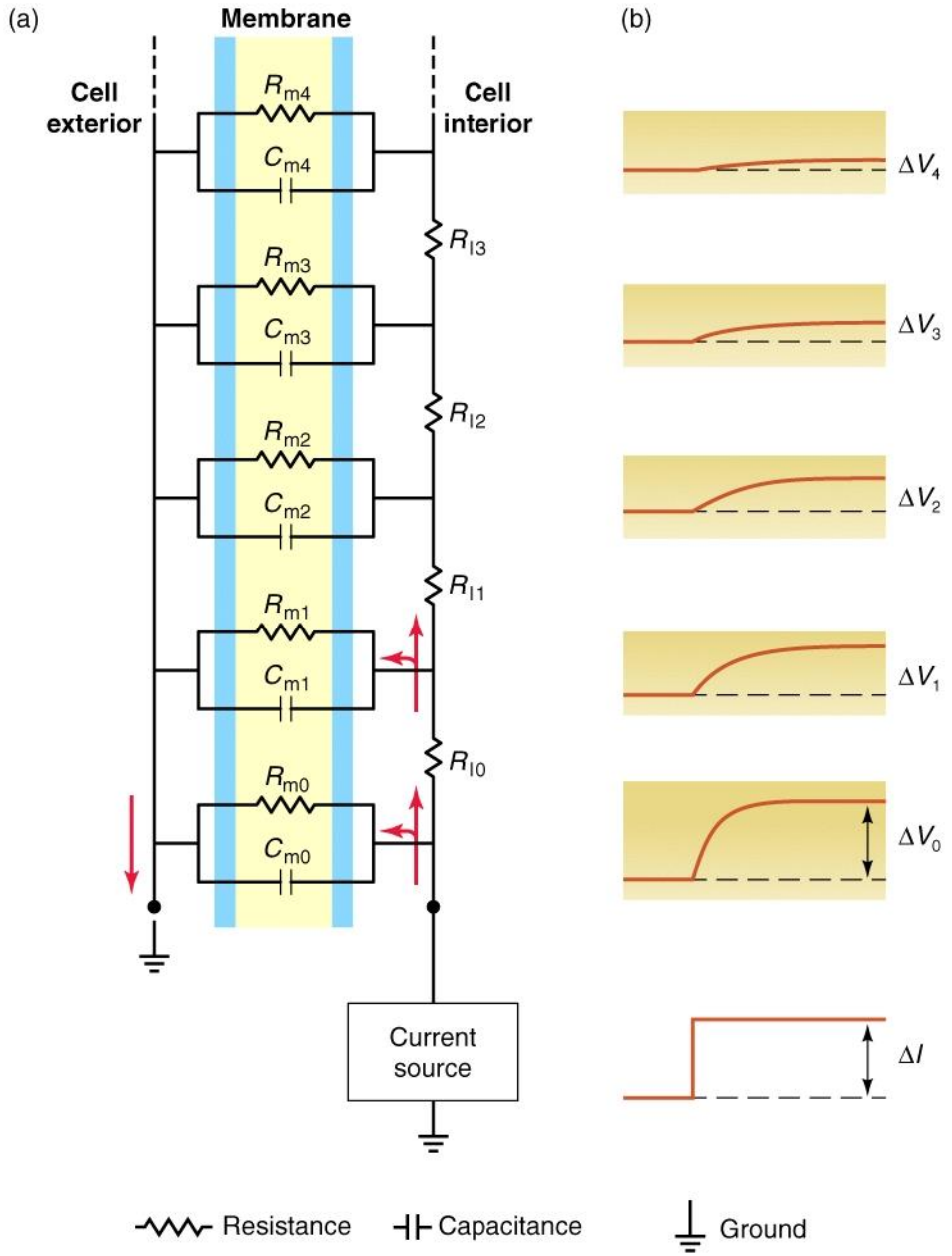
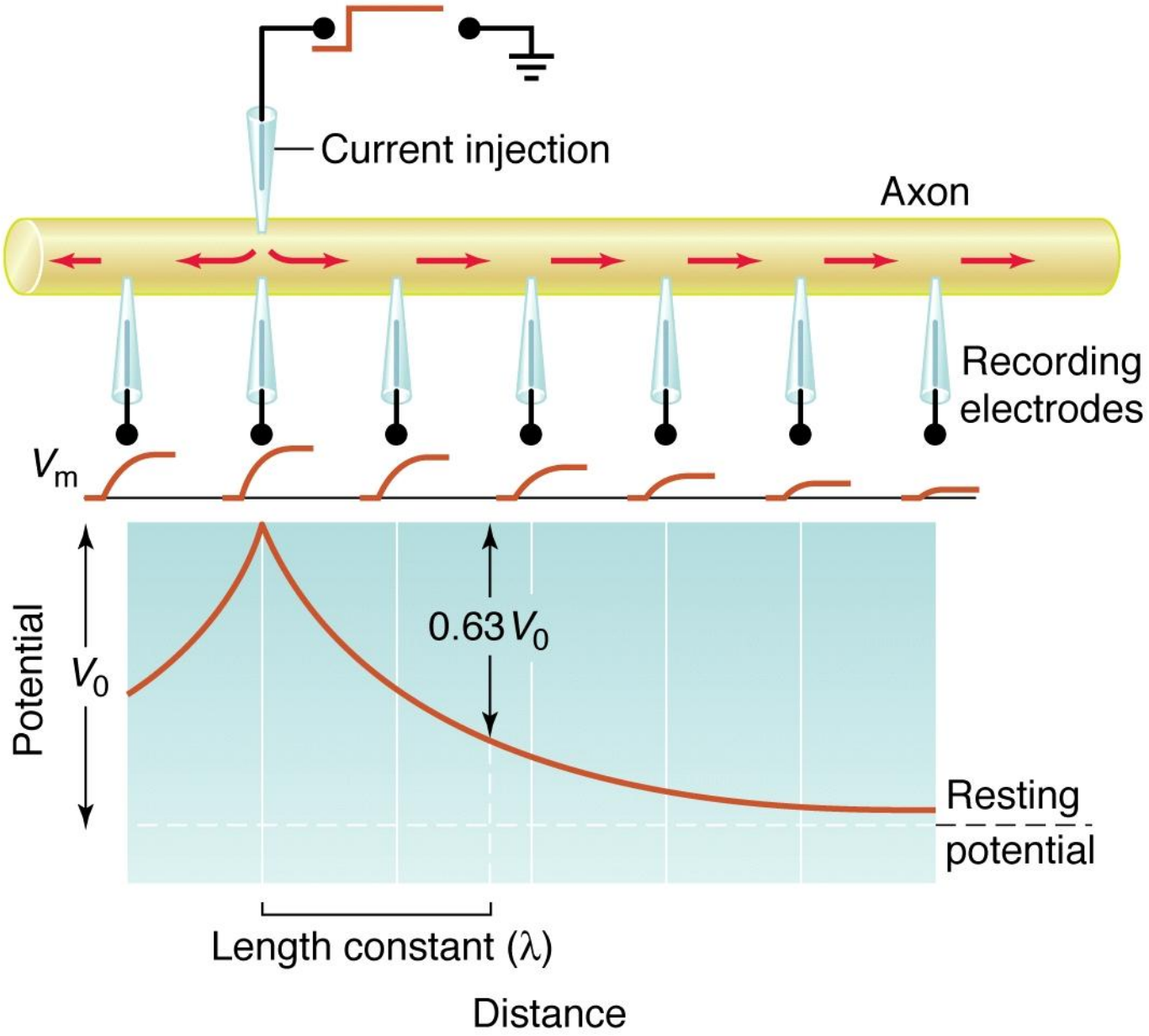
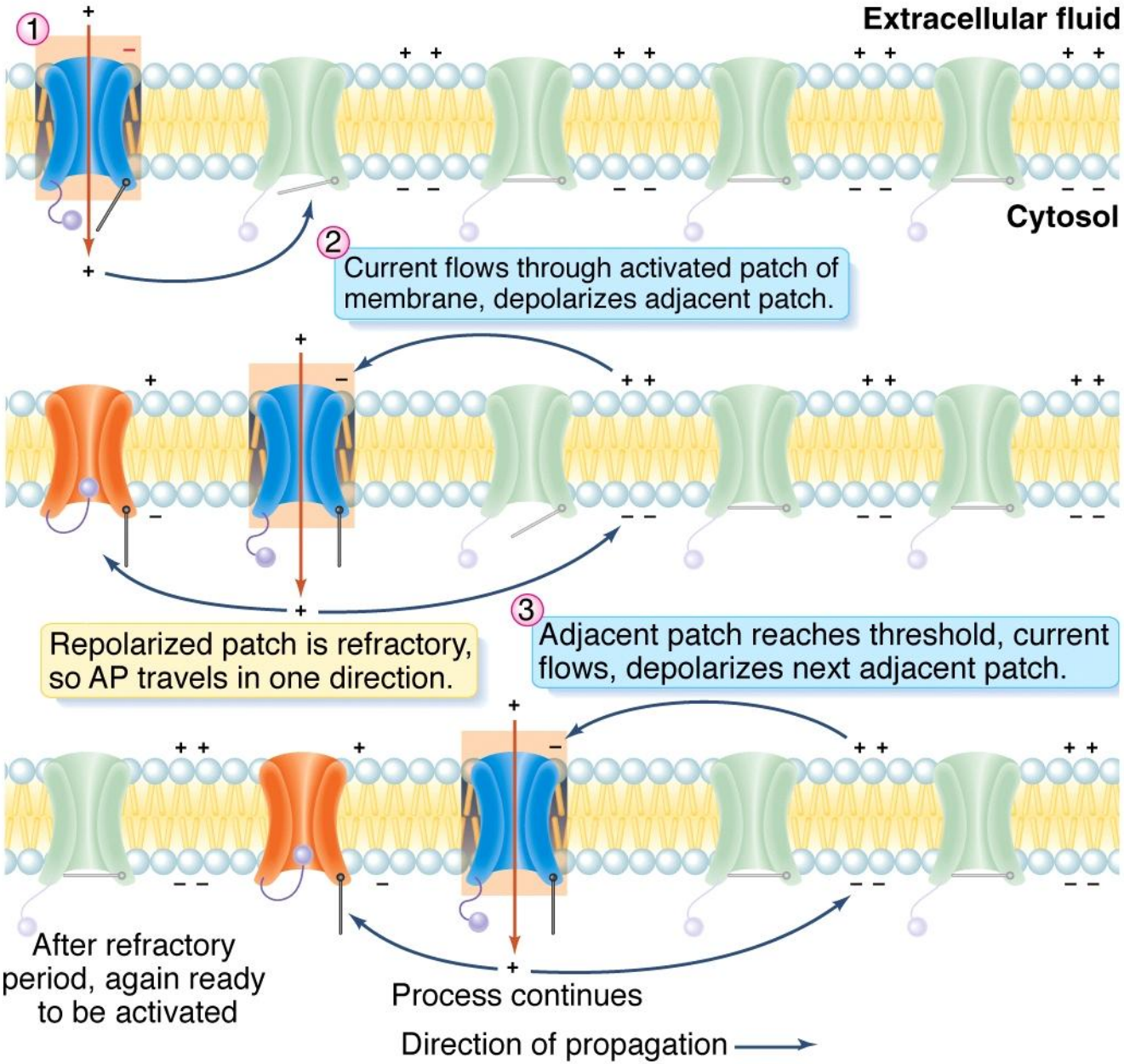
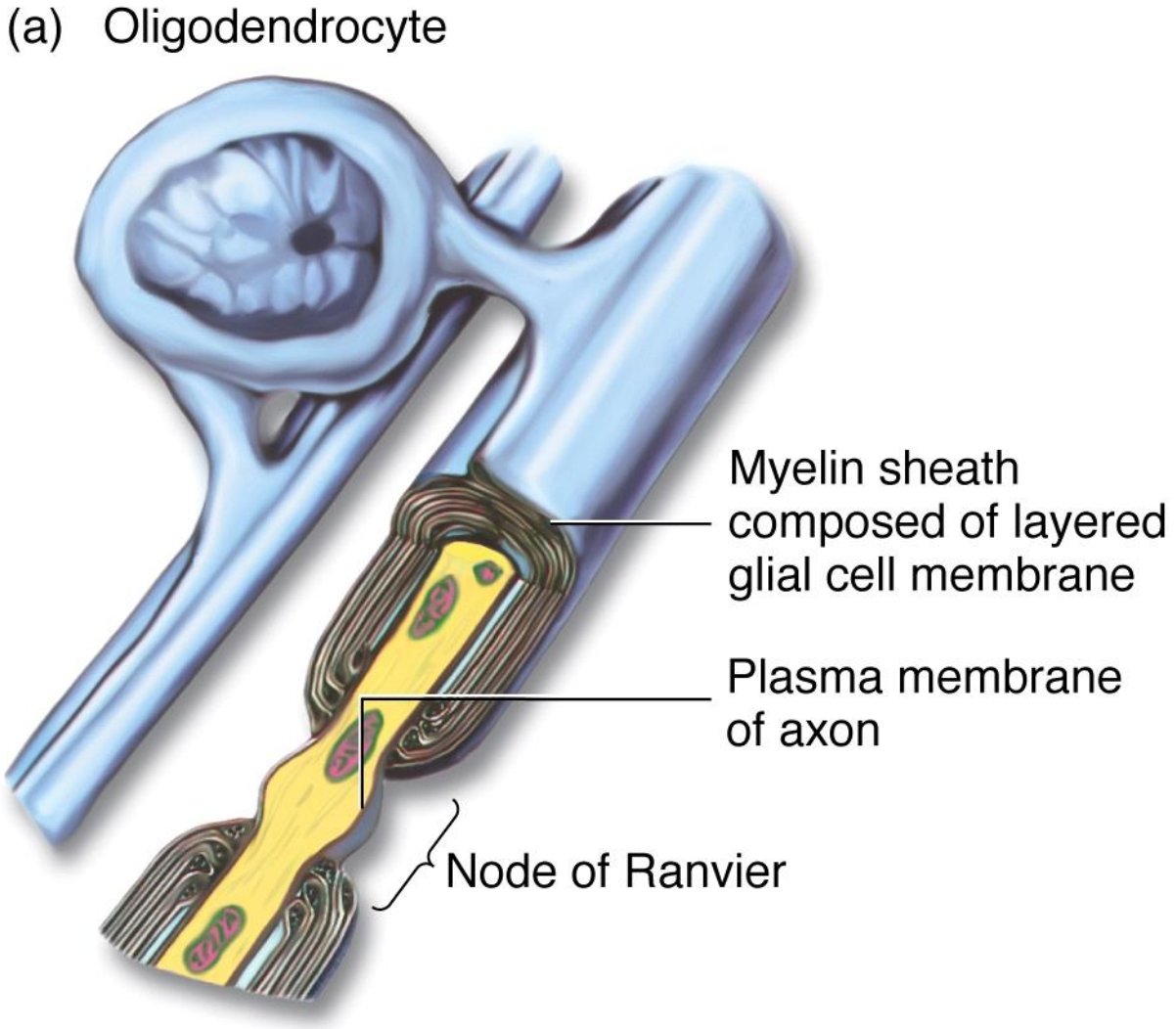
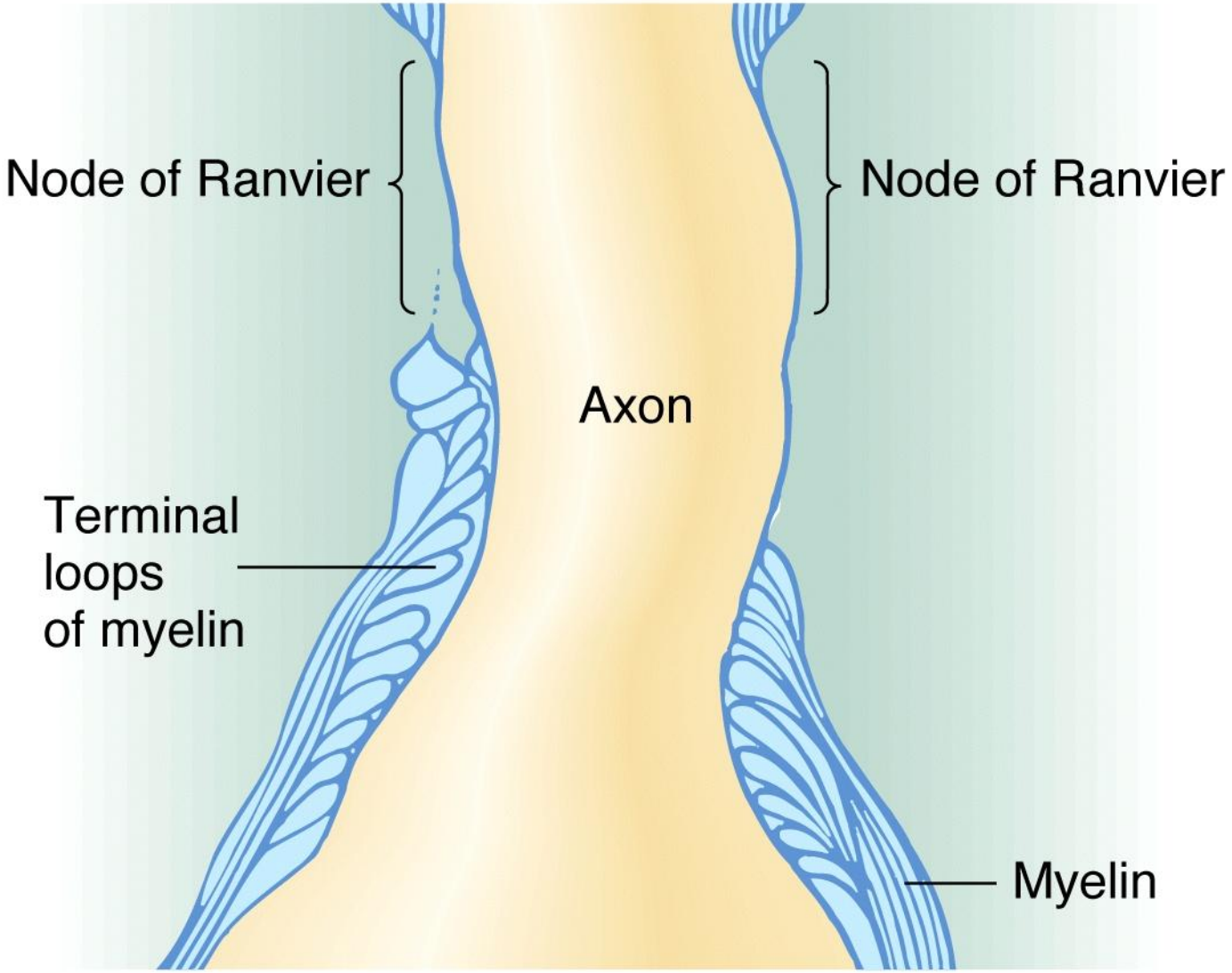

(a)
Membrane
(b)
Cell exterior
Cell interior
R_{m4}
C_{m4}
R_{I3}
R_{m3}
C_{m3}
R_{I2}
R_{m2}
C_{m2}
R_{I1}
R_{m1}
C_{m1}
R_{I0}
R_{m0}
C_{m0}
Current source
ΔV_4
ΔV_3
ΔV_2
ΔV_1
ΔV_0
ΔI
Resistance
Capacitance
Ground


Current injection
Axon
Recording electrodes
V_m
Potential
V_0
0.63 V_0
Resting potential
Length constant (λ)
Distance


Extracellular fluid
Cytosol
1
2
Current flows through activated patch of membrane, depolarizes adjacent patch.
Repolarized patch is refractory, so AP travels in one direction.
3
Adjacent patch reaches threshold, current flows, depolarizes next adjacent patch.
After refractory period, again ready to be activated
Process continues
Direction of propagation


(a) Oligodendrocyte
Myelin sheath composed of layered glial cell membrane
Plasma membrane of axon
Node of Ranvier


Node of Ranvier
Node of Ranvier
Axon
Terminal
loops
of myelin
Myelin

(b)

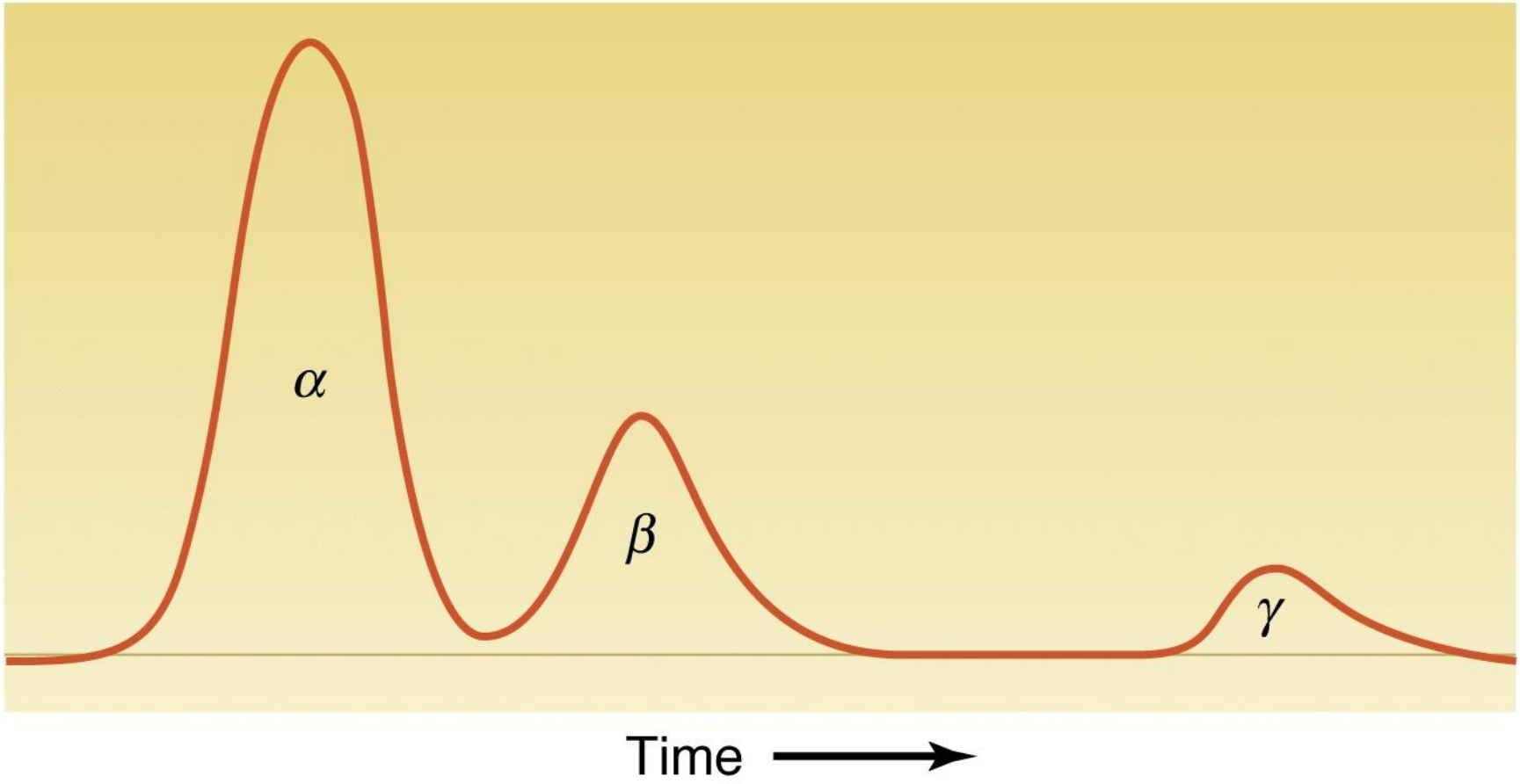
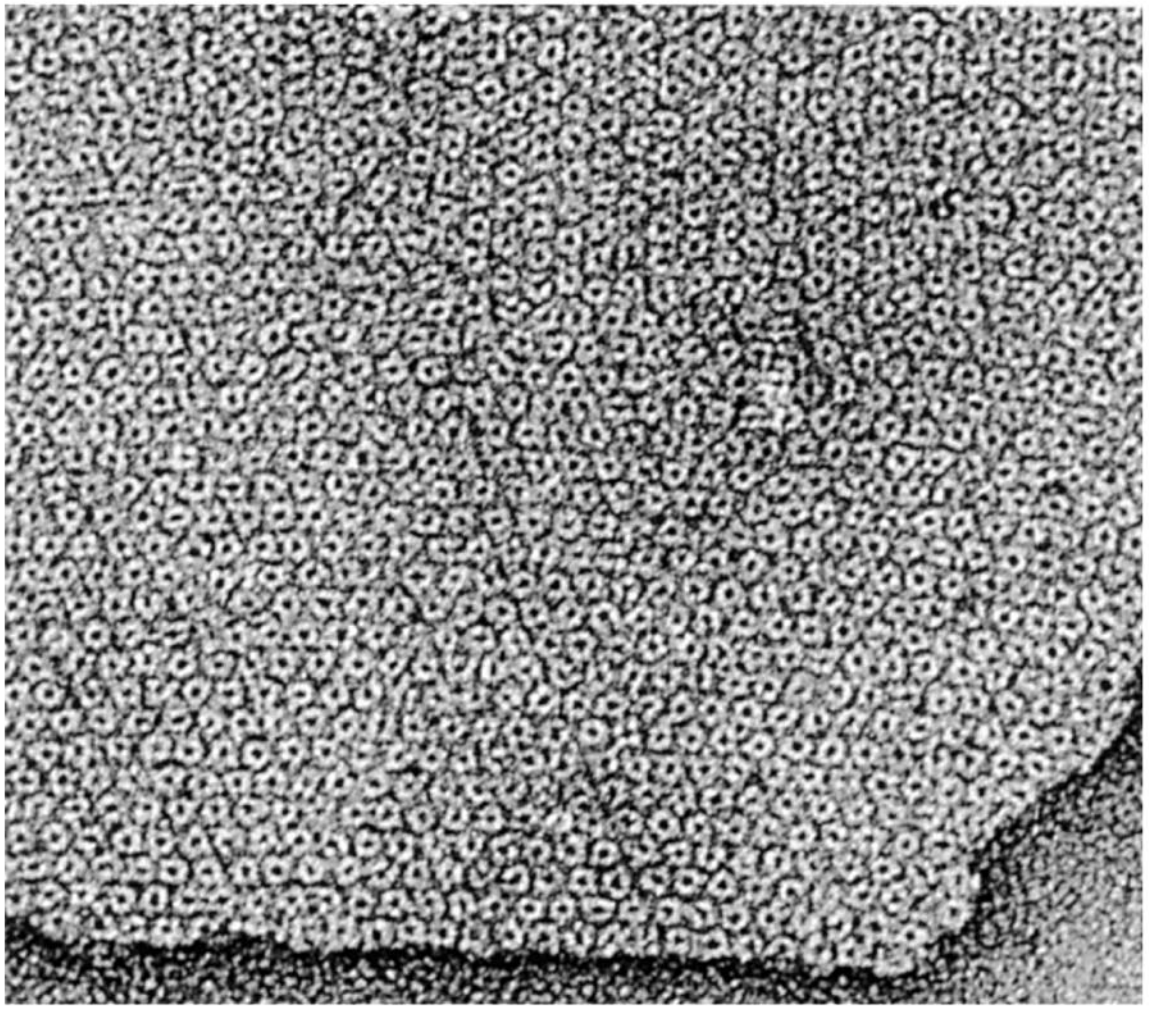


Table 6-1 The diameter of frog axons and the presence or absence of myelination control the conduction velocity.

