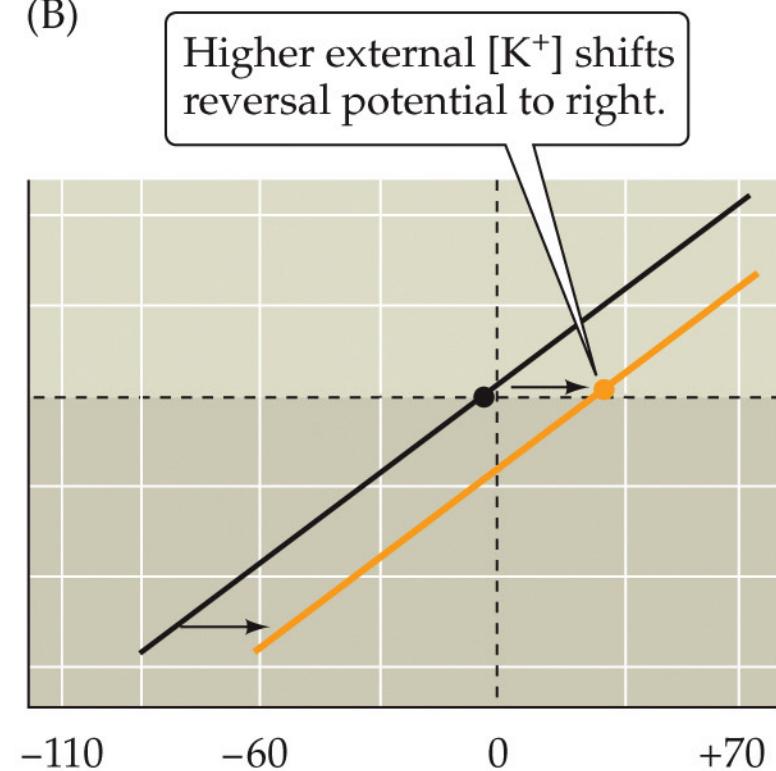
After Takeuchi and Takeuchi (1960). *J. Physiol.* 154: 52–67.

Reversal potential of the end plate current changes when ion gradients change

(A)



(B)

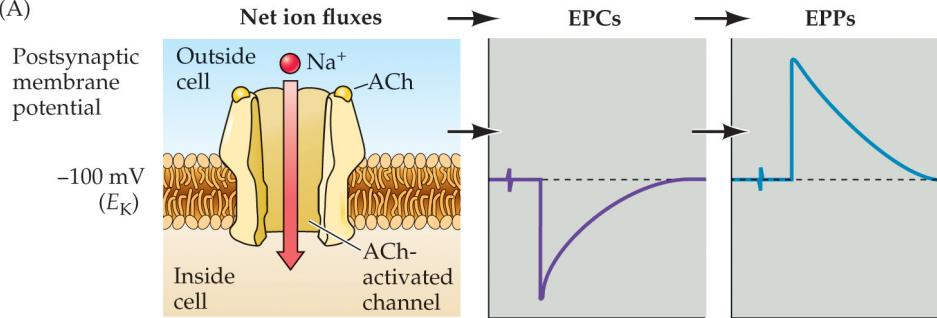


After Takeuchi and Takeuchi (1960) *J. Physiol.* 154: 52–67.

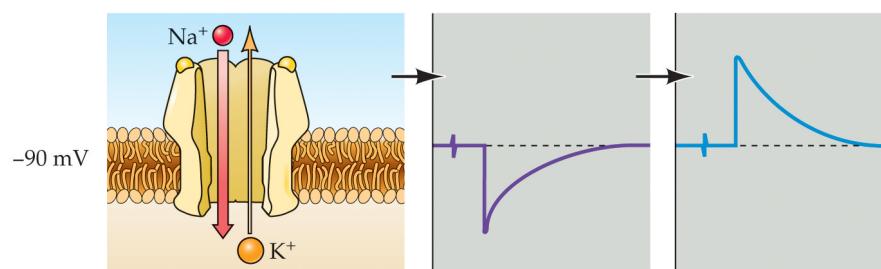
NEUROSCIENCE 6e, Figure 5.17
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Na^+ and K^+ movements during EPCs and EPPs

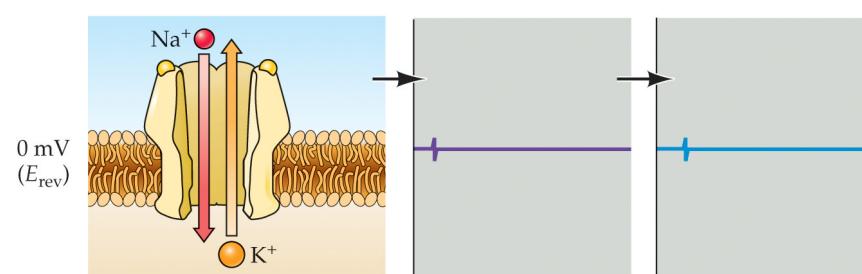
(A)