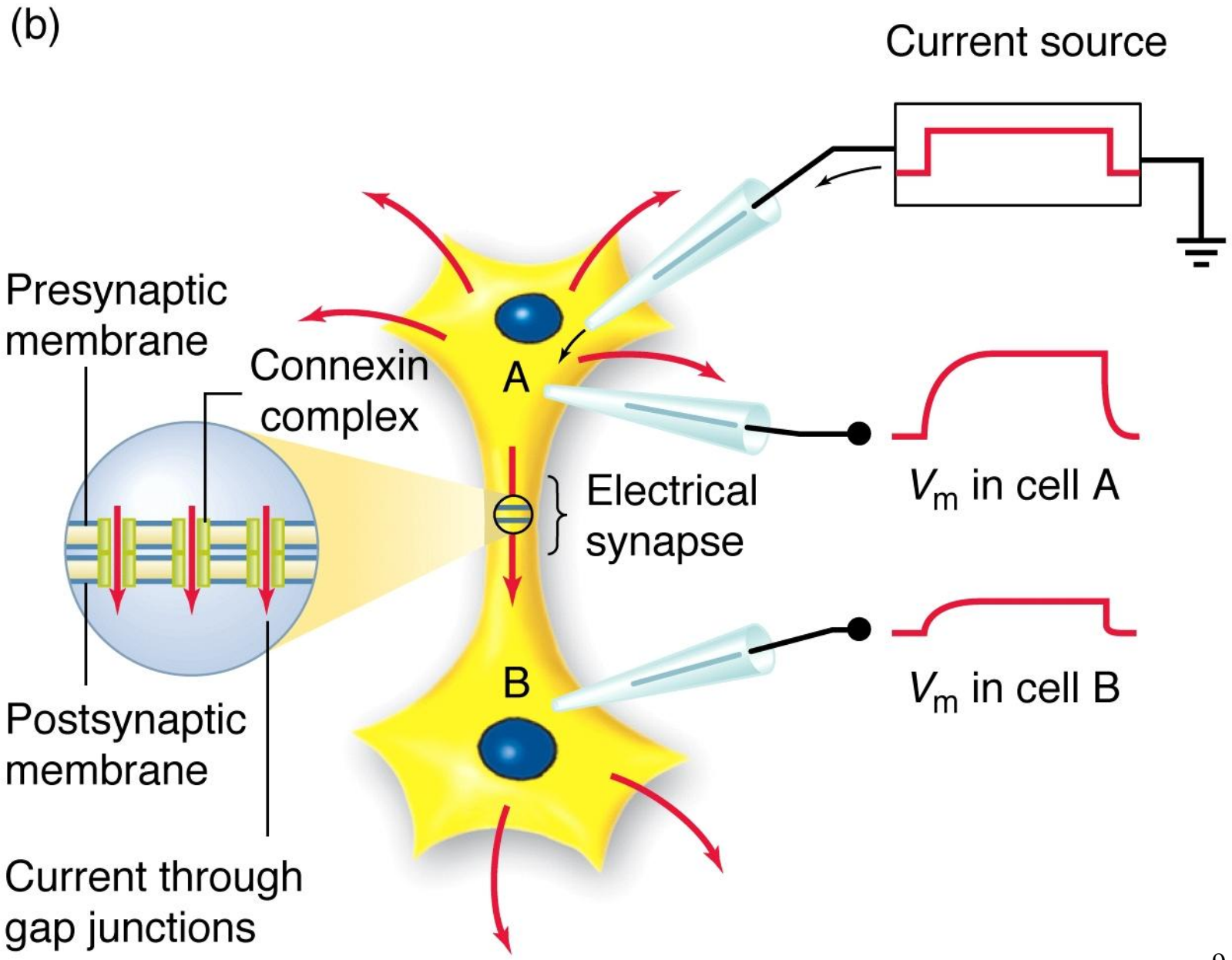
Fiber type	Average axon diameter (μm)	Conduction velocity ($m \cdot s^{-1}$)
Myelinated fibers		
Aα	18.5	42
Aβ	14.0	25
Aγ	11.0	17
B	Approximately 3.0	4.2
Unmyelinated fibers		
C	2.5	0.4–0.5

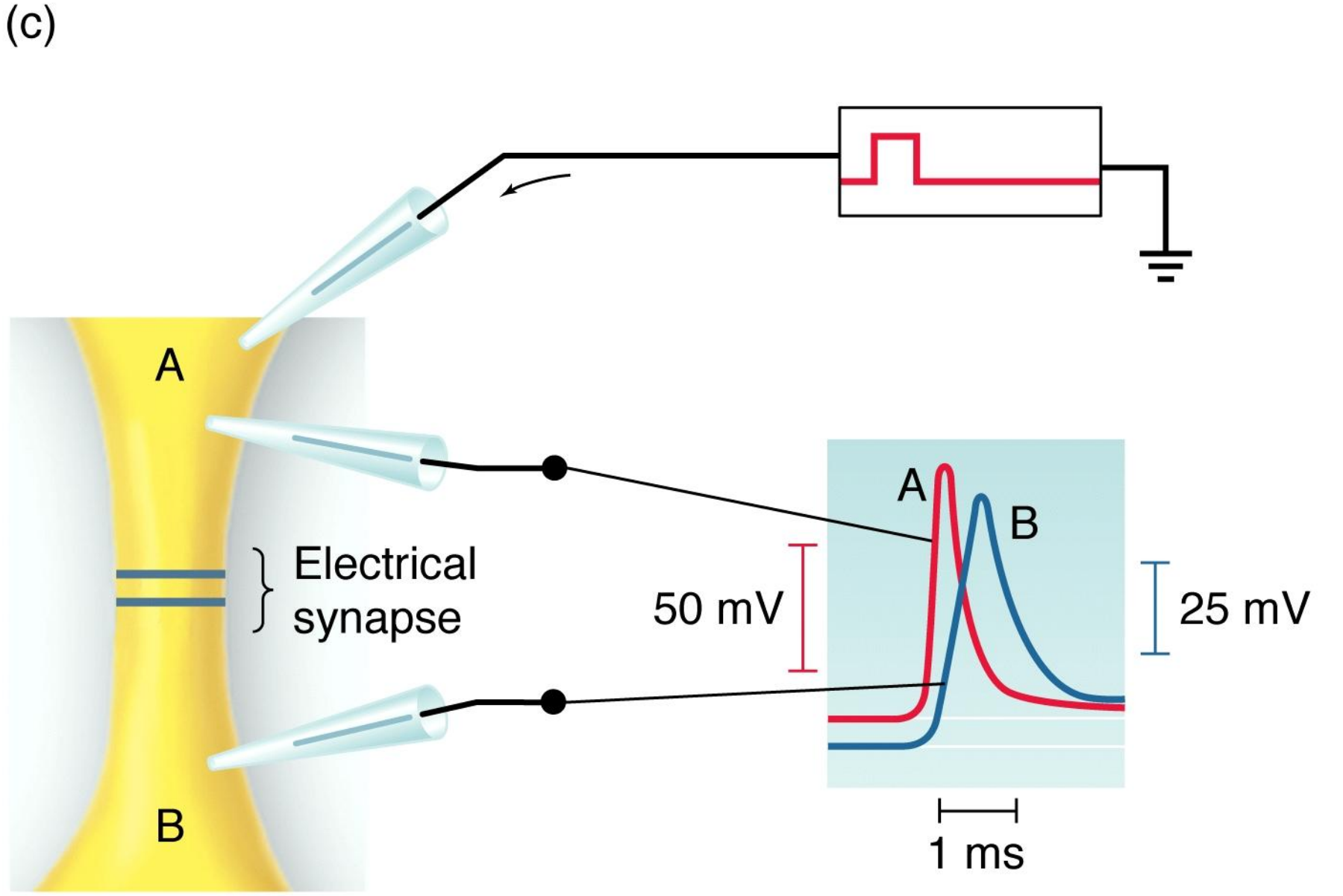
Source: Erlanger and Gasser, 1937.

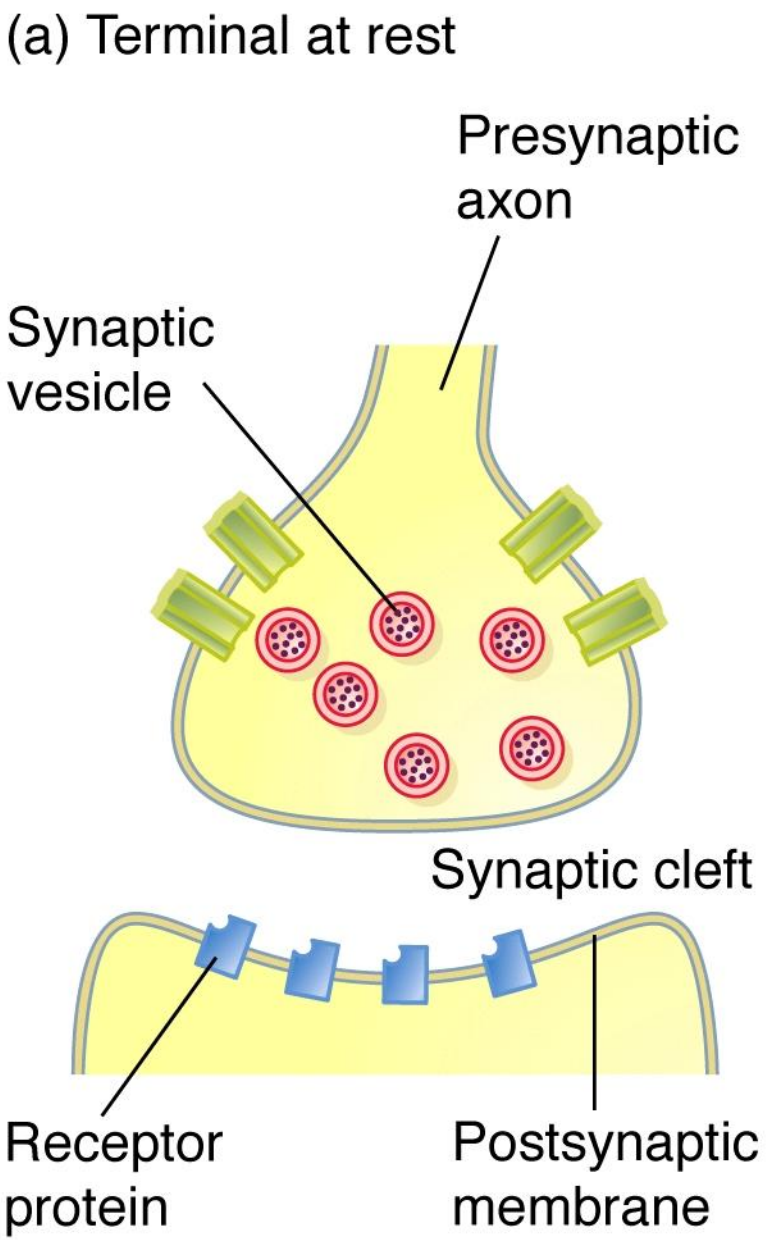
(a)



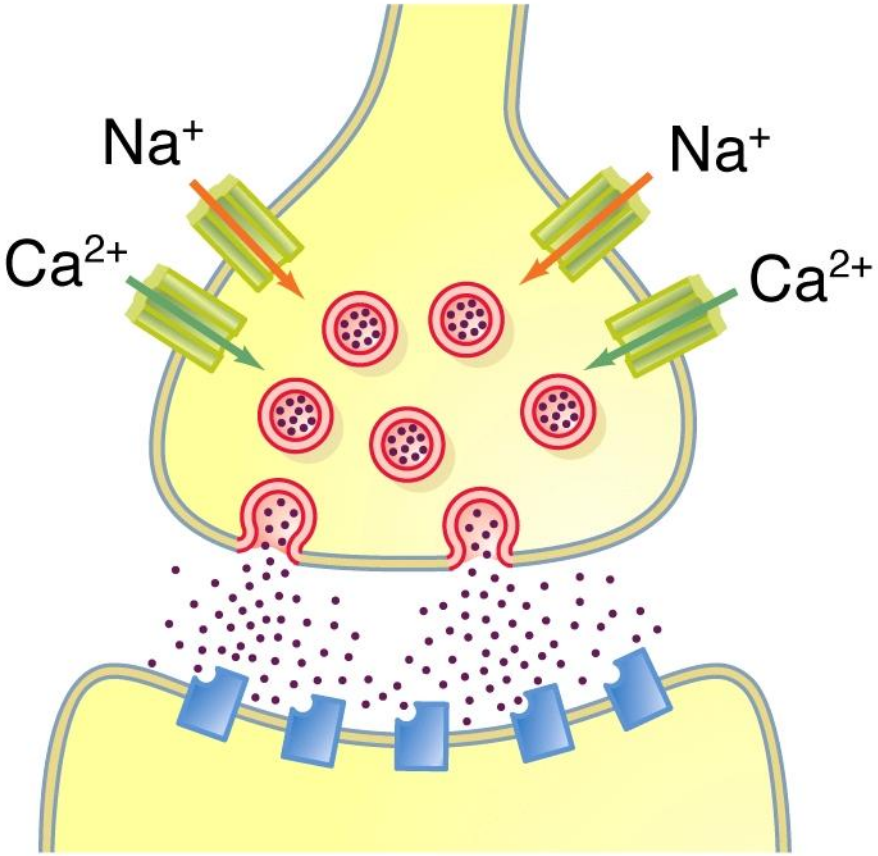
50 nm


(b)
Current source
Presynaptic membrane
Connexin complex
A
Electrical synapse
V_m in cell A
V_m in cell B
B
Postsynaptic membrane
Current through gap junctions

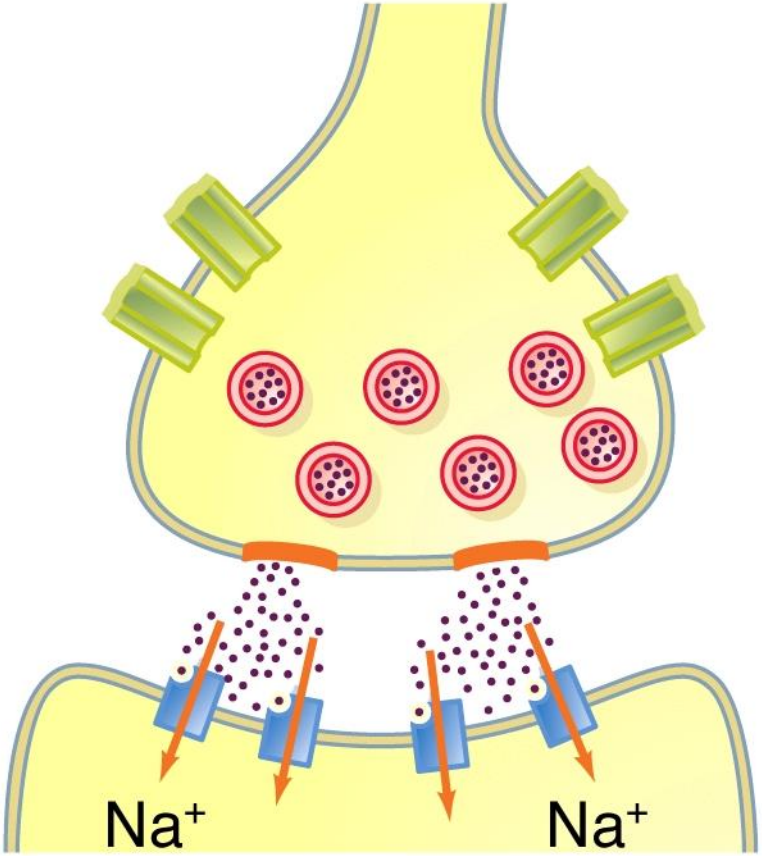

(c)
A
B
Electrical synapse
50 mV
A
B
25 mV
1 ms


(a) Terminal at rest
Presynaptic axon
Synaptic vesicle
Synaptic cleft
Receptor protein
Postsynaptic membrane

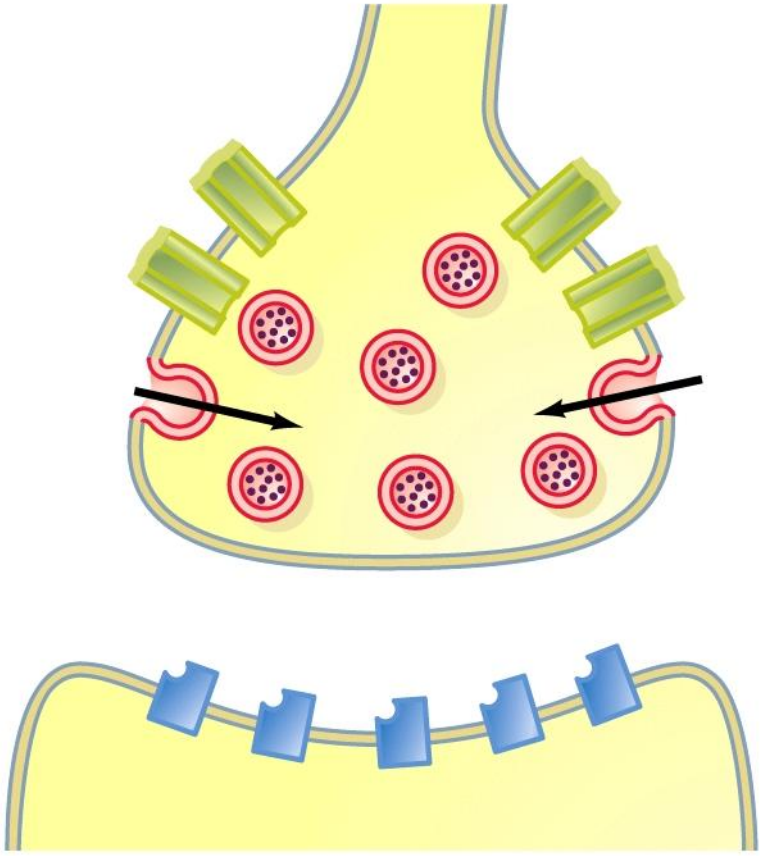
(b) AP arrives; vesicles fuse with terminal membrane, producing exocytosis of transmitter.



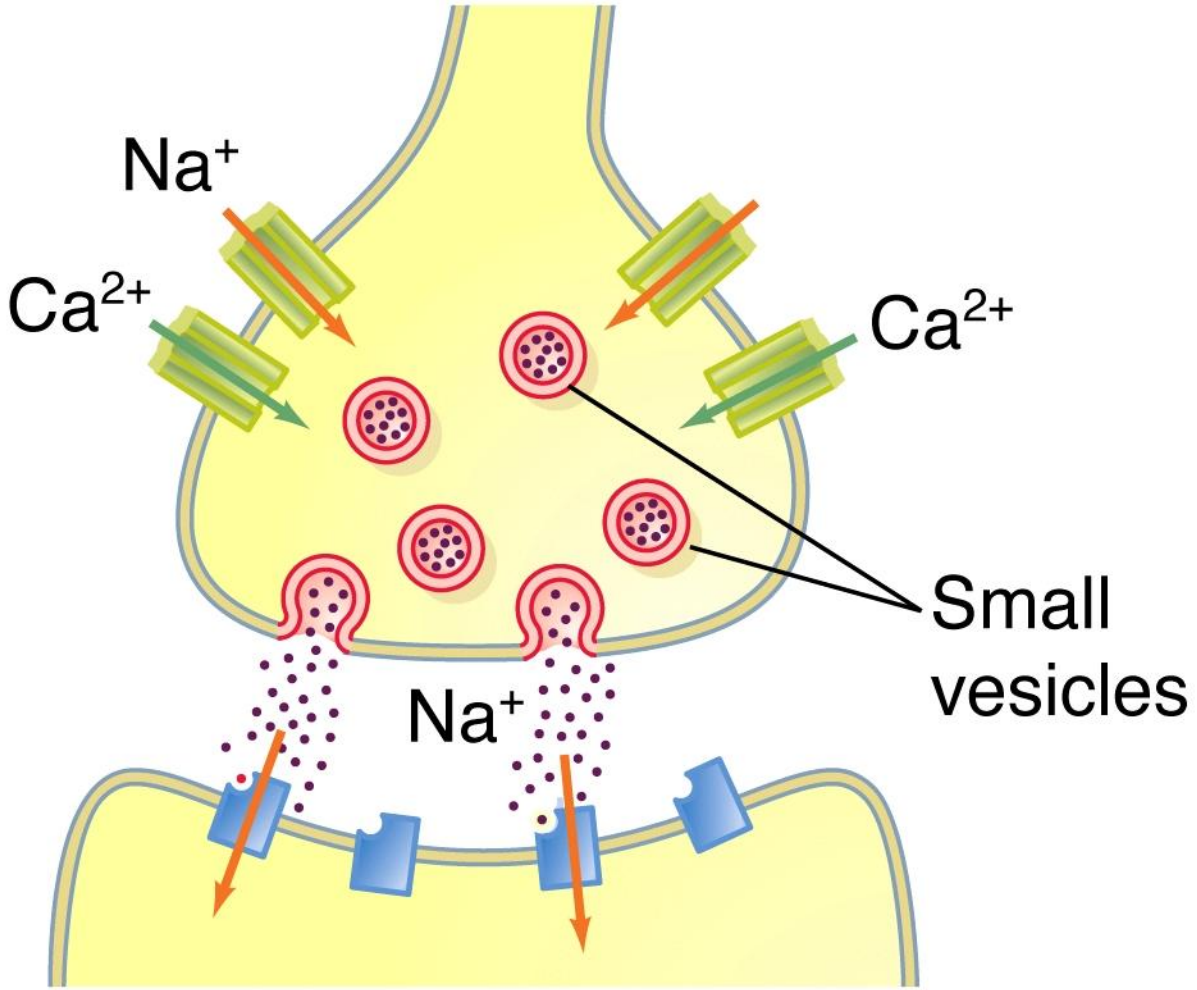
(c) Transmitter binds to postsynaptic receptor proteins; ion channels open.

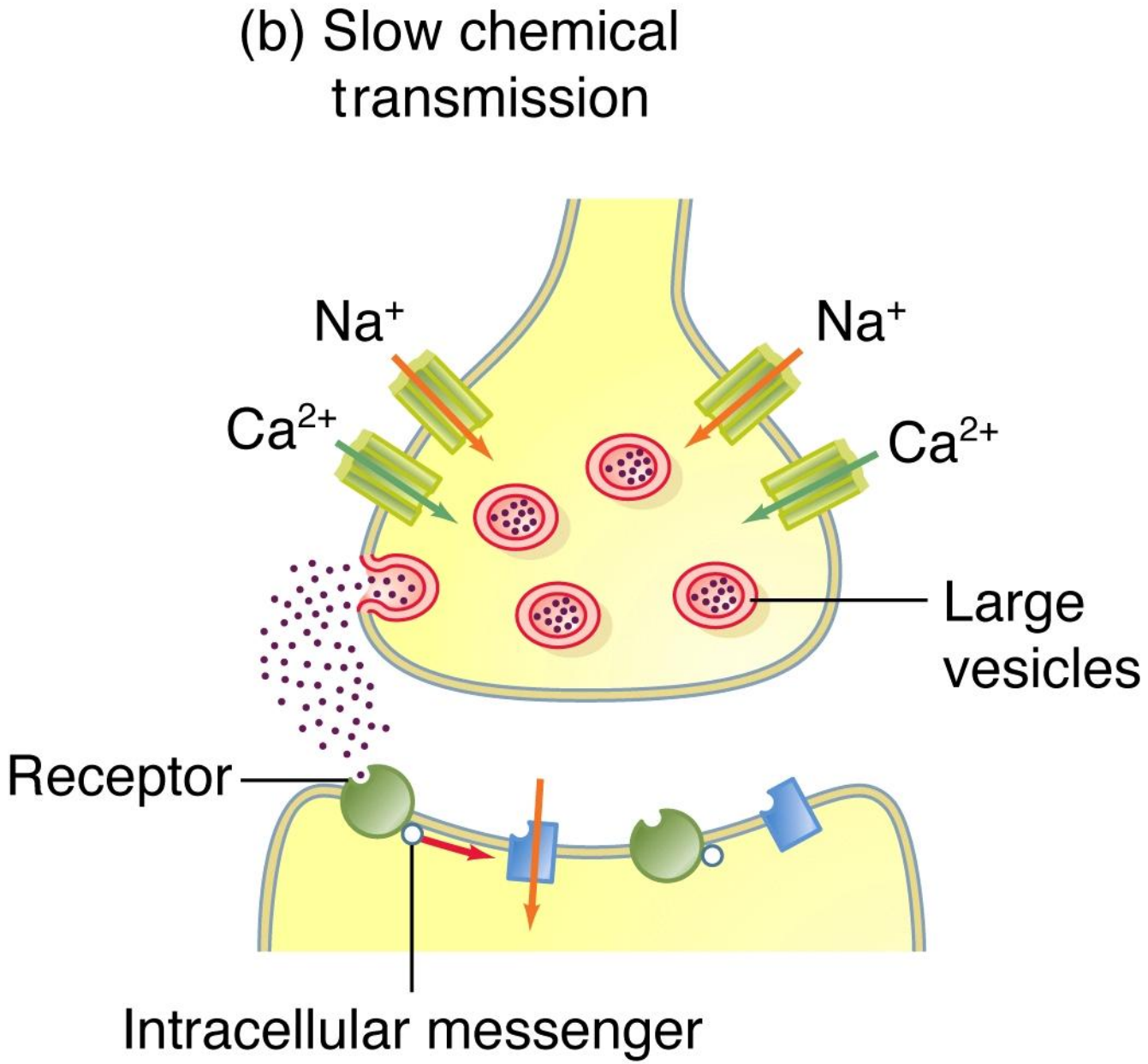


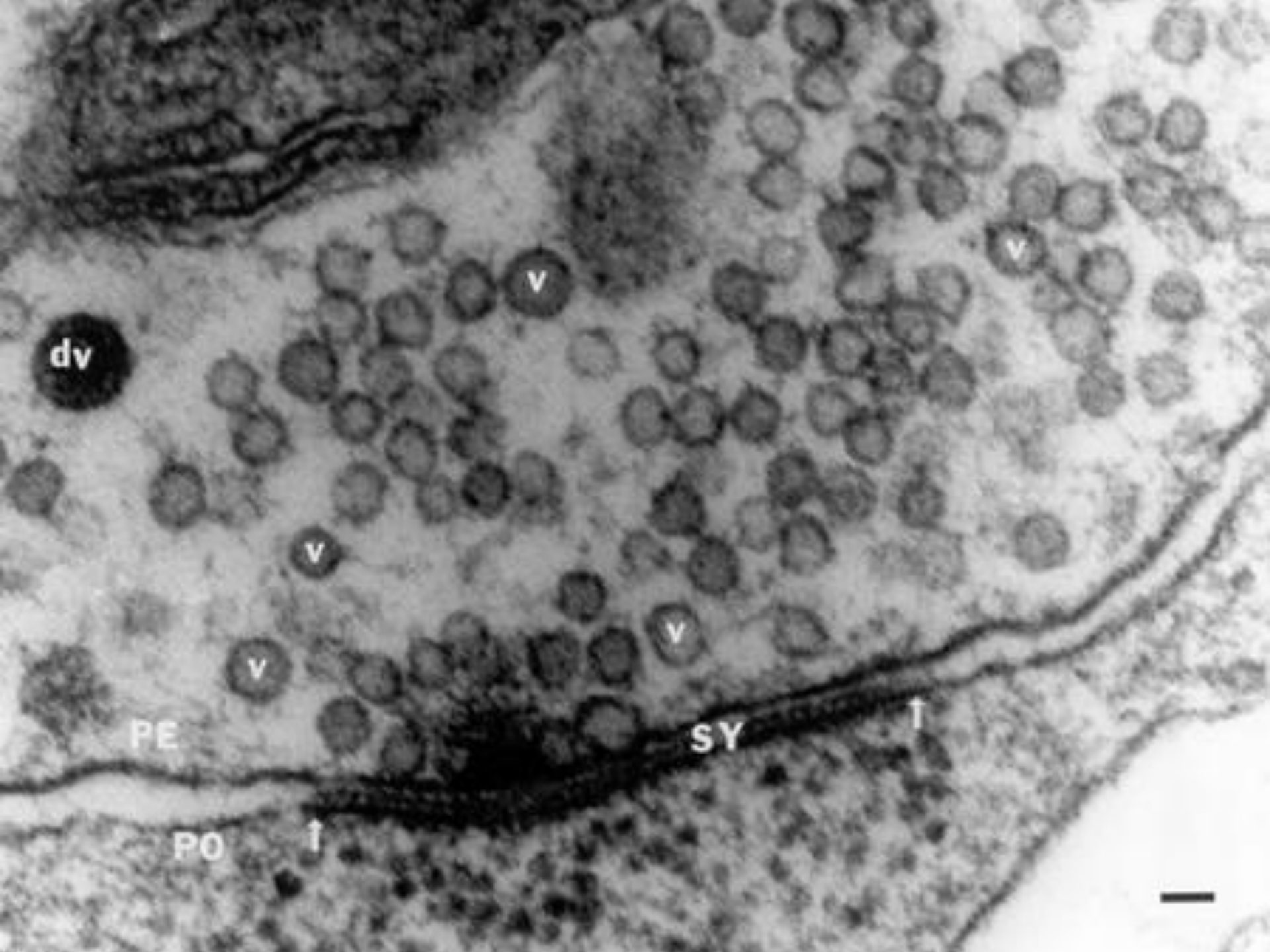
(d) Transmitter is removed from cleft; fused membrane is recycled.

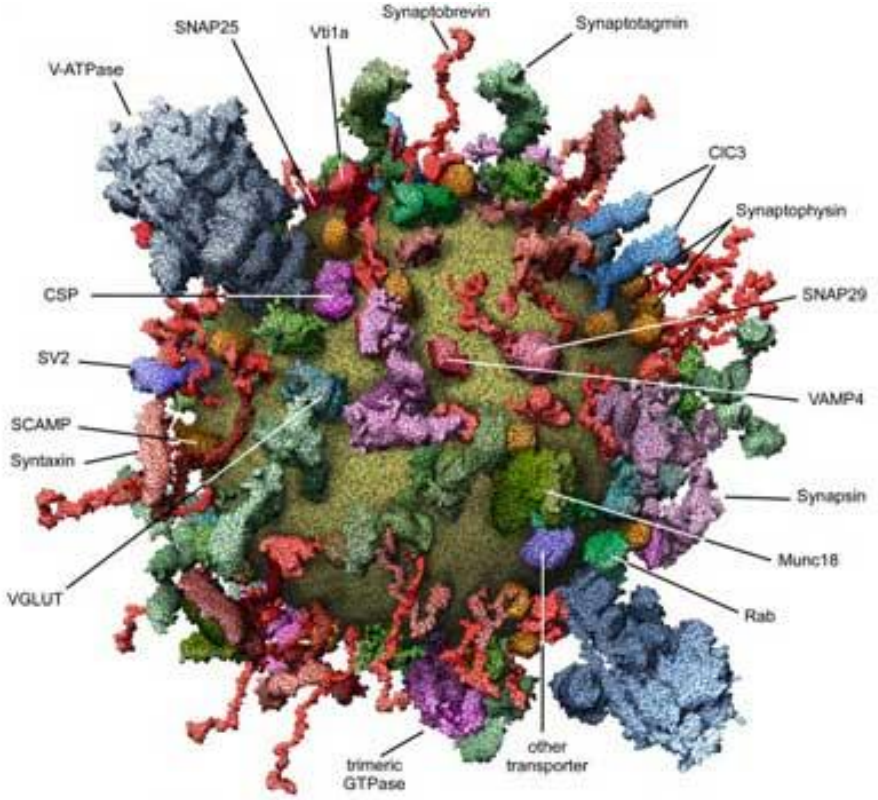


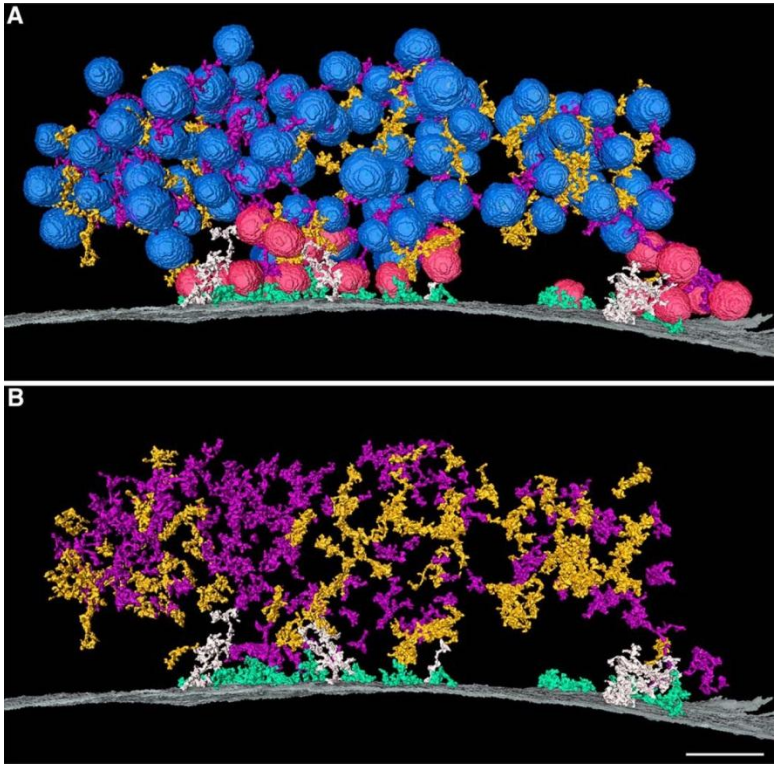
(a) Fast chemical transmission




(b) Slow chemical transmission
Na+
Na+
Ca2+
Ca2+
Large vesicles
Receptor
Intracellular messenger

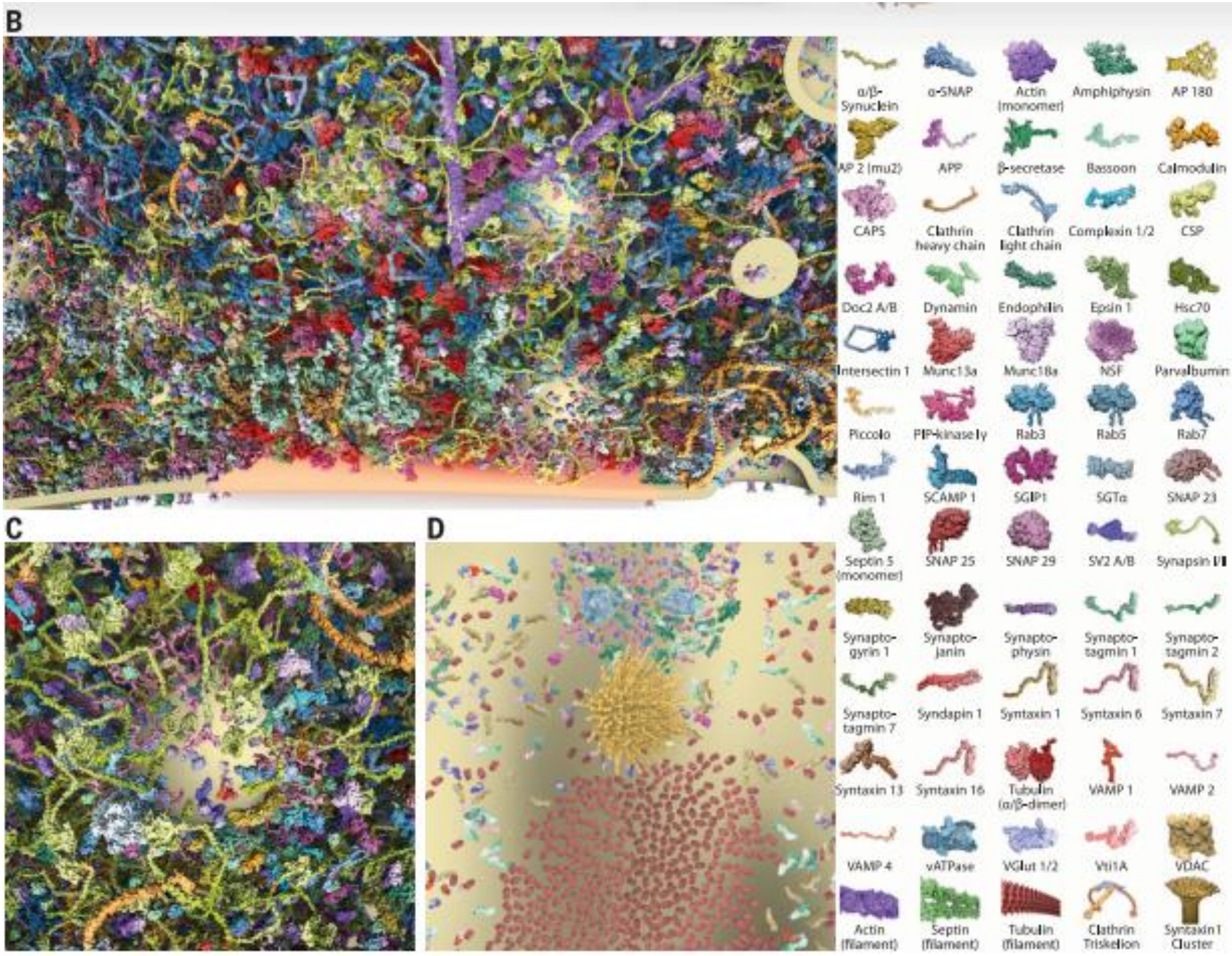

dv
v
v
v
v
v
PE
SY
PO

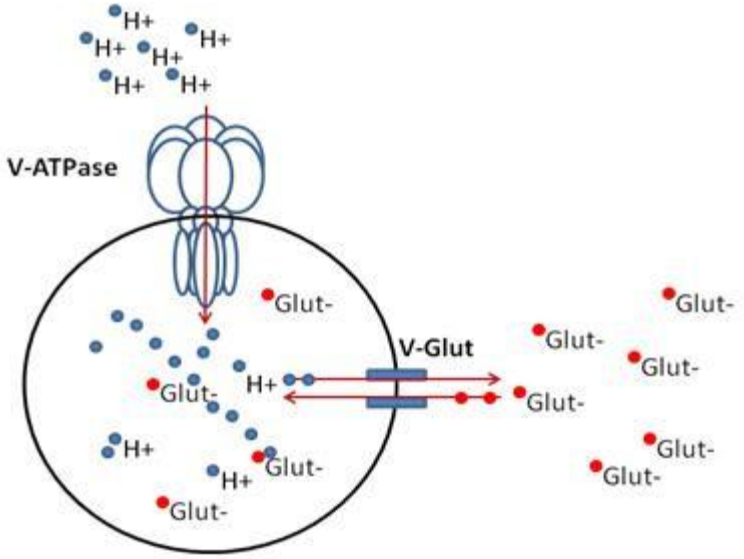


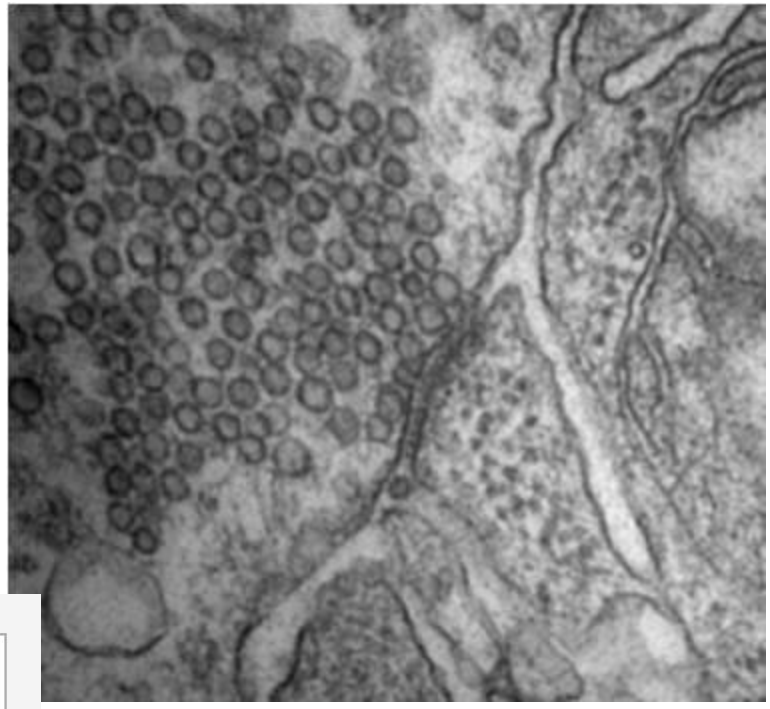


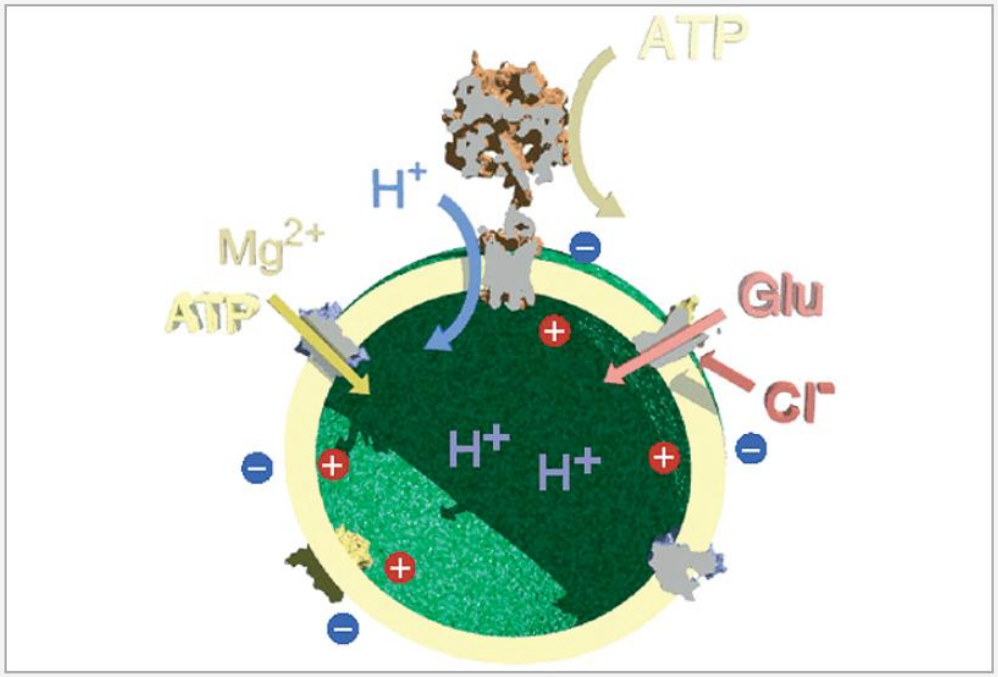
Sudhof, T.C. (2004), Annu. Rev. Neurosci. 27, 509–547

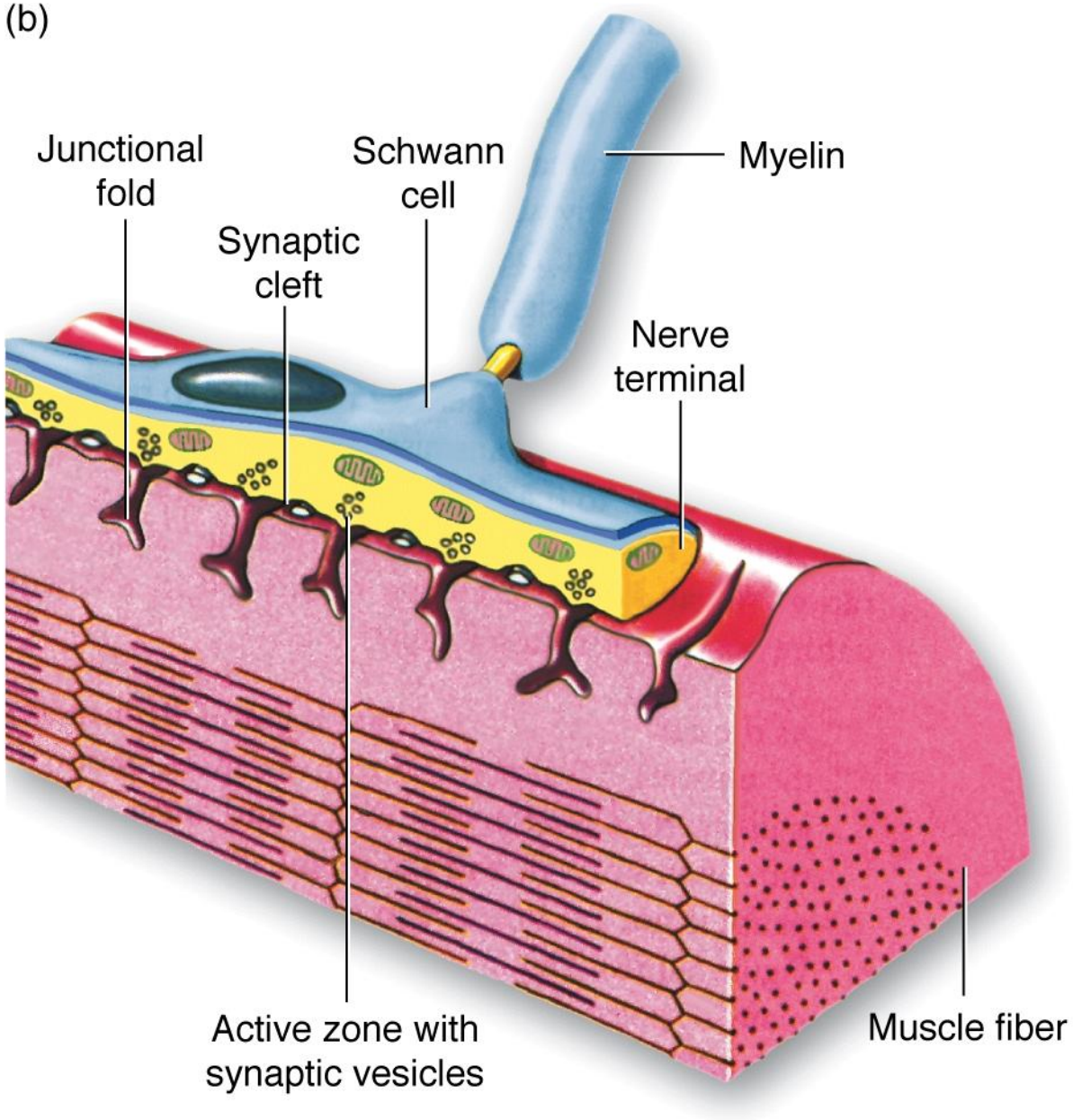
Andy A. Cole, Xiaobing Chen and Tho
Journal of Neuroscience. 2016, 36 (11)