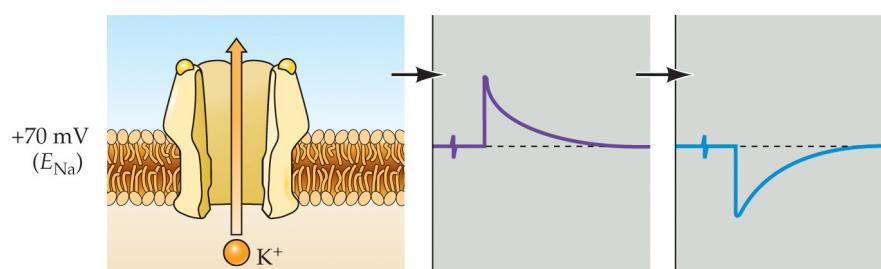
(B)



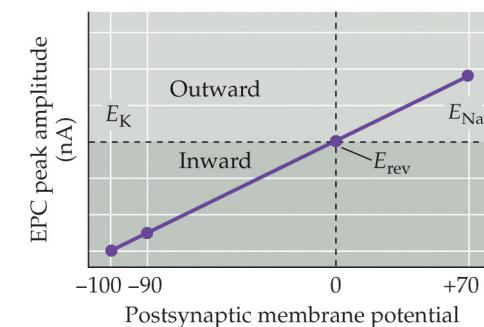
(C)



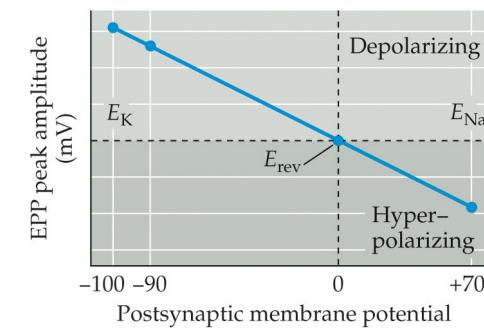
(D)



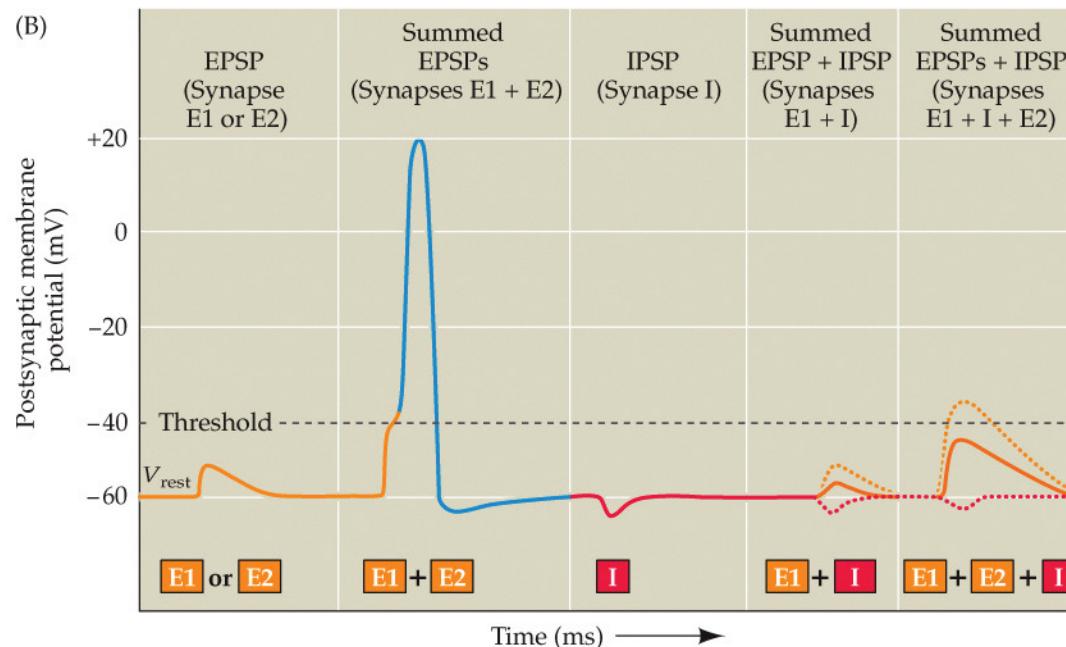
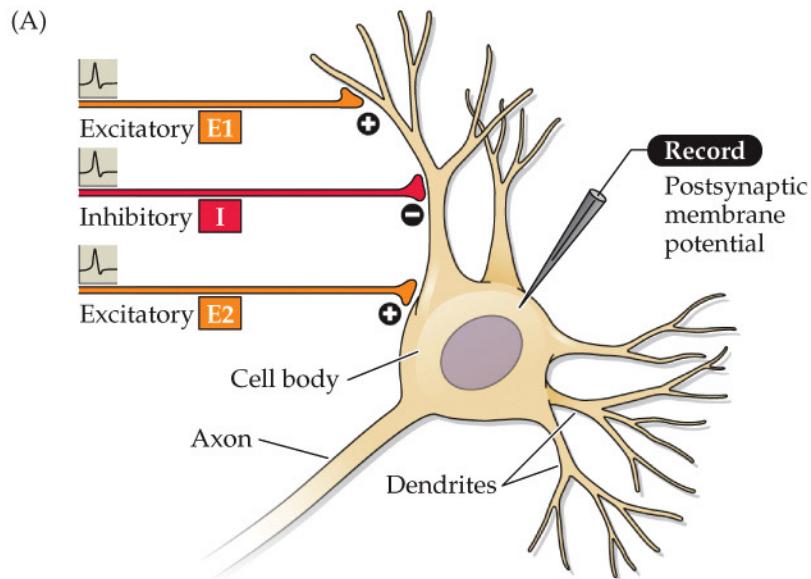
(E)



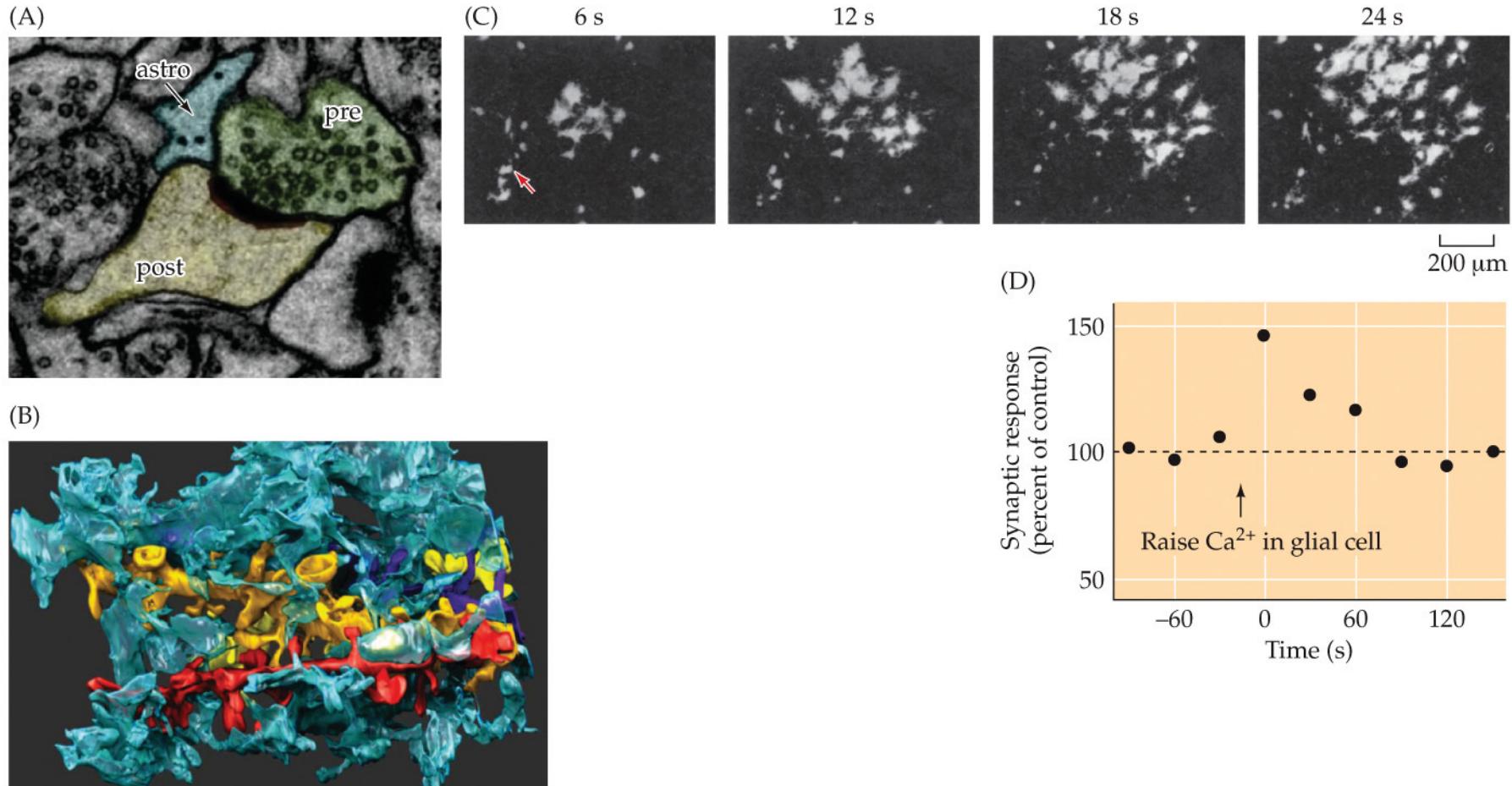
(F)



Summation of postsynaptic potentials



The Tripartite Synapse



A,B from Witcher et al.(2007) *Glia* 55: 13–24. C from Cornell-Bell et al. (1990) *Science* 247: 470-473. D from Perea and Araque (2007) *Science* 317: 1083–1086.

Overview of postsynaptic signaling