B
C
D
α/β-Synuclein
α-SNAP
Actin (monomer)
Amphiphysin
AP 180
AP 2 (mu2)
APP
β-secretase
Bassoon
Calmodulin
CAPS
Clathrin heavy chain
Clathrin light chain
Complexin 1/2
CSP
Doc2 A/B
Dynamin
Endophilin
Epsin 1
Hsc70
Intersectin 1
Munc13a
Munc18a
NSF
Parvalbumin
Piccolo
PIP-kinase Iγ
Rab3
Rab6
Rab7
Rim 1
SCAMP 1
SGIP1
SGTα
SNAP 23
Septin 5 (monomer)
SNAP 25
SNAP 29
SV2 A/B
Synapsin I/II
Synapto-gyrin 1
Synapto-janin
Synapto-physin
Synapto-tagmin 1
Synapto-tagmin 2
Synapto-tagmin 7
Syndapin 1
Syntaxin 1
Syntaxin 6
Syntaxin 7
Syntaxin 13
Syntaxin 16
Tubulin (α/β-dimer)
VAMP 1
VAMP 2
VAMP 4
vATPase
VGlut 1/2
Vti1A
VDAC
Actin (filament)
Septin (filament)
Tubulin (filament)
Clathrin Triskelion
Syntaxin1 Cluster

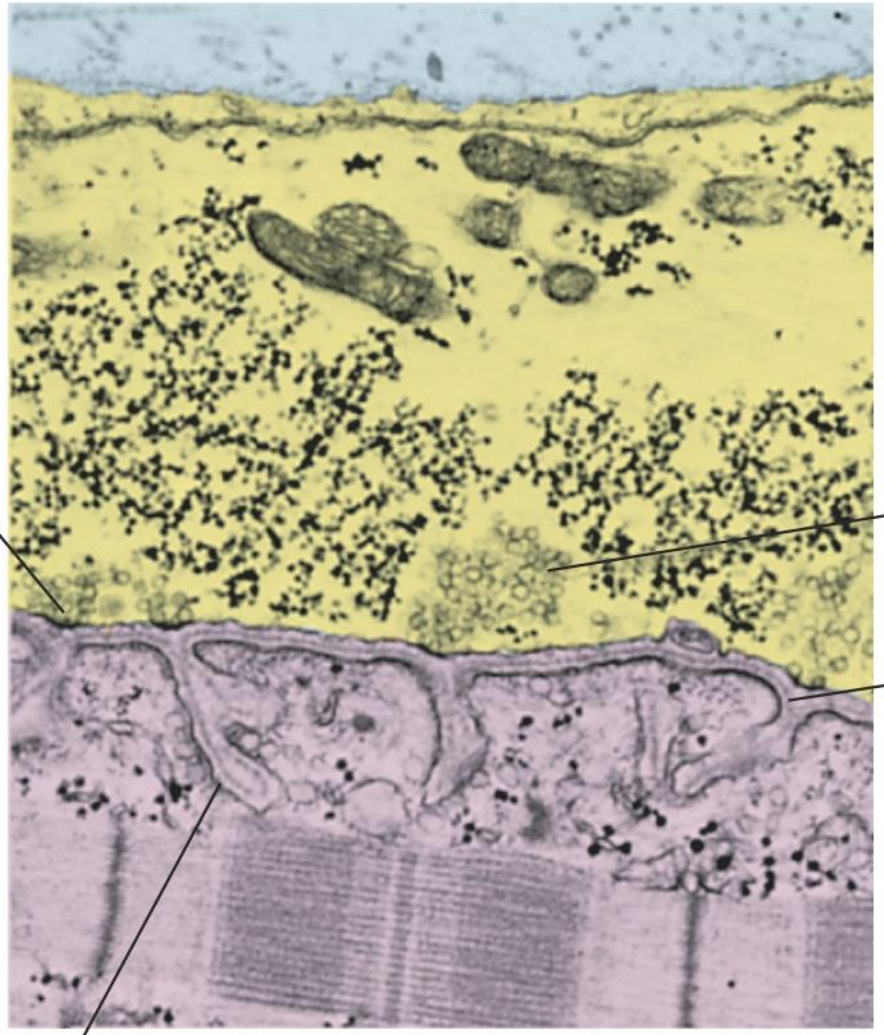

H+
V-ATPase
Glut-
V-Glut

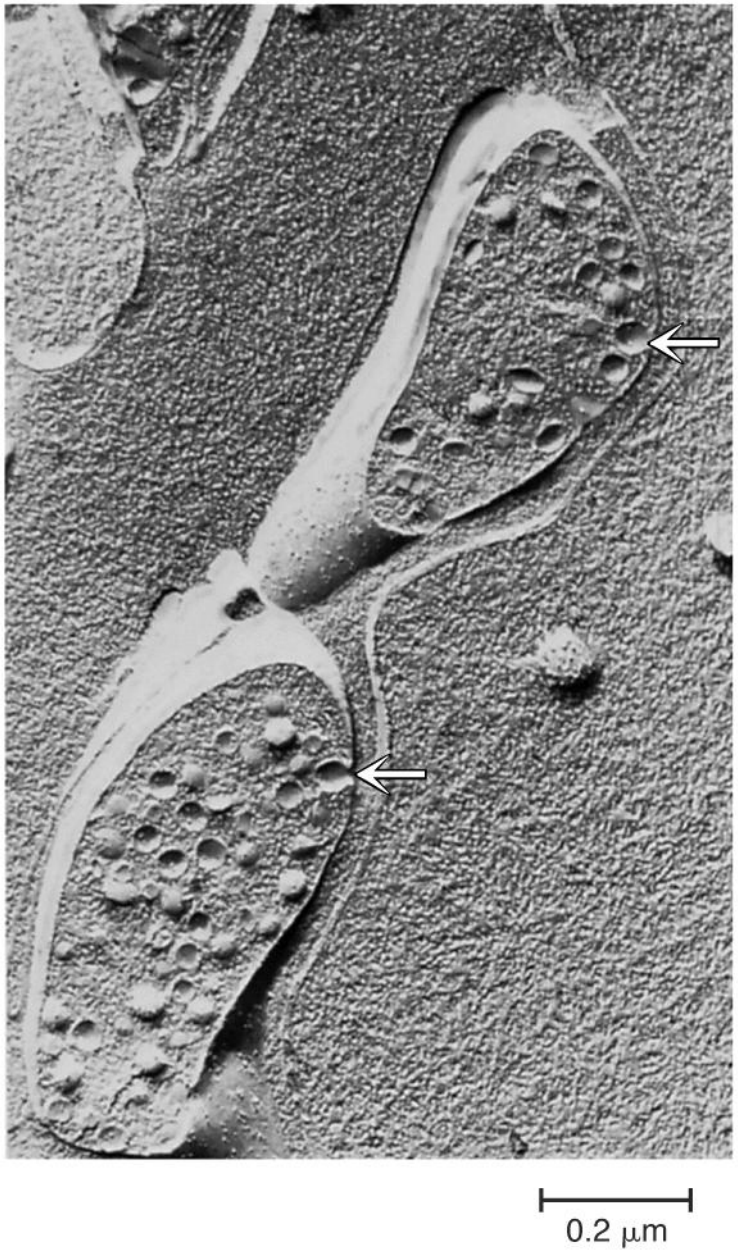


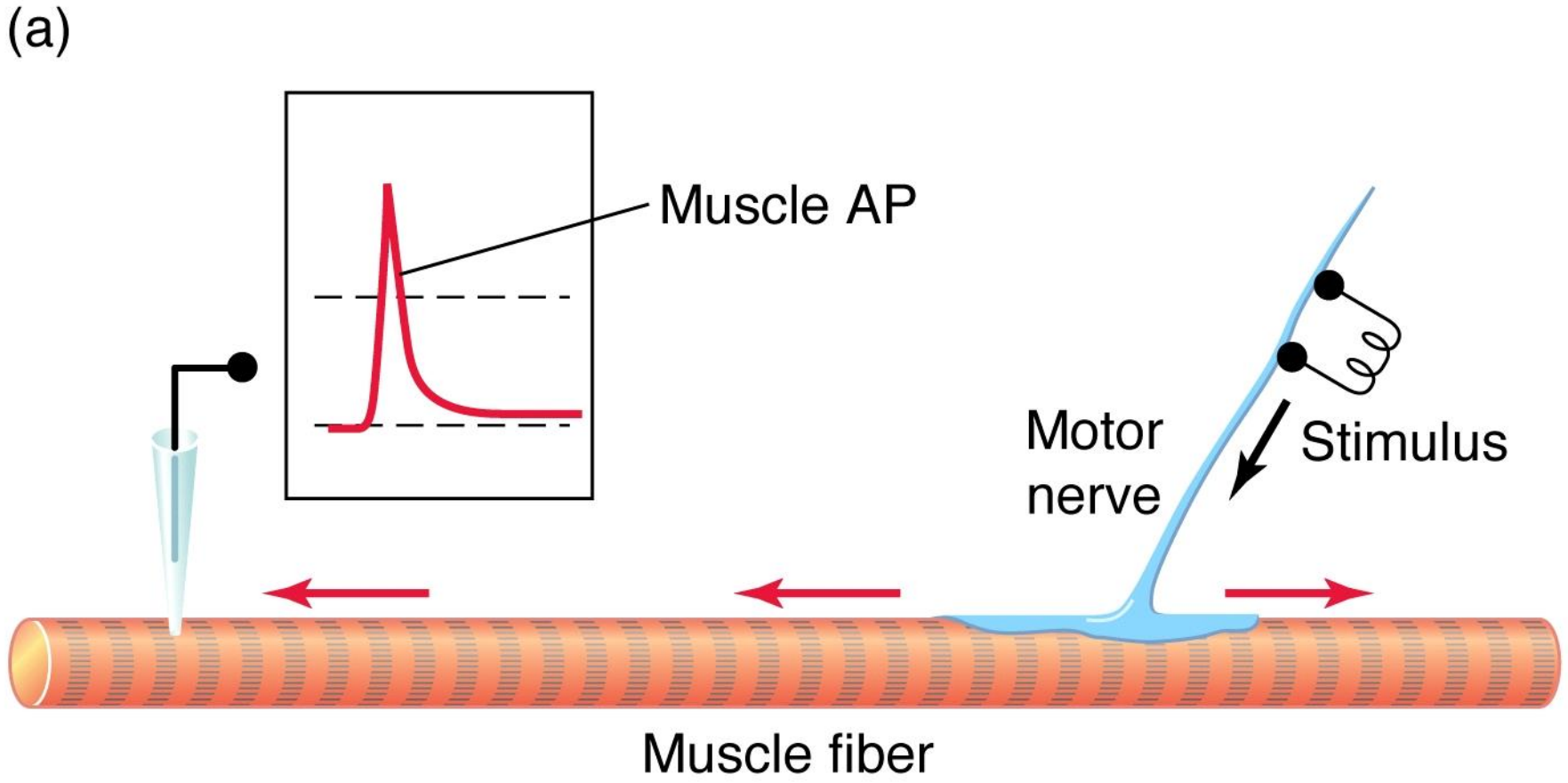

ATP
H+
Mg2+
ATP
Glu
Cl-


(b)
Junctional fold
Schwann cell
Myelin
Synaptic cleft
Nerve terminal
Active zone with synaptic vesicles
Muscle fiber

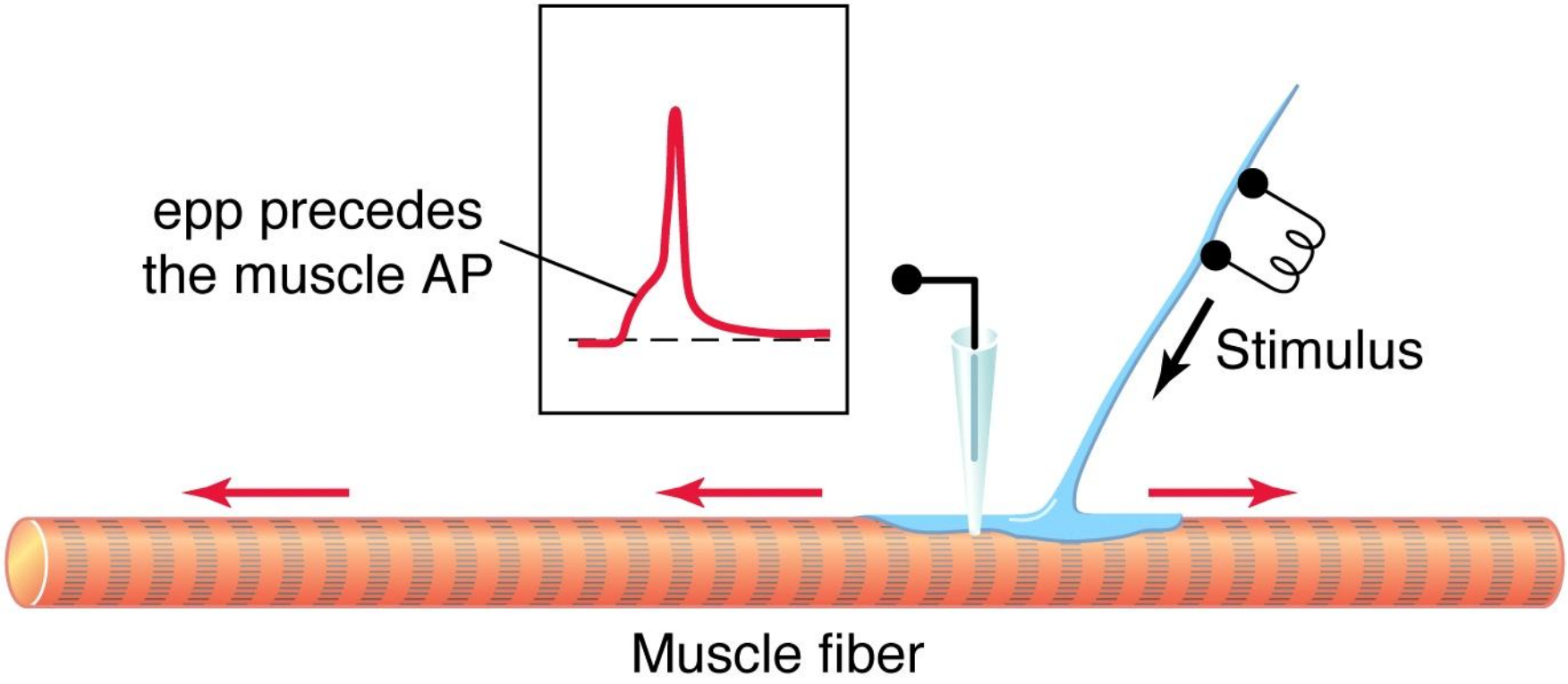
(c)

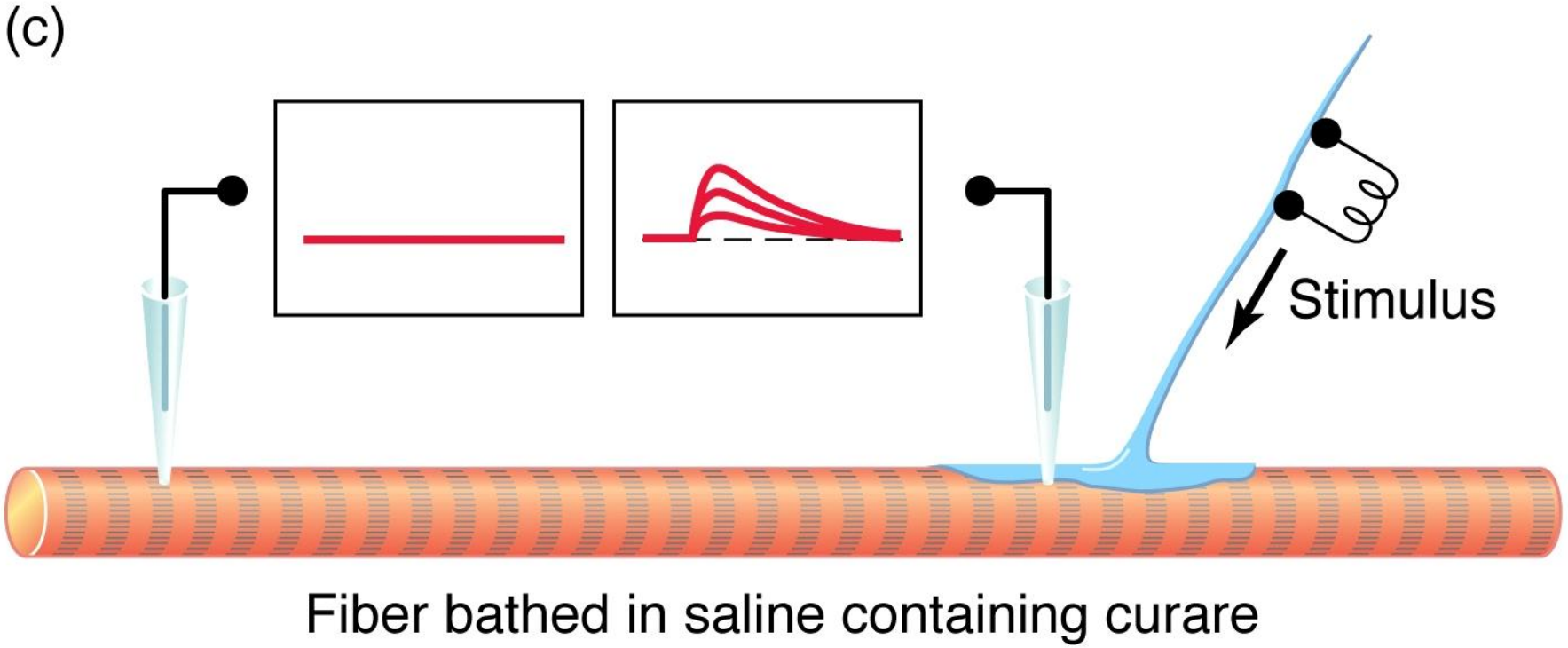

Thickened membrane
Synaptic vesicles
Synaptic cleft
Junctional fold
0.5 μm

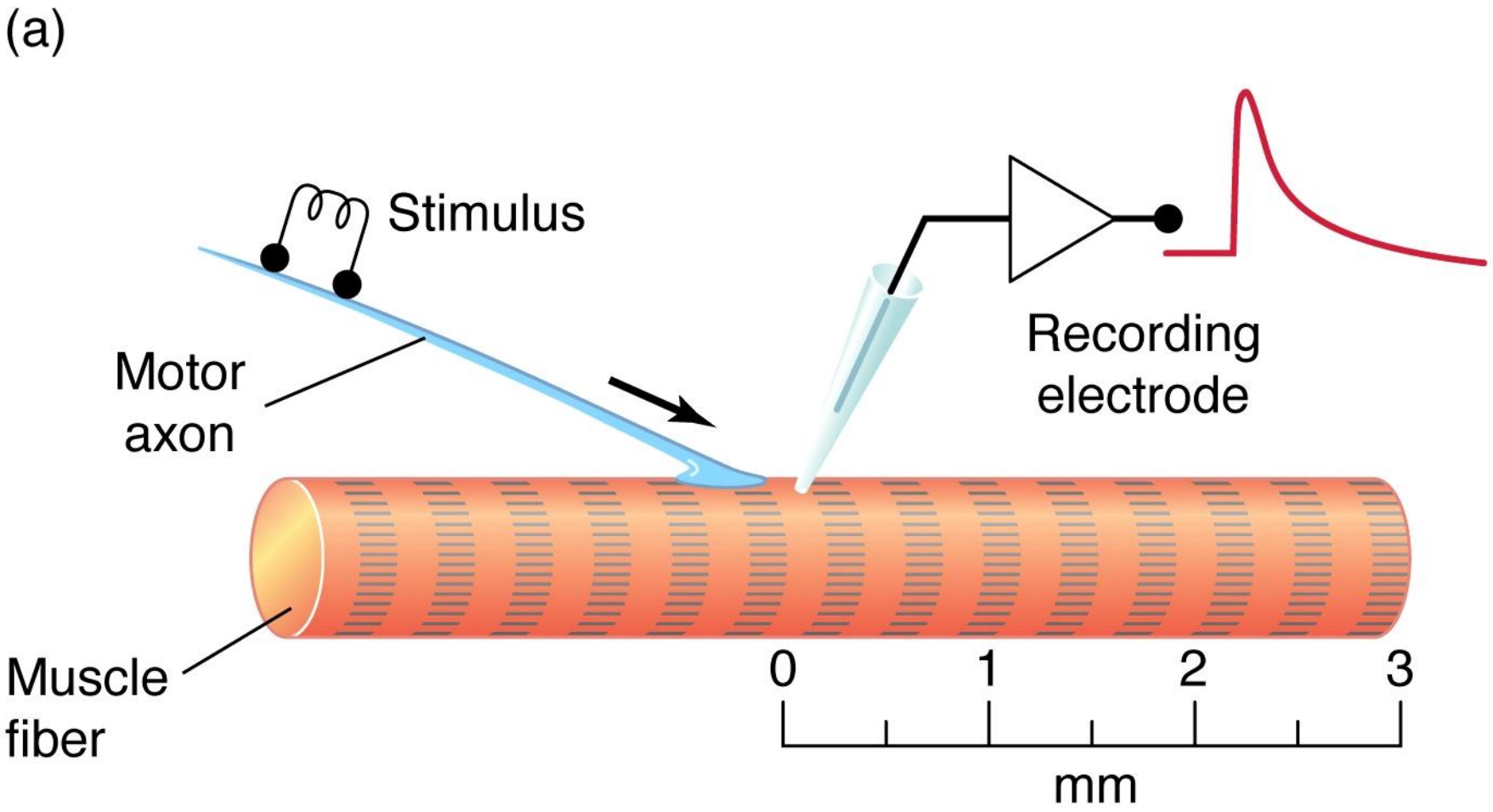

0.2 μm

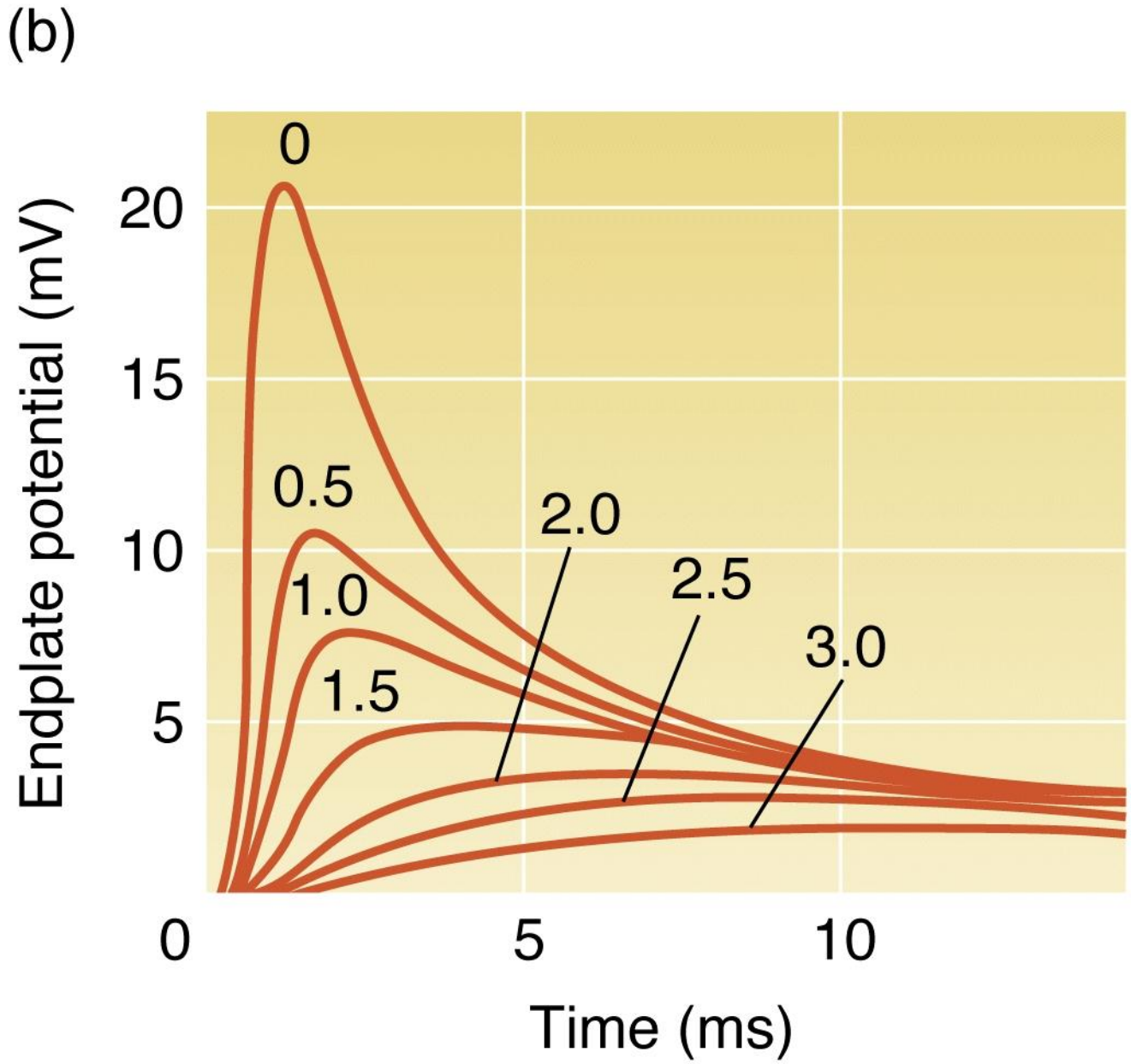

(a)
Muscle AP
Motor nerve
Stimulus
Muscle fiber

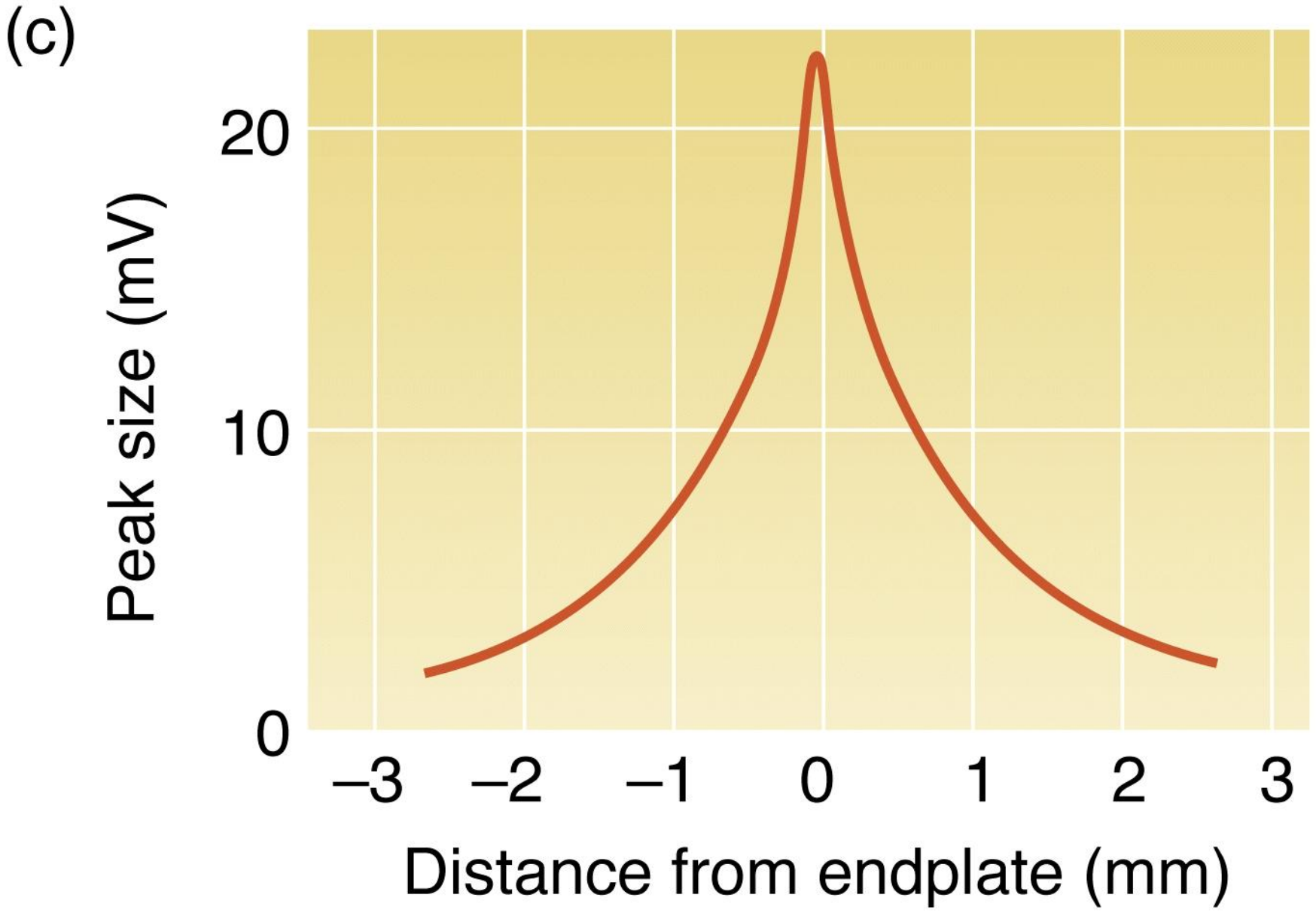
(b)

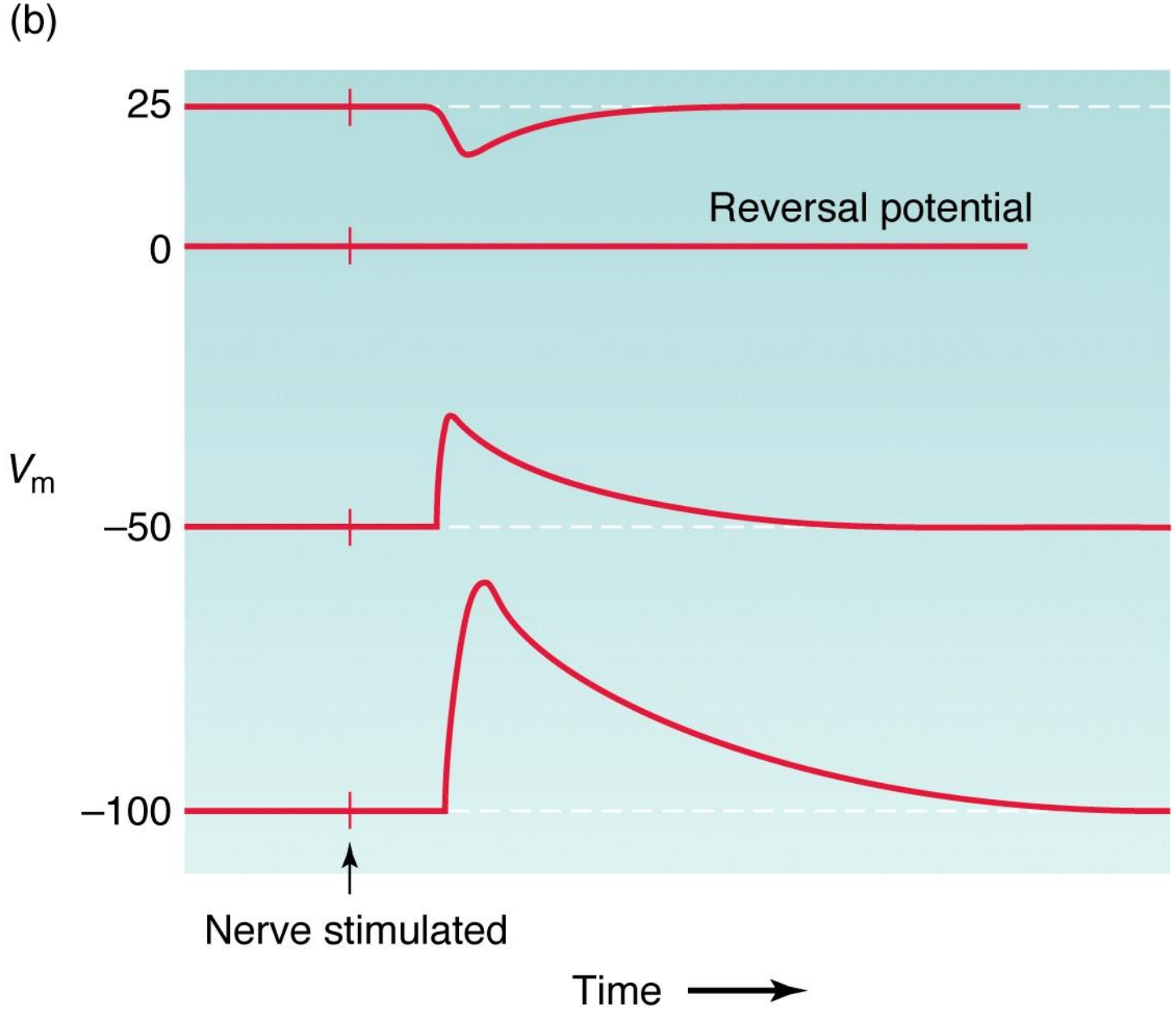


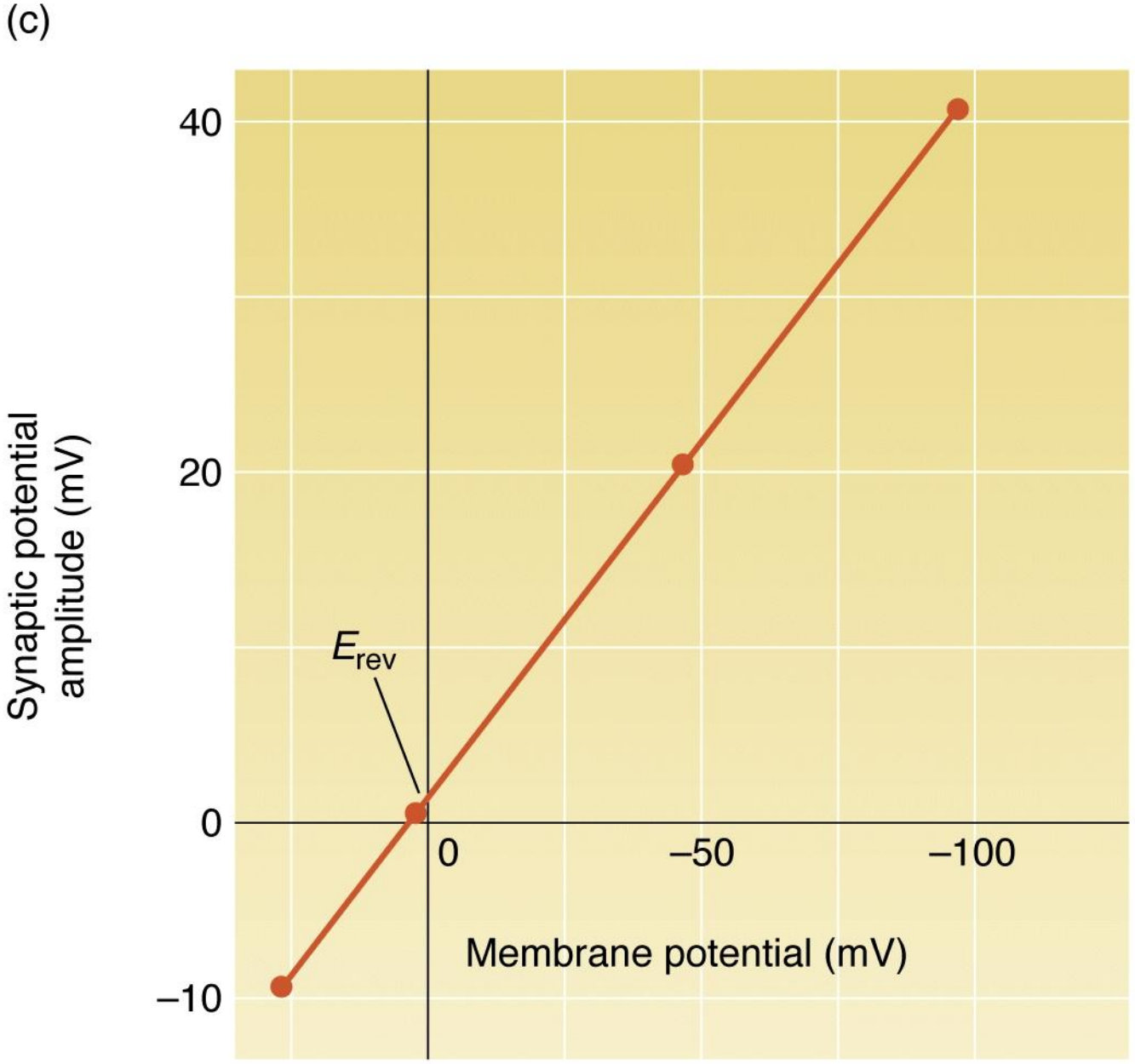

(c)
Stimulus
Fiber bathed in saline containing curare

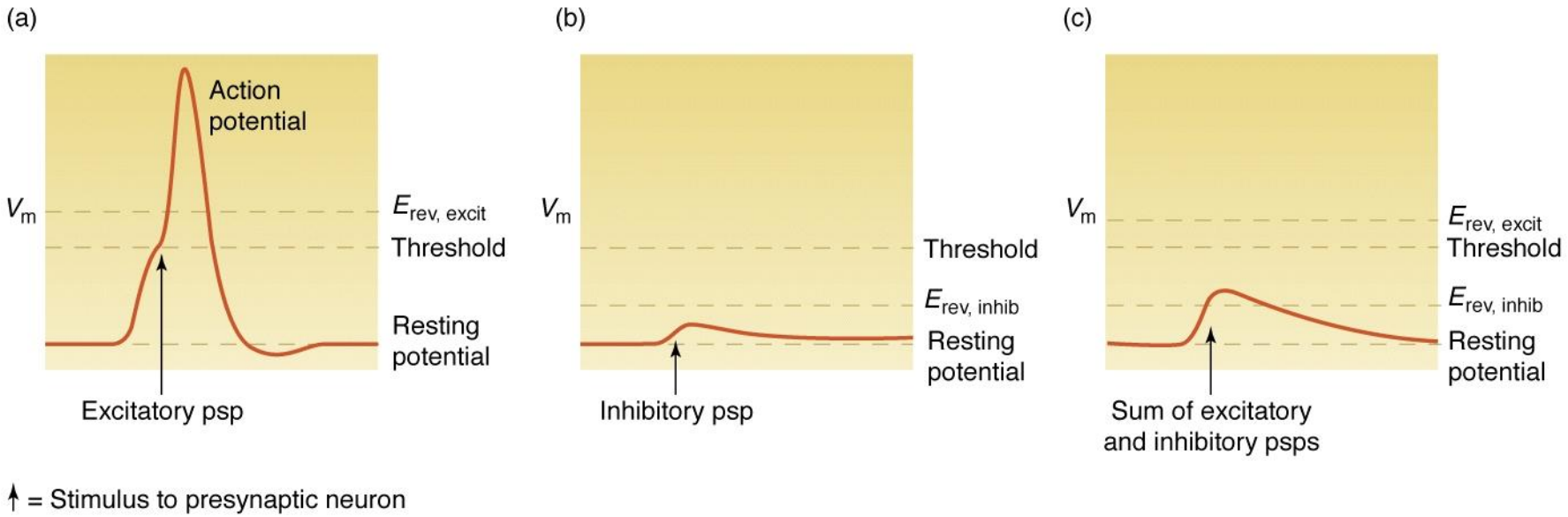

(a)
Stimulus
Motor
axon
Recording
electrode
Muscle
fiber
0
1
2
3
mm

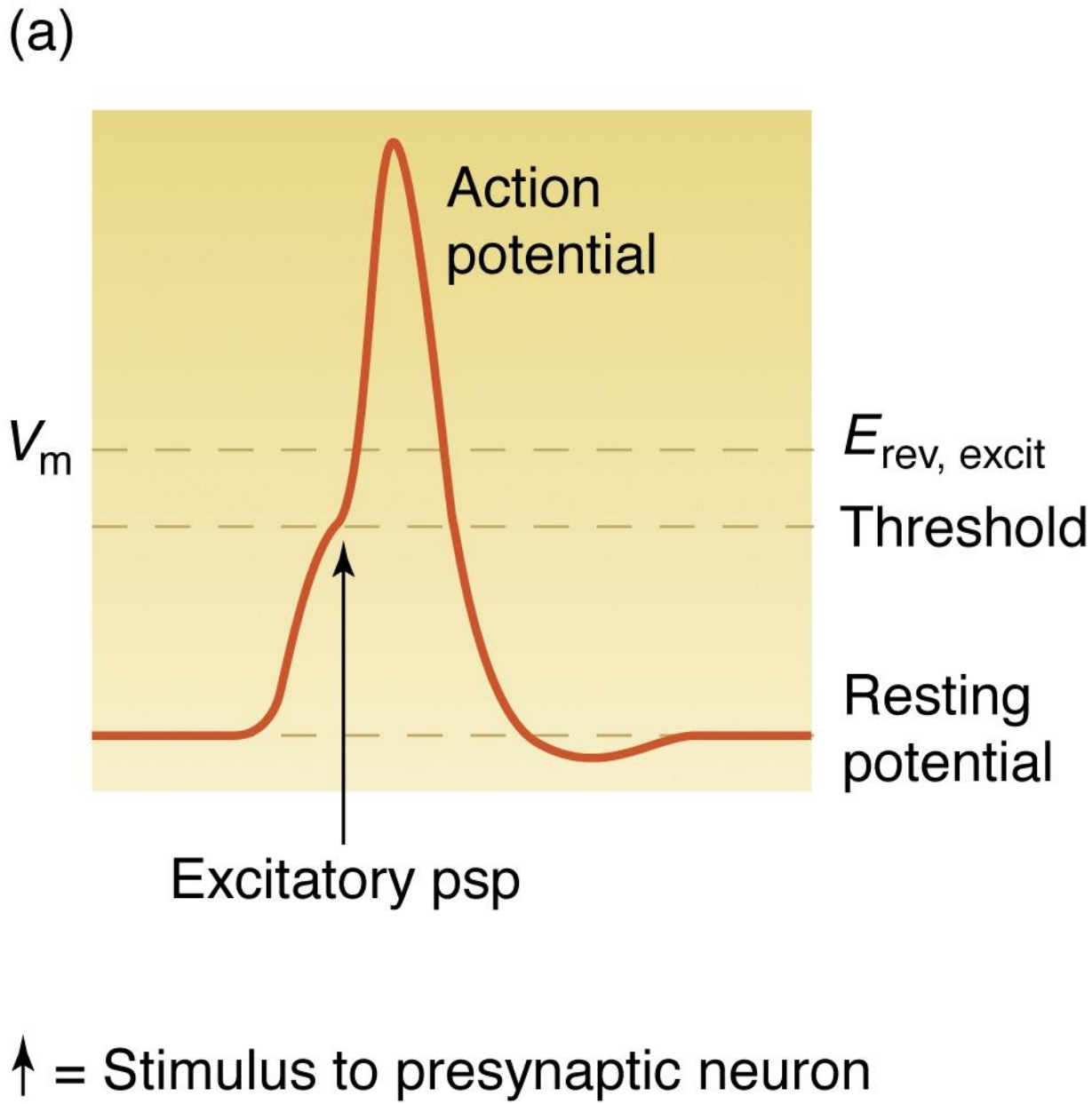

(b)
Endplate potential (mV)
20
15
10
5
0
0
0.5
1.0
1.5
2.0
2.5
3.0
0
5
10
Time (ms)

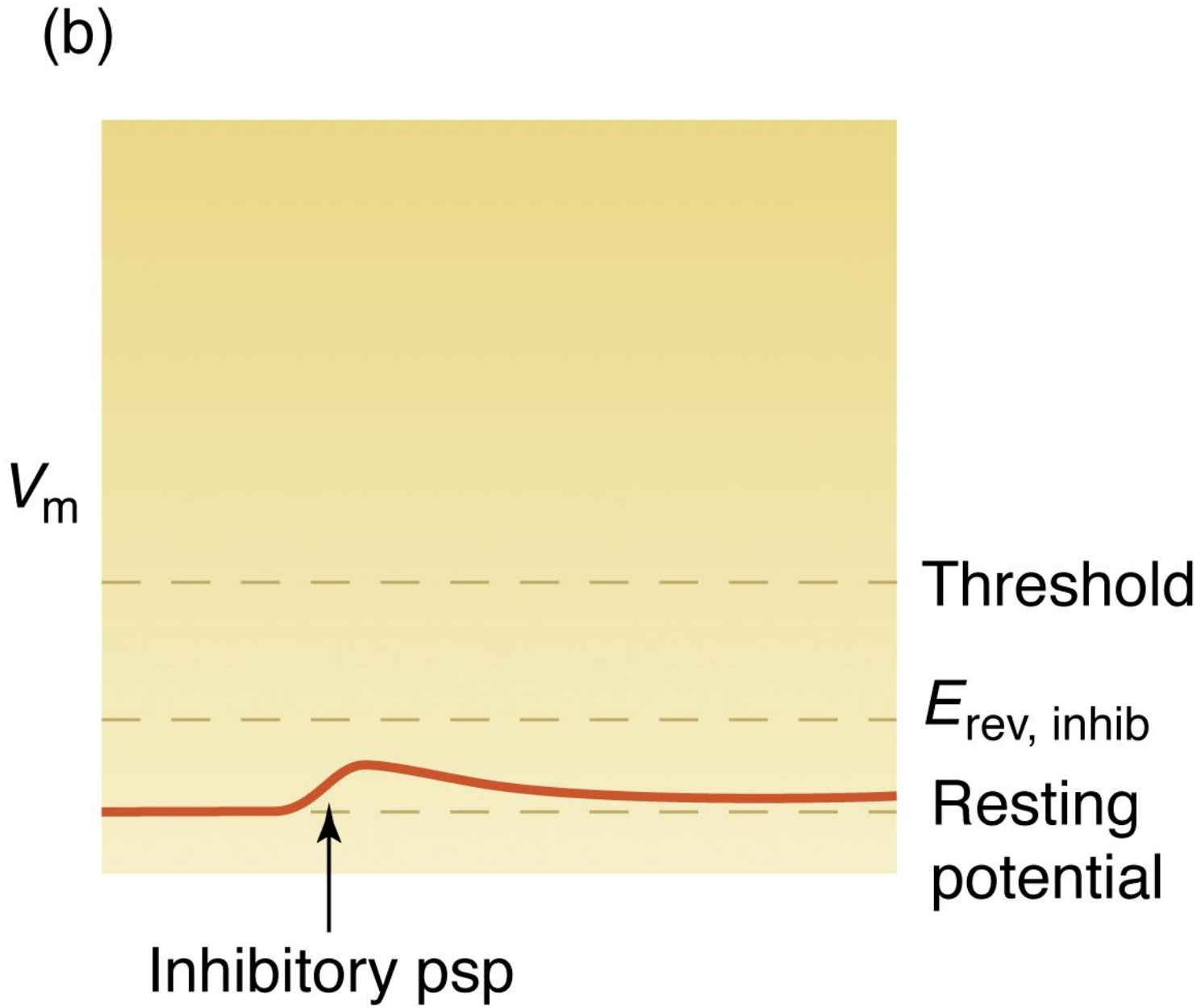

(c)
20
10
0
Peak size (mV)
–3
–2
–1
0
1
2
3
Distance from endplate (mm)

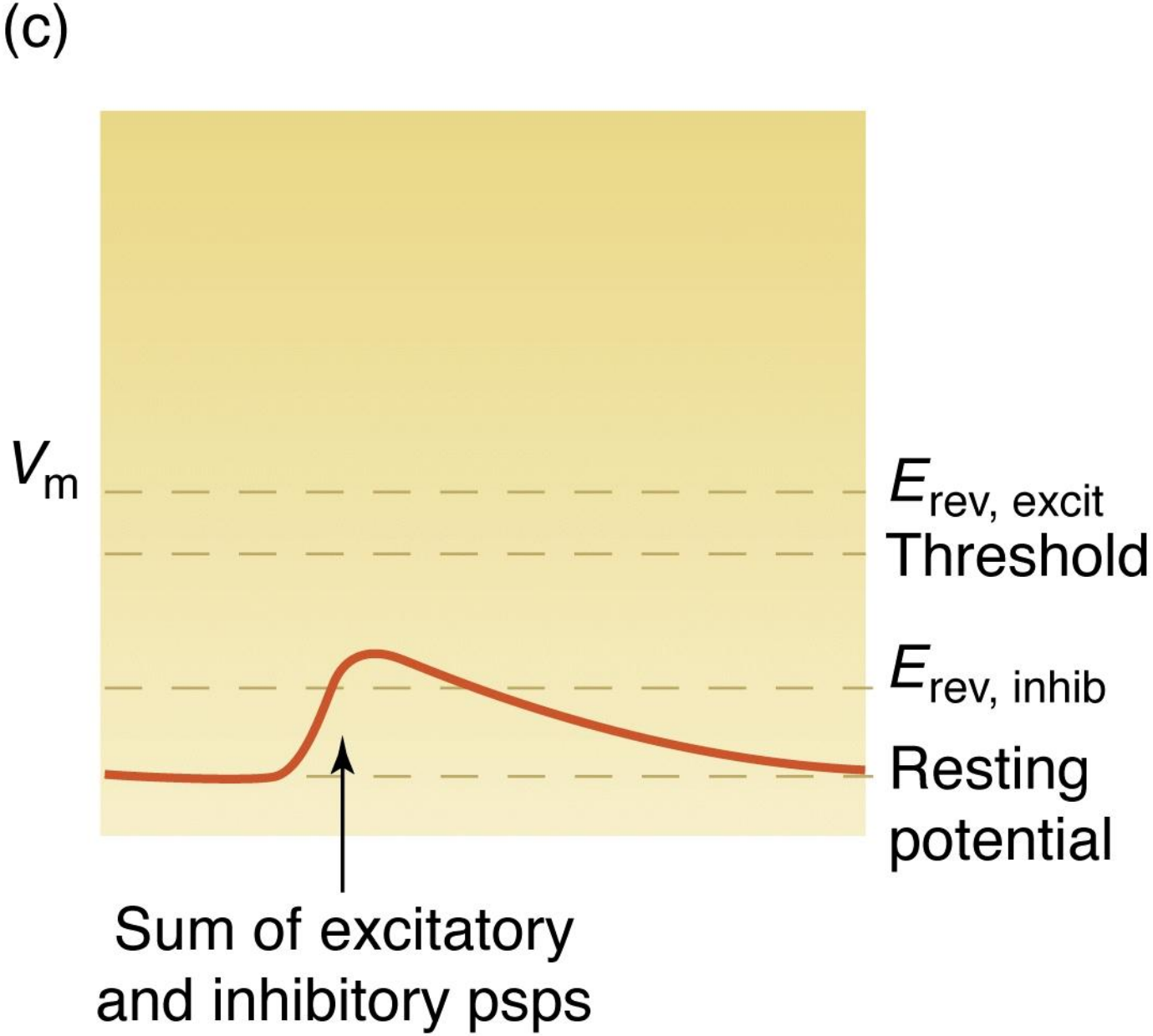

(b)
25
Reversal potential
0
V_m
–50
–100
Nerve stimulated
Time

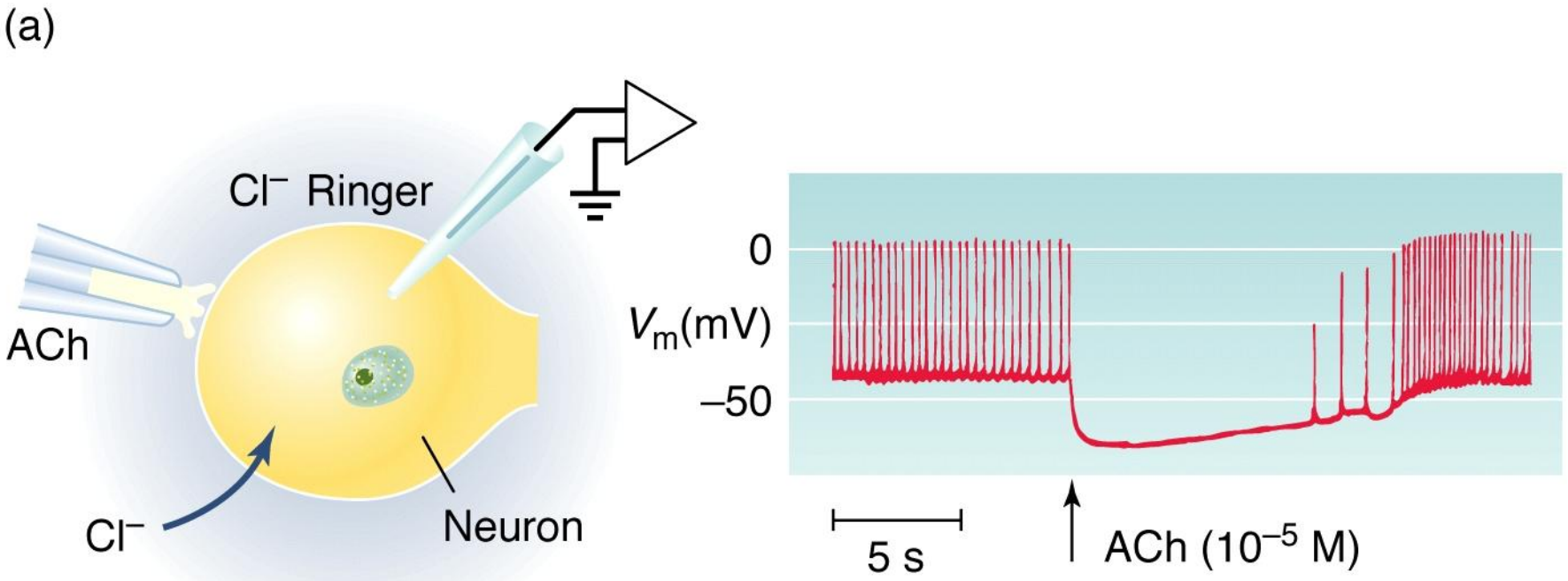

(c)
Synaptic potential amplitude (mV)
40
20
0
–10
E_{rev}
0
–50
–100
Membrane potential (mV)

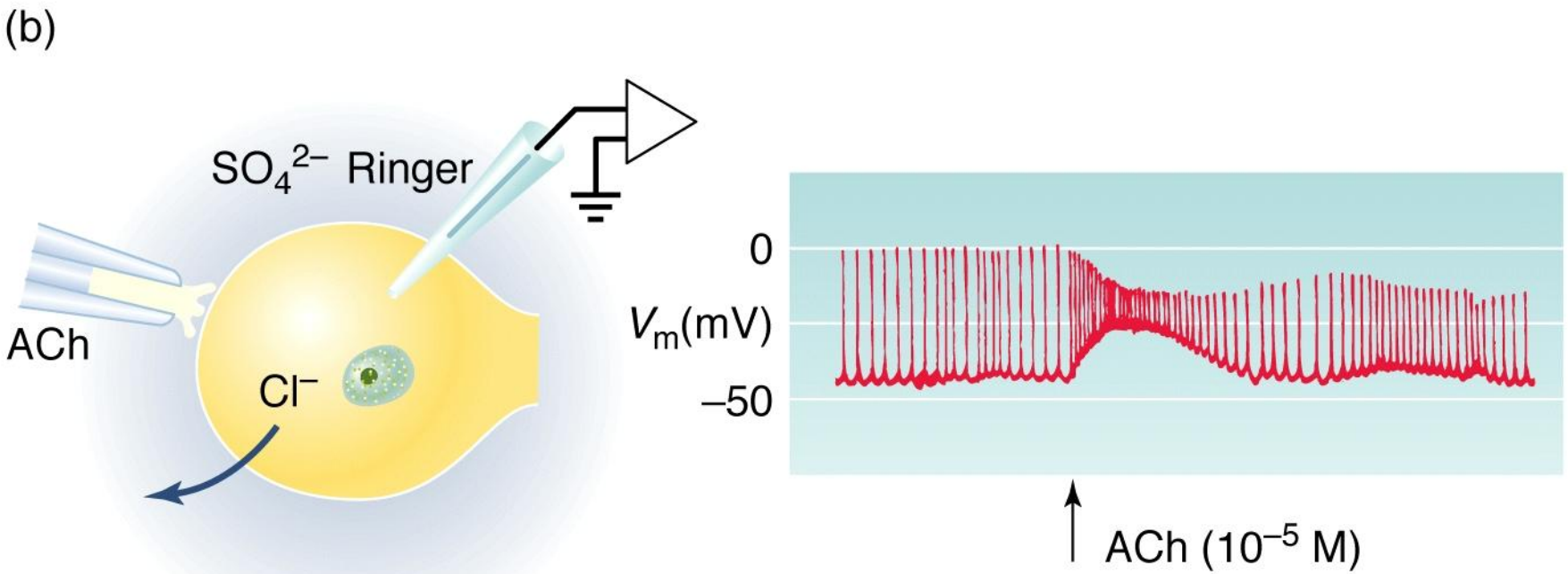

(a)
Action potential
V_m
$E_{rev, excit}$
Threshold
Resting potential
Excitatory psp
(b)
V_m
Threshold
$E_{rev, inhib}$
Resting potential
Inhibitory psp
(c)
V_m
$E_{rev, excit}$
Threshold
$E_{rev, inhib}$
Resting potential
Sum of excitatory and inhibitory psps
= Stimulus to presynaptic neuron

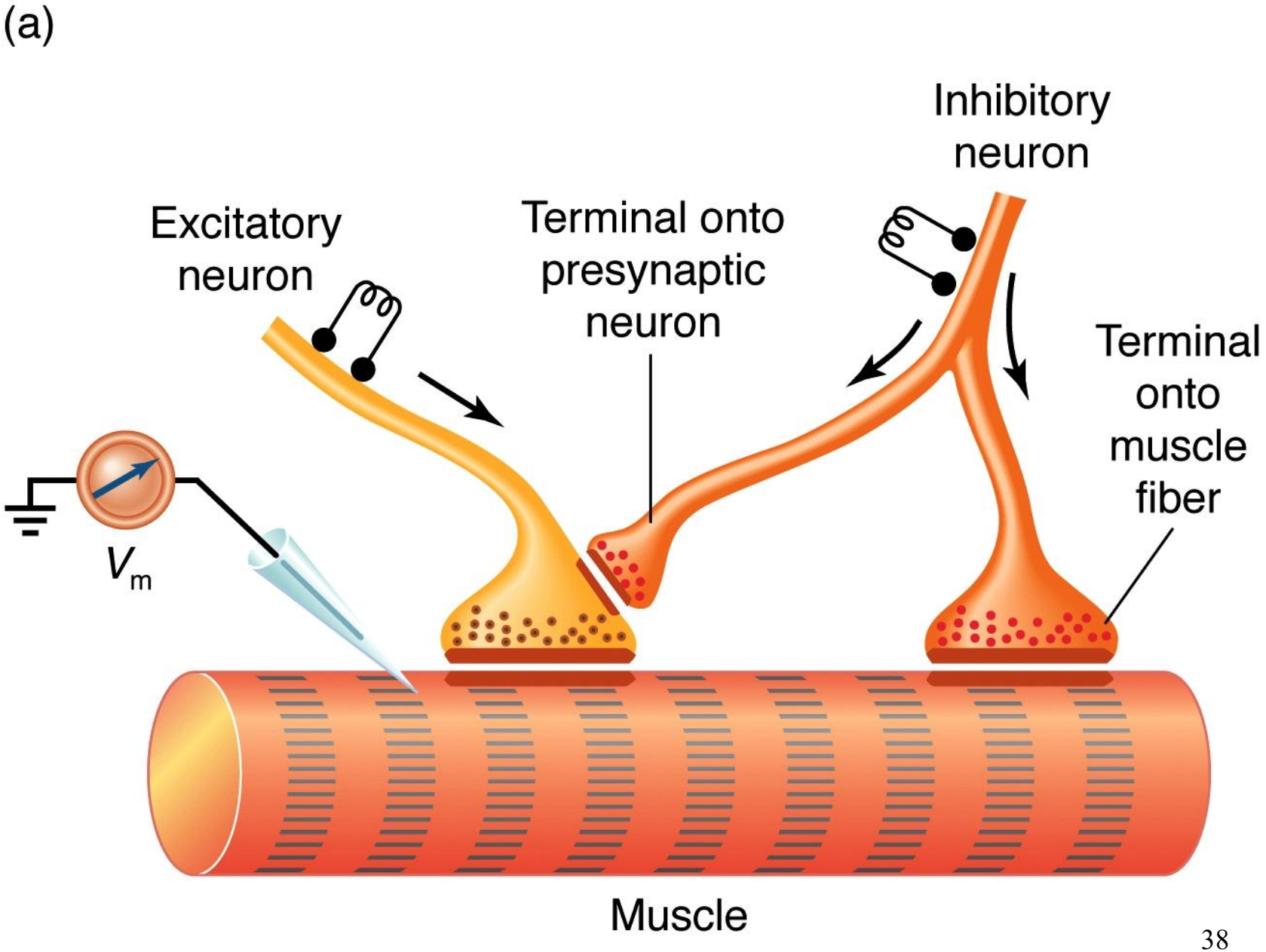

(a)
Action potential
V_m
$E_{rev, excit}$
Threshold
Resting potential
Excitatory psp
= Stimulus to presynaptic neuron

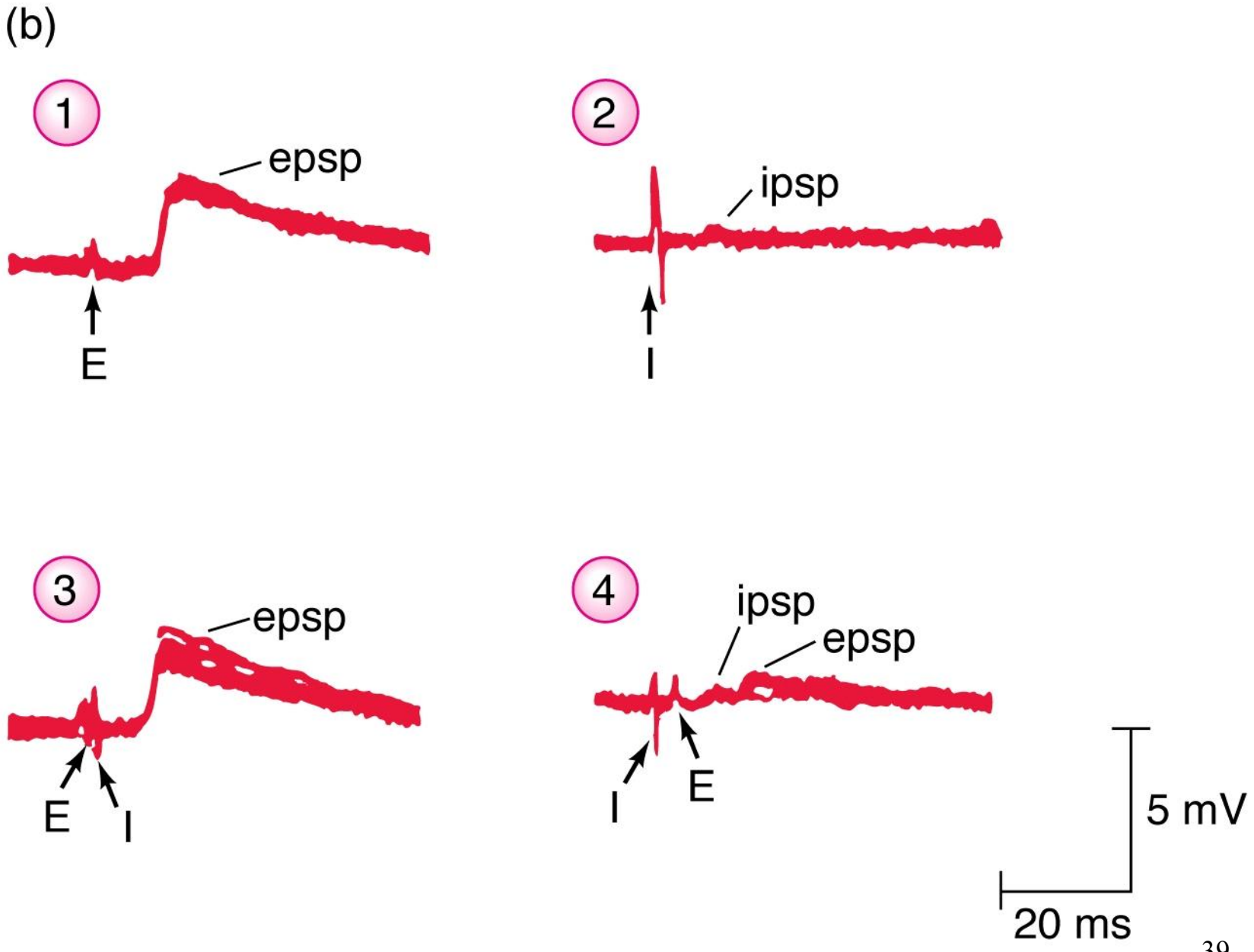

(b)
V_m
Threshold
$E_{rev, inhib}$
Resting potential
Inhibitory psp

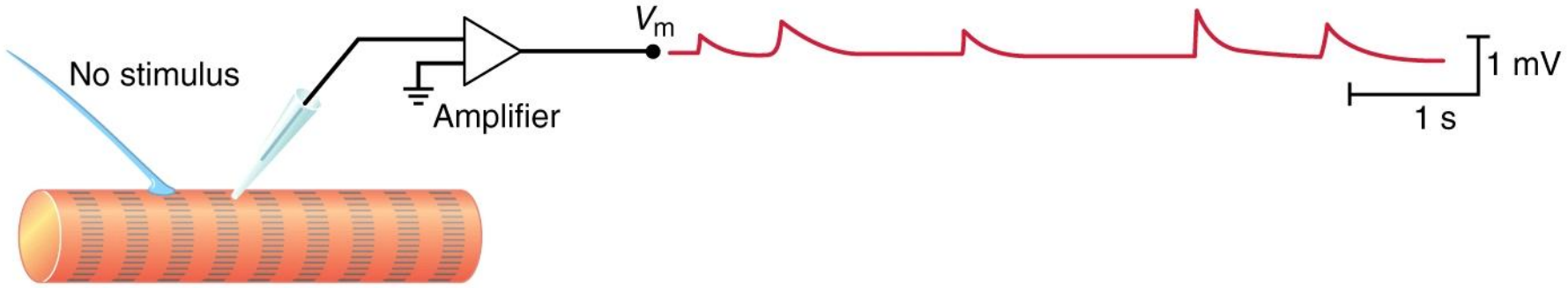

(c)
V_m
$E_{rev, excit}$
Threshold
$E_{rev, inhib}$
Resting potential
Sum of excitatory and inhibitory psps

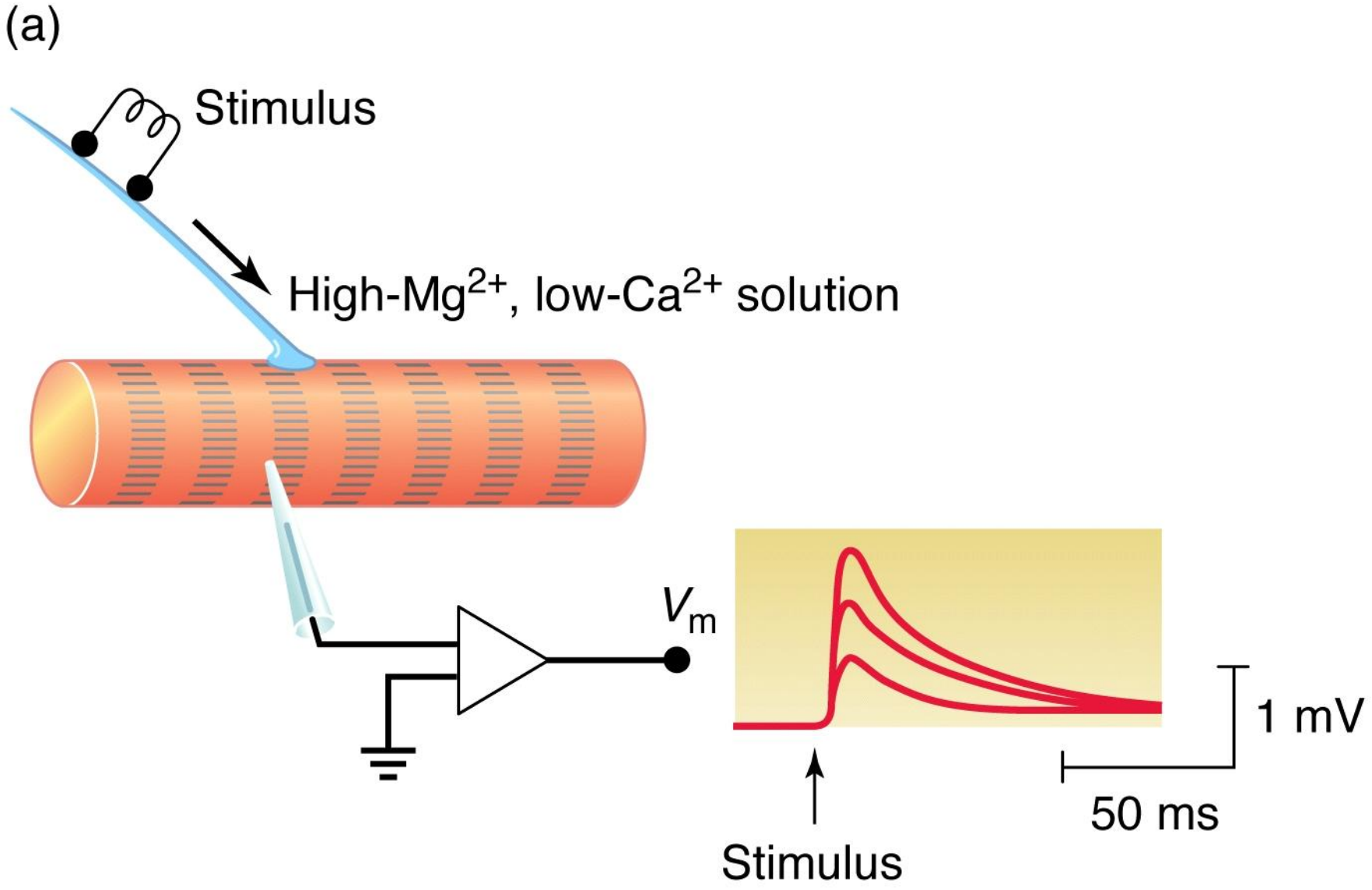

(a)
Cl⁻ Ringer
ACh
Cl⁻
Neuron
0
V_m(mV)
–50
5 s
ACh (10^{-5} M)

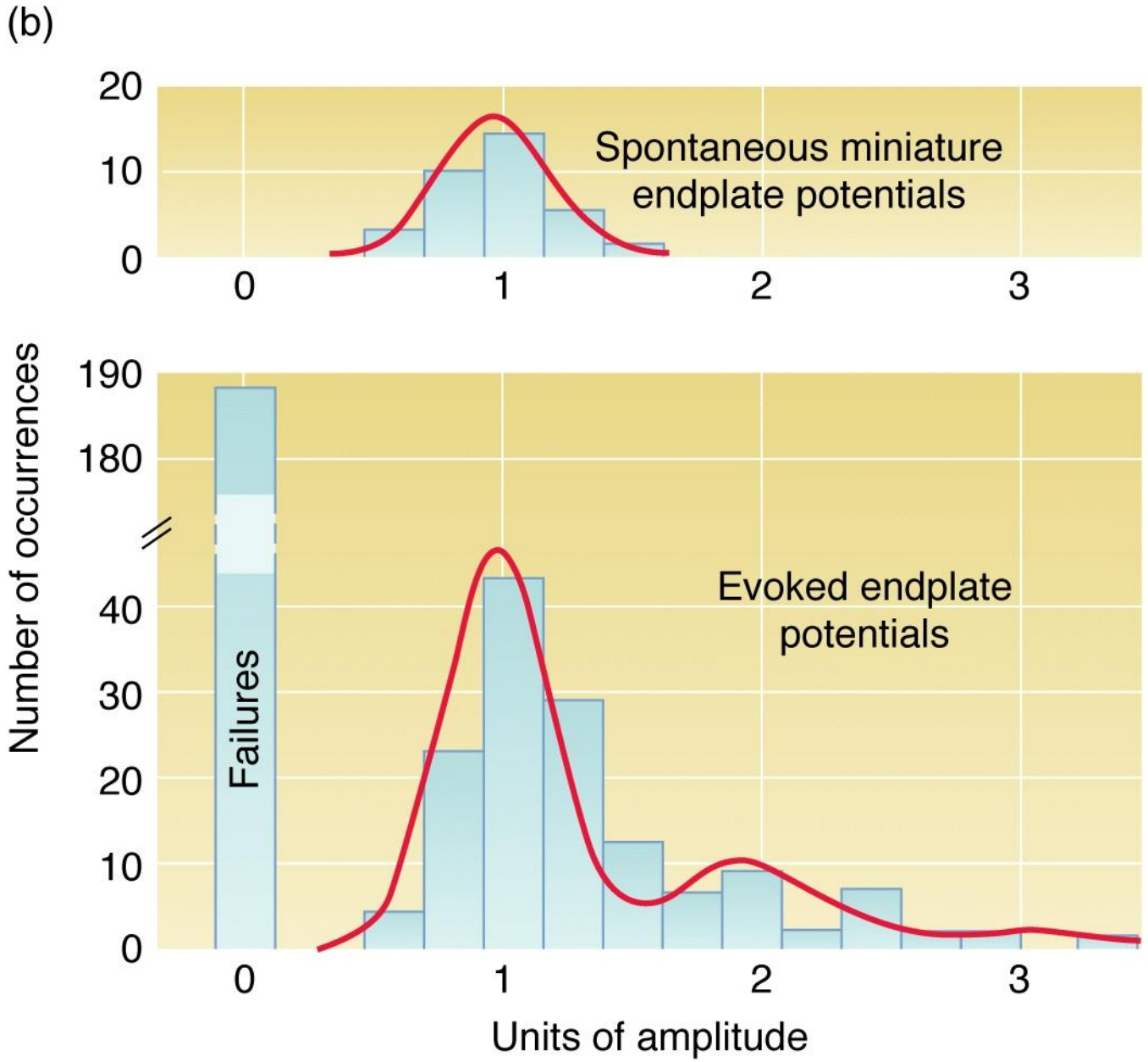

(b)
SO_4^{2-} Ringer
ACh
Cl^-
0
V_m(mV)
–50
ACh (10^{-5} M)

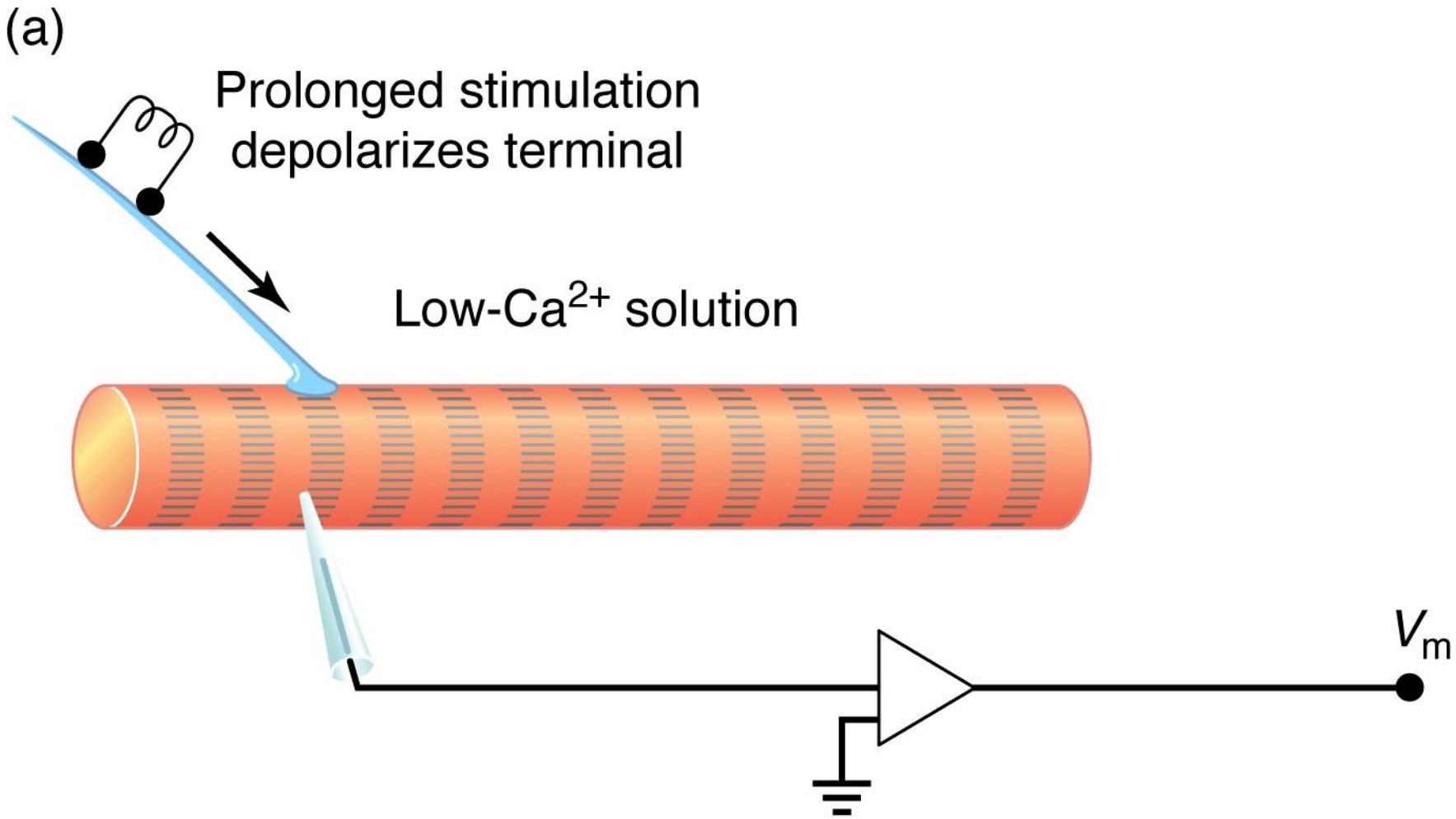

(a)
Inhibitory neuron
Excitatory neuron
Terminal onto presynaptic neuron
Terminal onto muscle fiber
V_m
Muscle


(b)
1
epsp
E
2
ipsp
I
3
epsp
E
I
4
ipsp
epsp
I
E
5 mV
20 ms

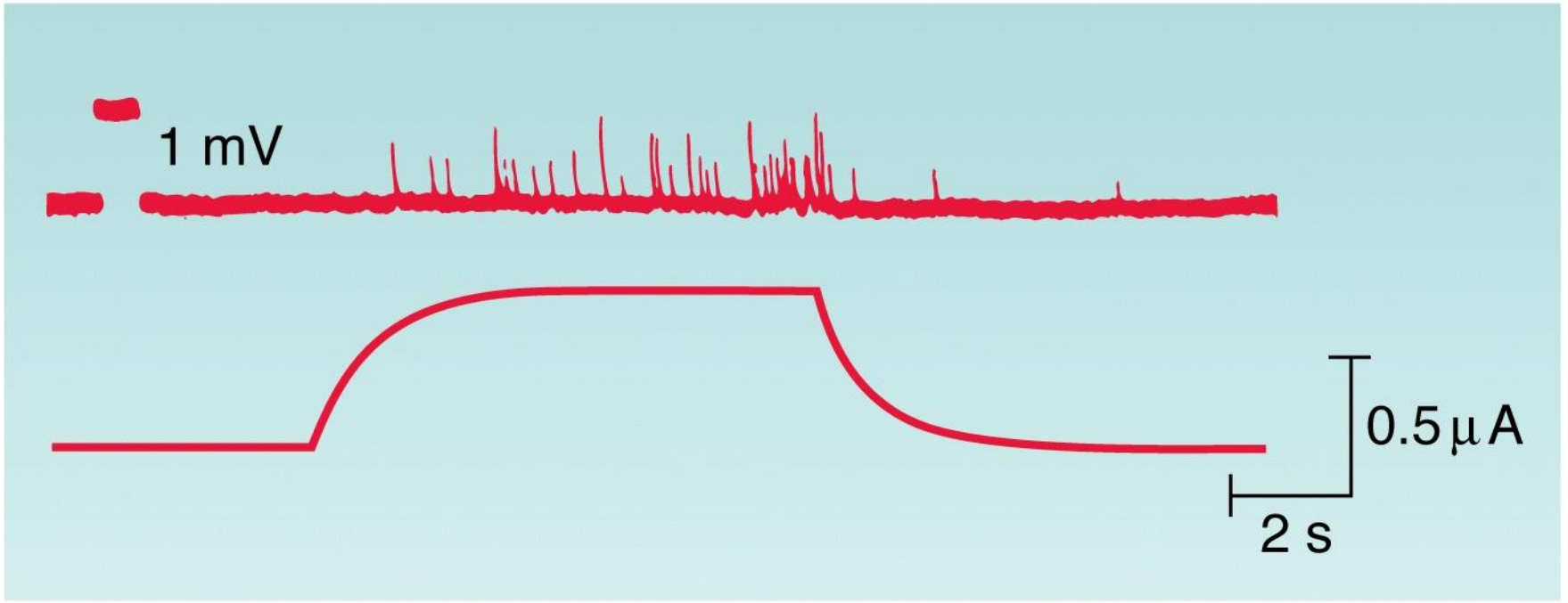

No stimulus
Amplifier
V_m
1 mV
1 s

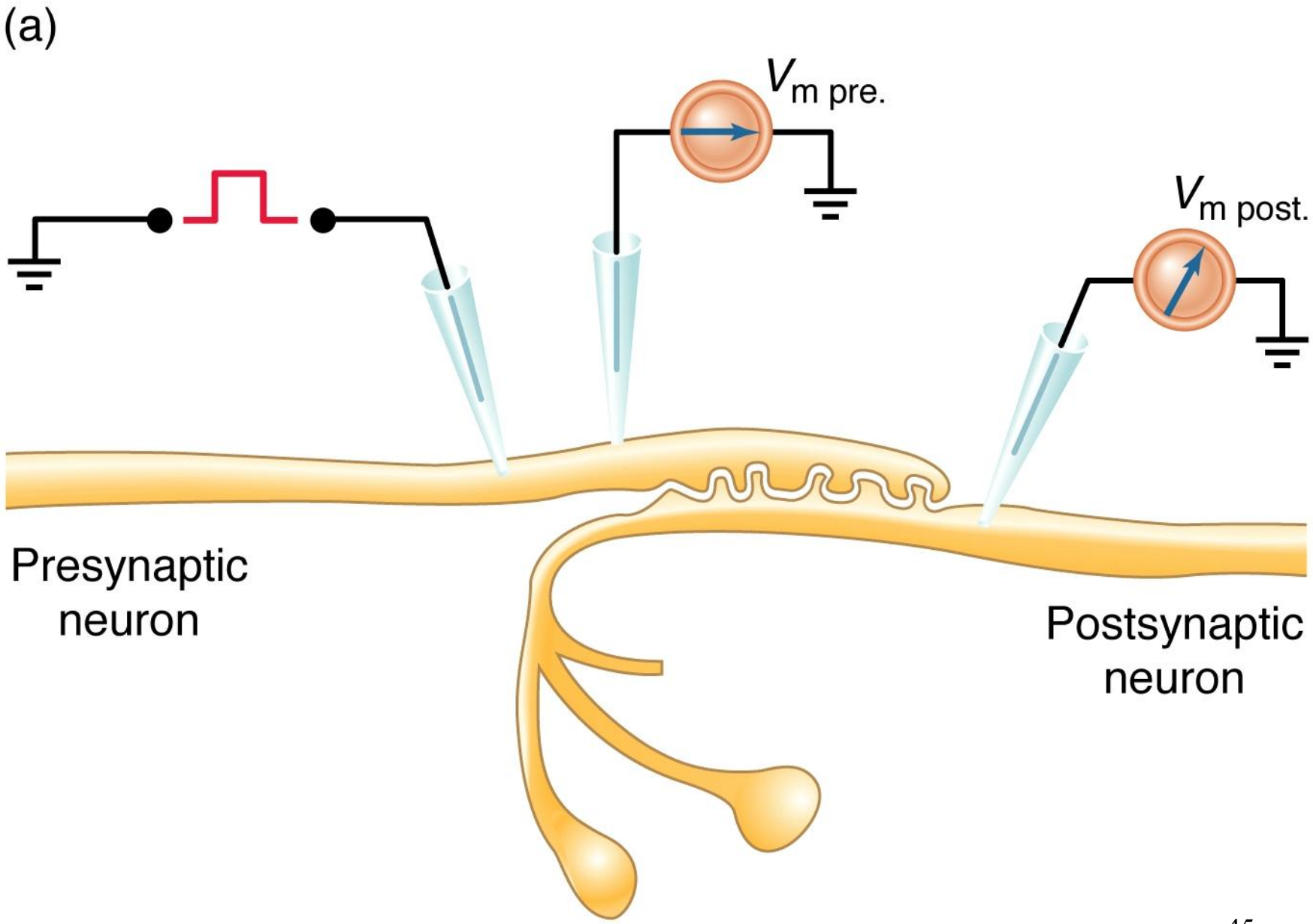

(a)
Stimulus
High-Mg2+, low-Ca2+ solution
Vm
1 mV
50 ms
Stimulus

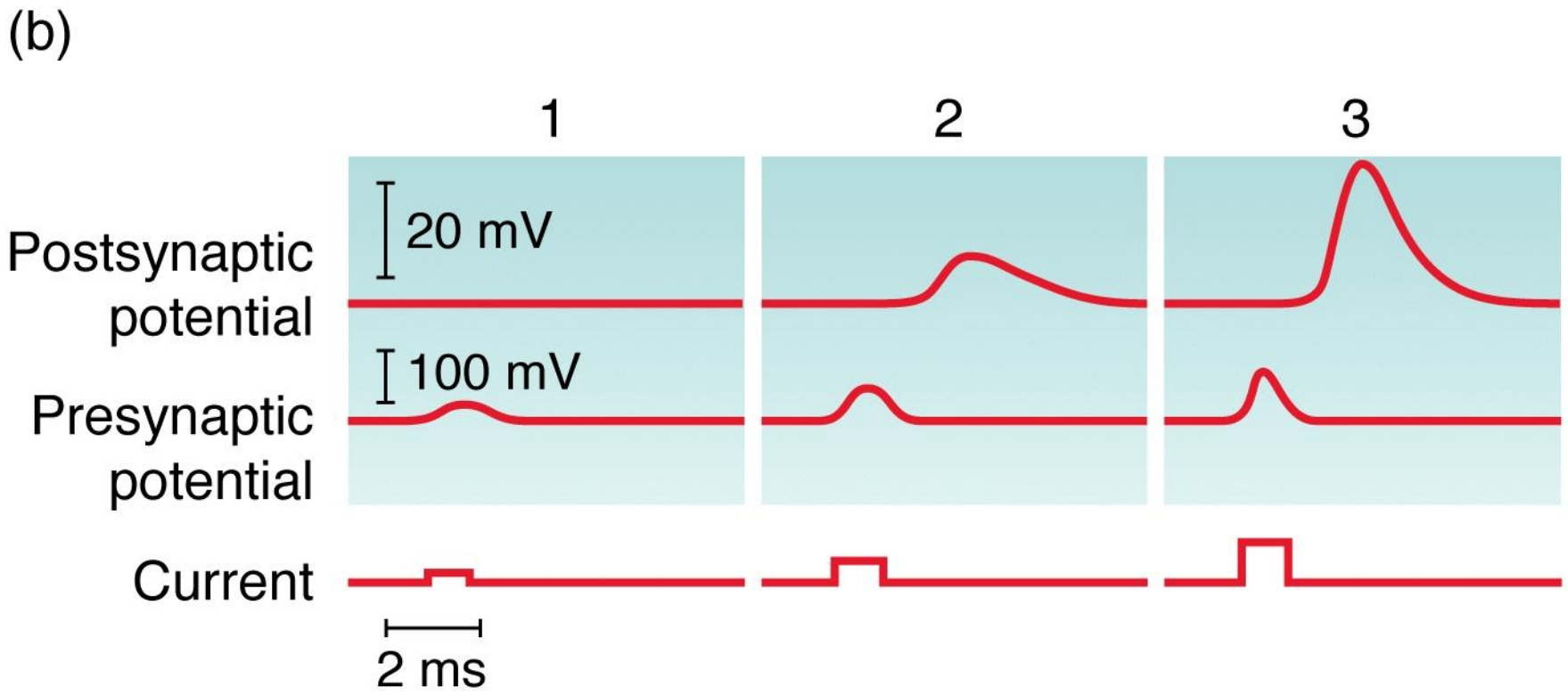

(b)
20
10
0
Spontaneous miniature endplate potentials
0
1
2
3
Number of occurrences
190
180
40
30
20
10
0
Failures
Evoked endplate potentials
0
1
2
3
Units of amplitude

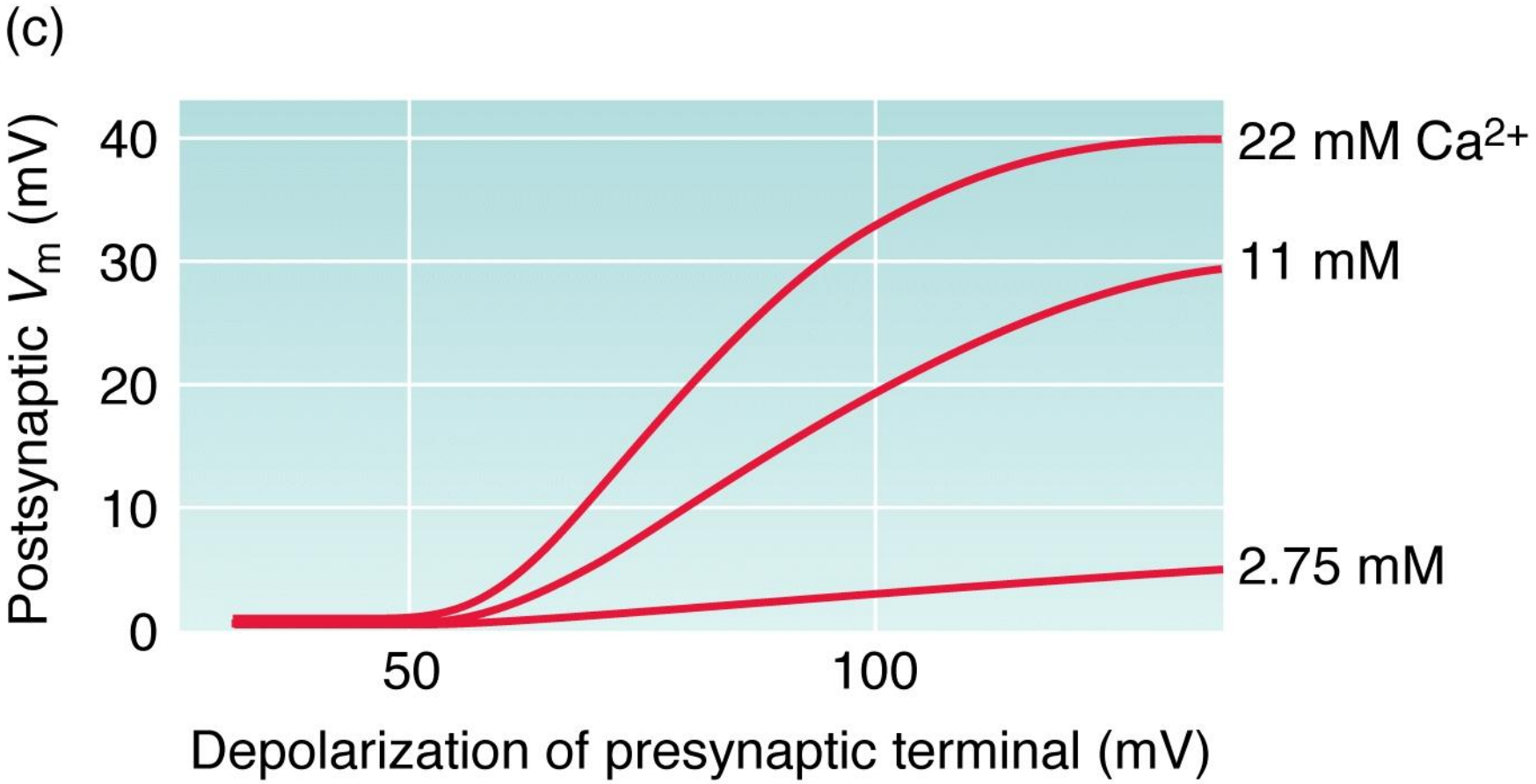

(a)
Prolonged stimulation
depolarizes terminal
Low-Ca2+ solution
Vm

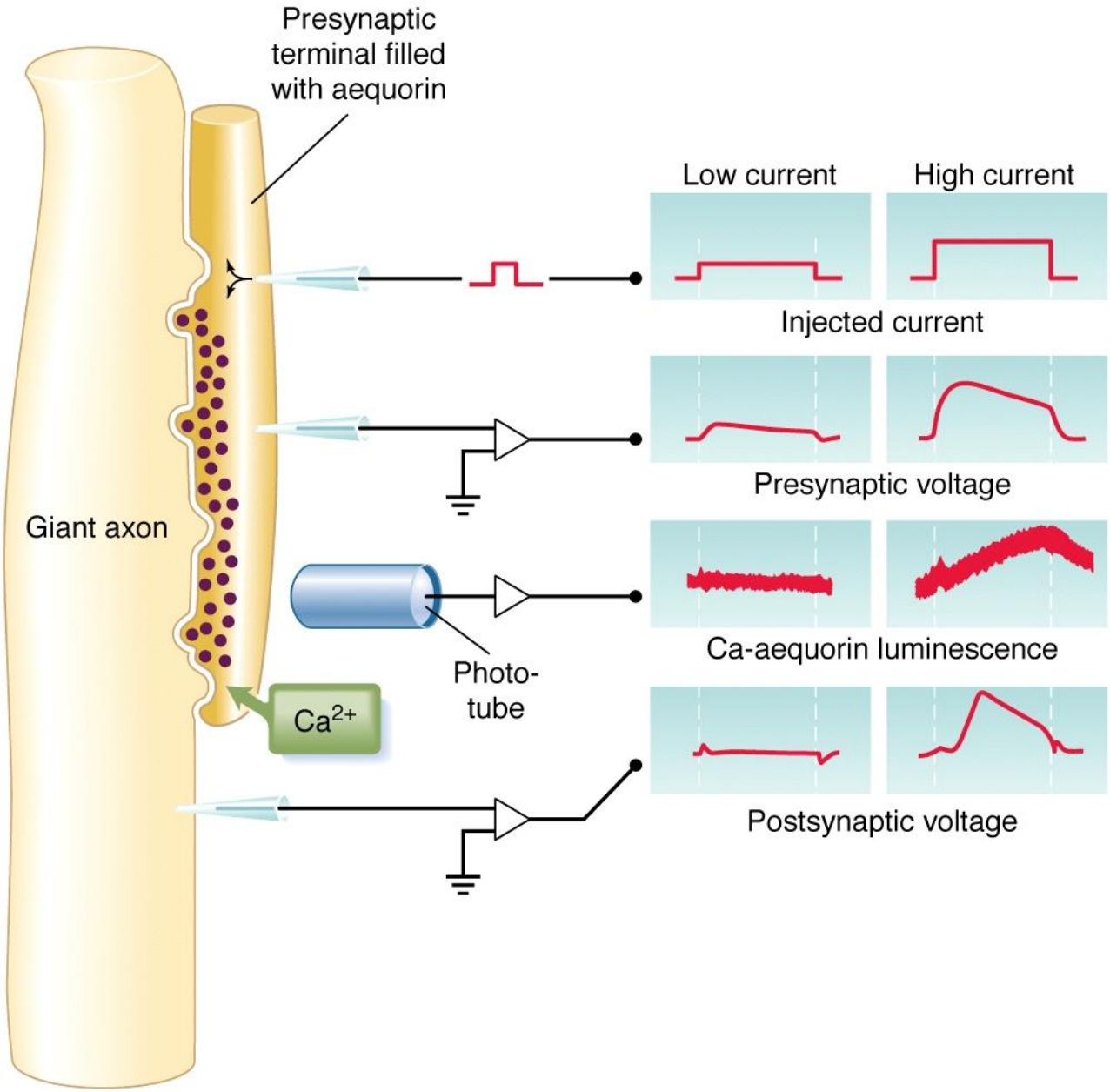
(b)

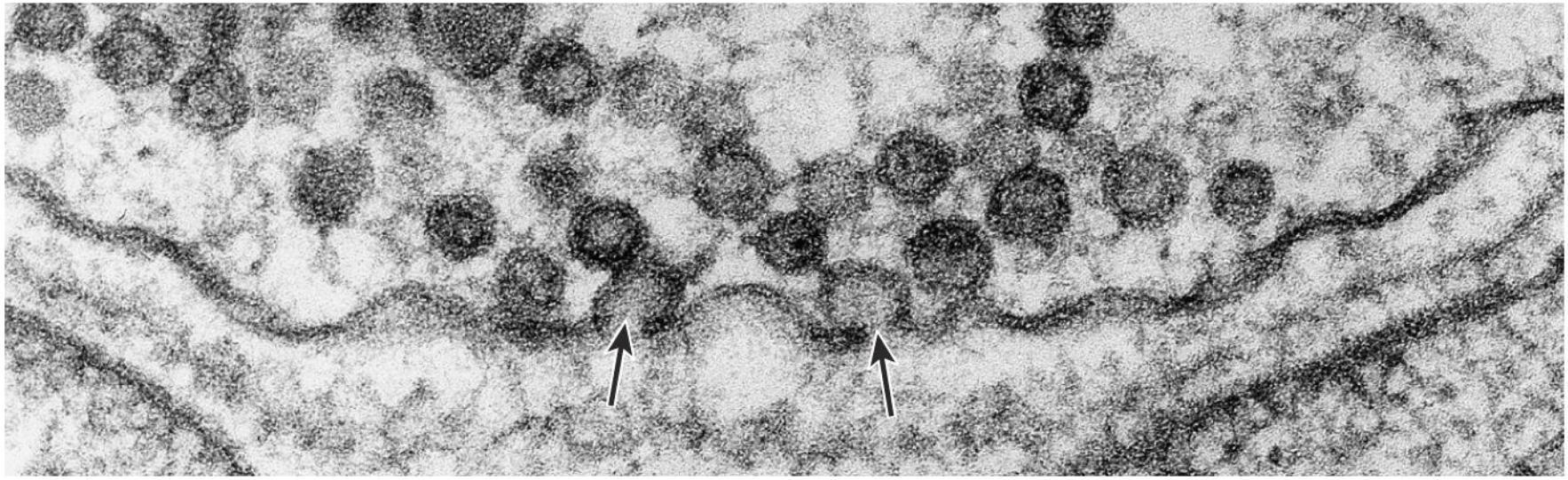



(a)
$V_{m\ pre.}$
$V_{m\ post.}$
Presynaptic neuron
Postsynaptic neuron


(b)
1
2
3
20 mV
Postsynaptic potential
100 mV
Presynaptic potential
Current
2 ms

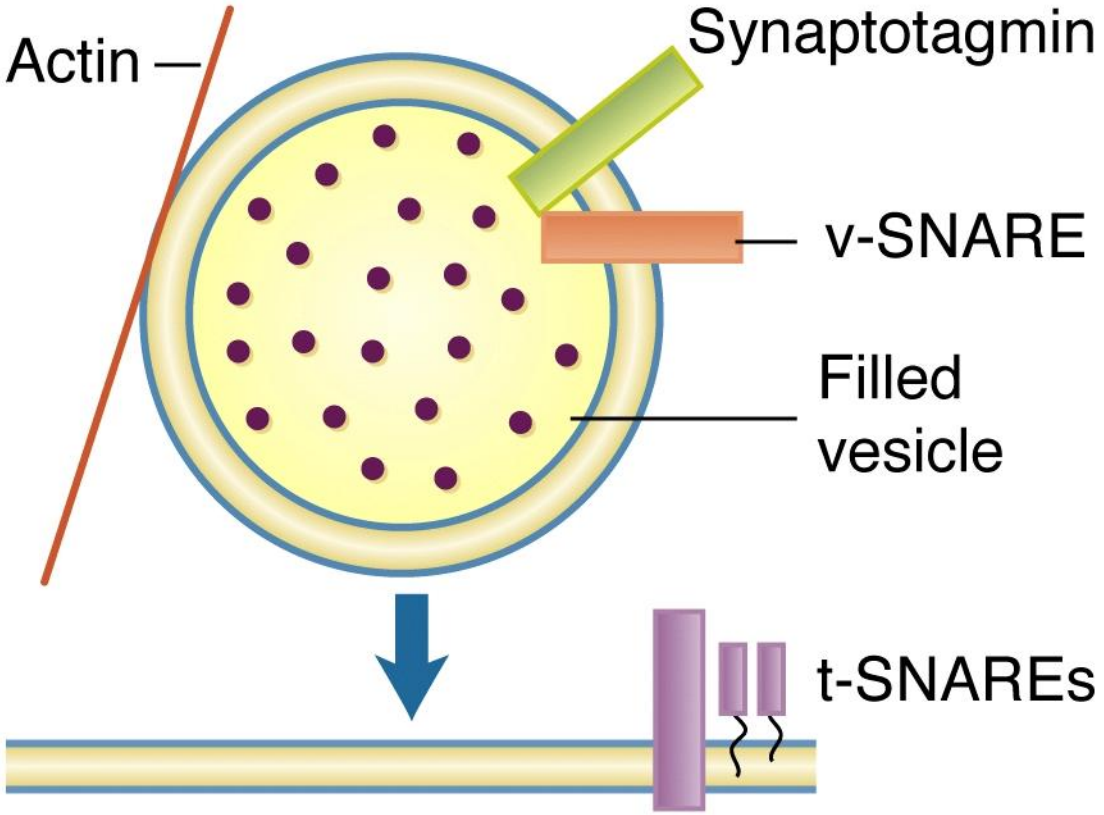

(c)
Postsynaptic V_m (mV)
40
30
20
10
0
50
100
Depolarization of presynaptic terminal (mV)
22 mM Ca^{2+}
11 mM
2.75 mM


Presynaptic terminal filled with aequorin
Low current
High current
Injected current
Giant axon
Presynaptic voltage
Photo-tube
Ca-aequorin luminescence
Ca2+
Postsynaptic voltage



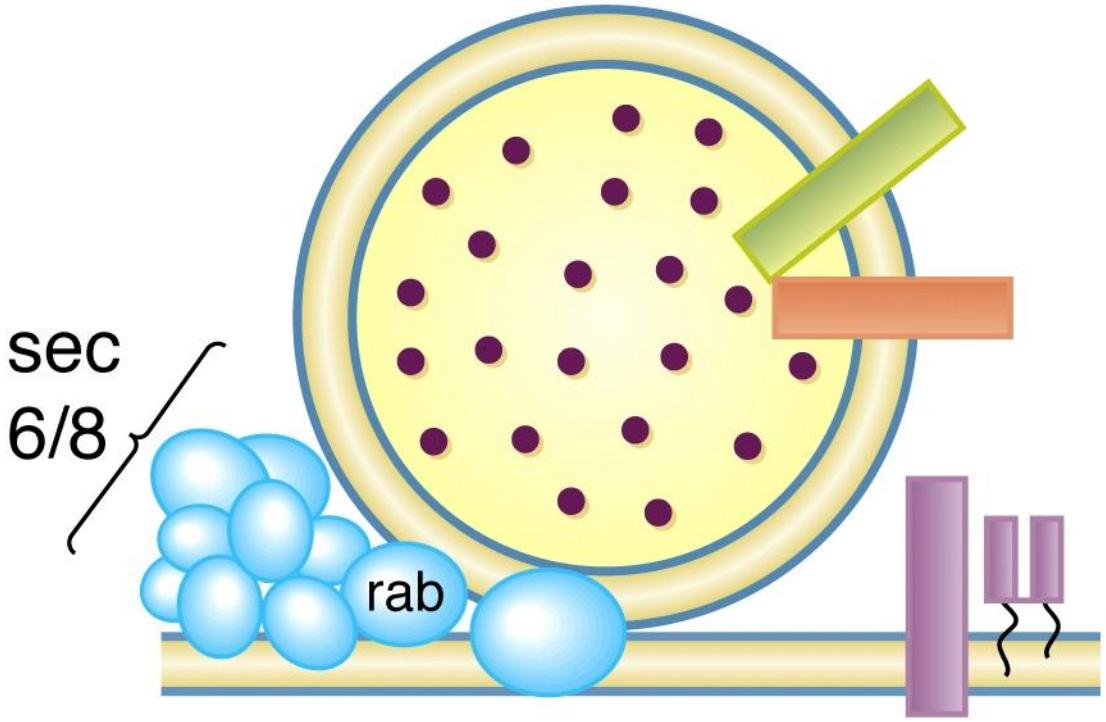
1

Vesicle moves to the active zone.



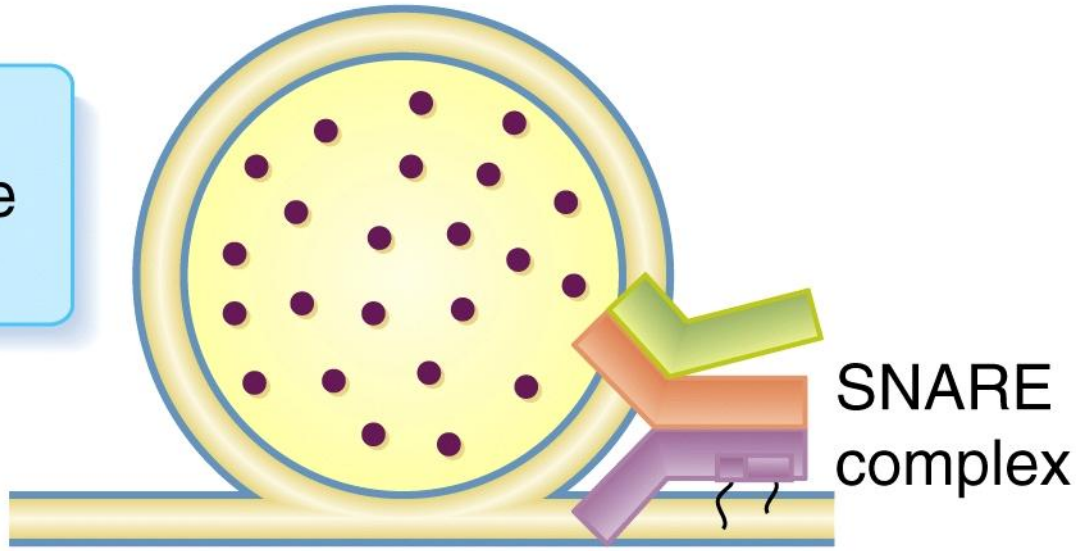
2

Several proteins participate in attaching vesicle to the active zone.



3

Complex of SNARE proteins docks vesicle to membrane.



4

Fusion between vesicle and membrane requires an increase of [Ca^{2+}] in cytoplasm.

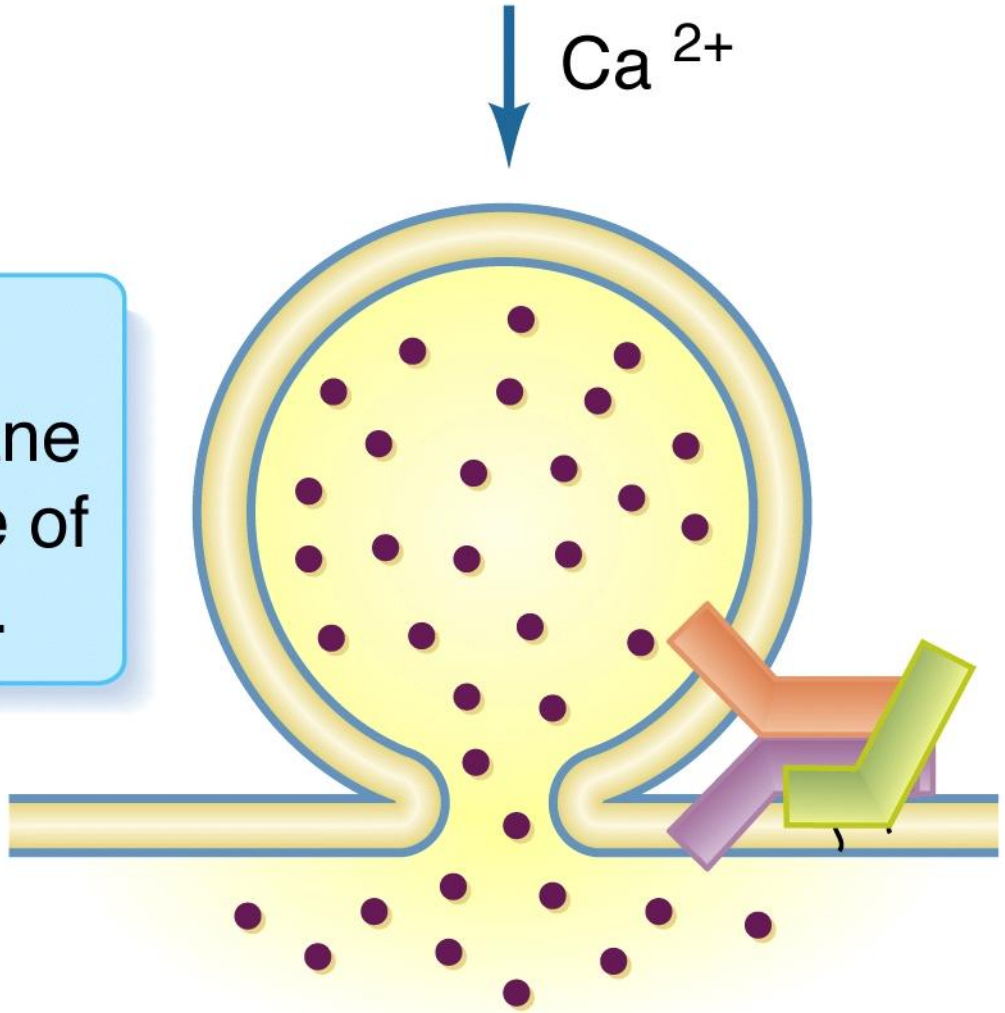
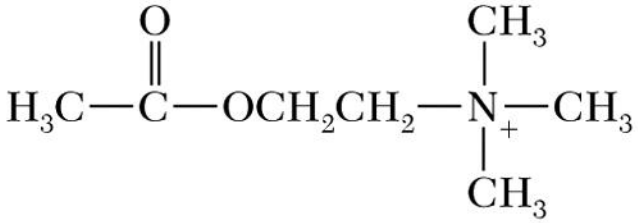
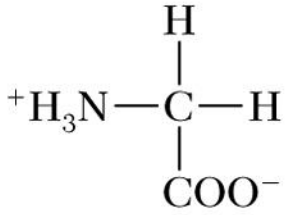
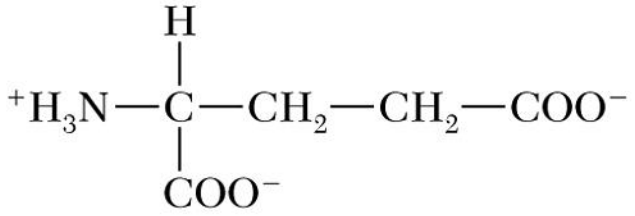
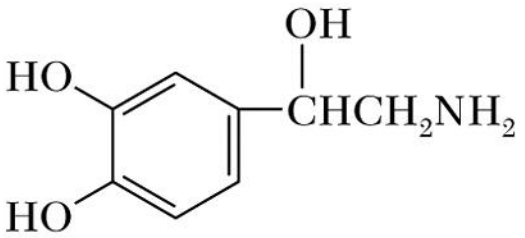
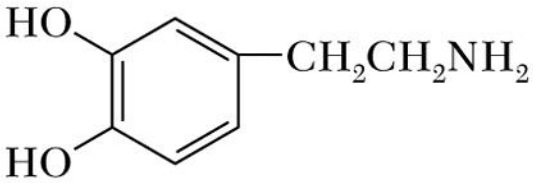
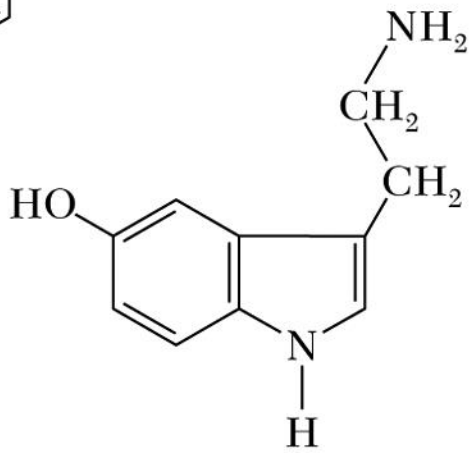


Table 6-2 Typical small neurotransmitters, their structures, and functions

Neurotransmitter	Typical effects*	Structure
Acetylcholine (ACh)	Fast excitation; slow inhibition	
Glycine (Gly)	Fast inhibition	
γ-Aminobutyric acid (GABA)	Fast inhibition; slow inhibition	
Glutamate (Glu)	Fast excitation; slow change in postsynaptic metabolism	

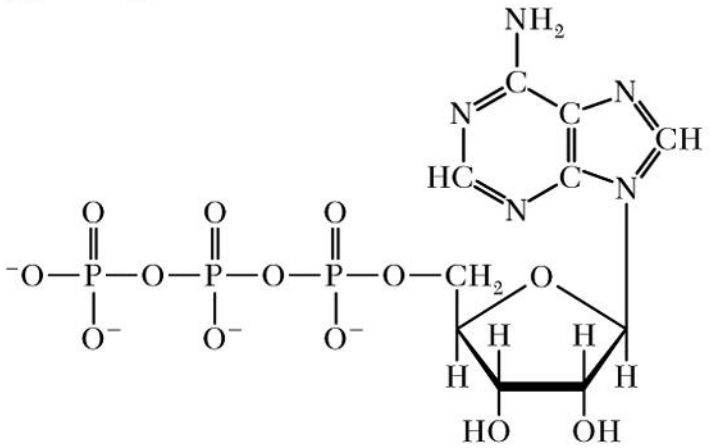
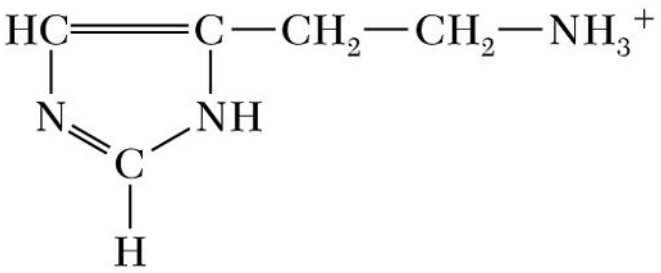
*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

Table 6-2 Typical small neurotransmitters, their structures, and functions

Neurotransmitter	Typical effects*	Structure
Norepinephrine (Nor-epi)	Slow excitation; slow inhibition	
Dopamine	Differs with location but causes slow postsynaptic effects	
Serotonin (5-HT = 5-hydroxytryptamine)	Slow excitation or slow inhibition	

*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

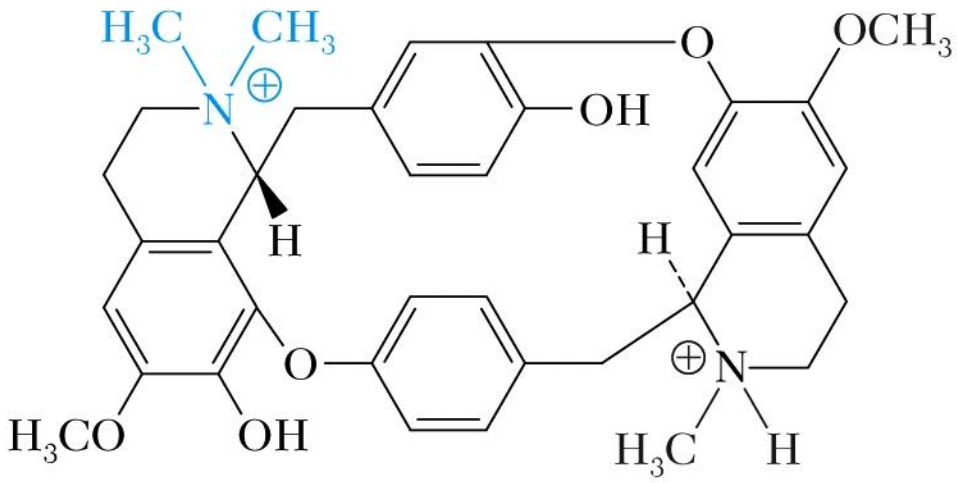
Table 6-2 Typical small neurotransmitters, their structures, and functions

Neurotransmitter	Typical effects*	Structure
Nitrogen oxide (NO)	Synaptic modulation	
Adenosine triphosphate (ATP)	Both fast and slow synaptic transmission	
Histamine	Slow modulation	

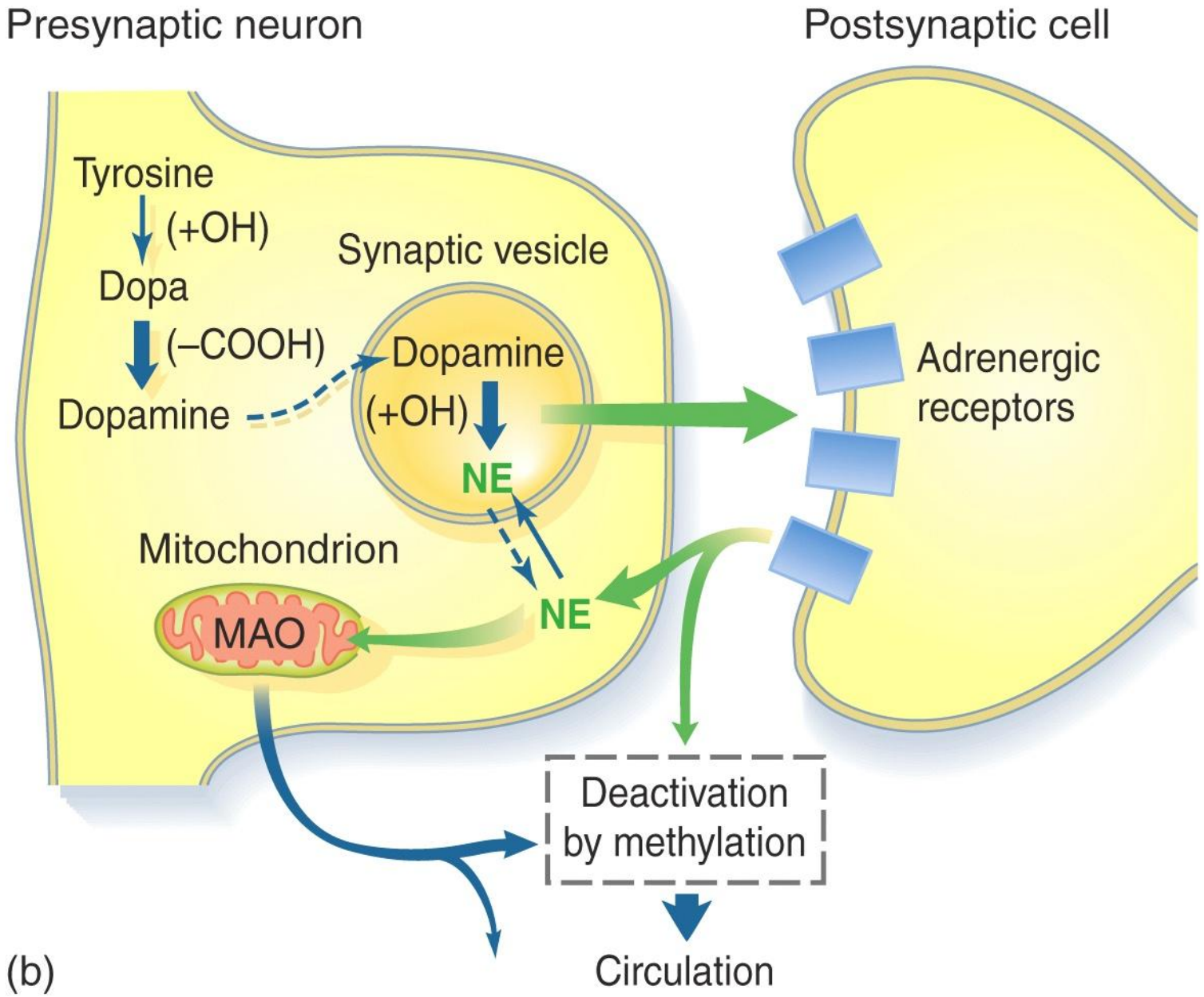
*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

Acetylcholine (ACh)

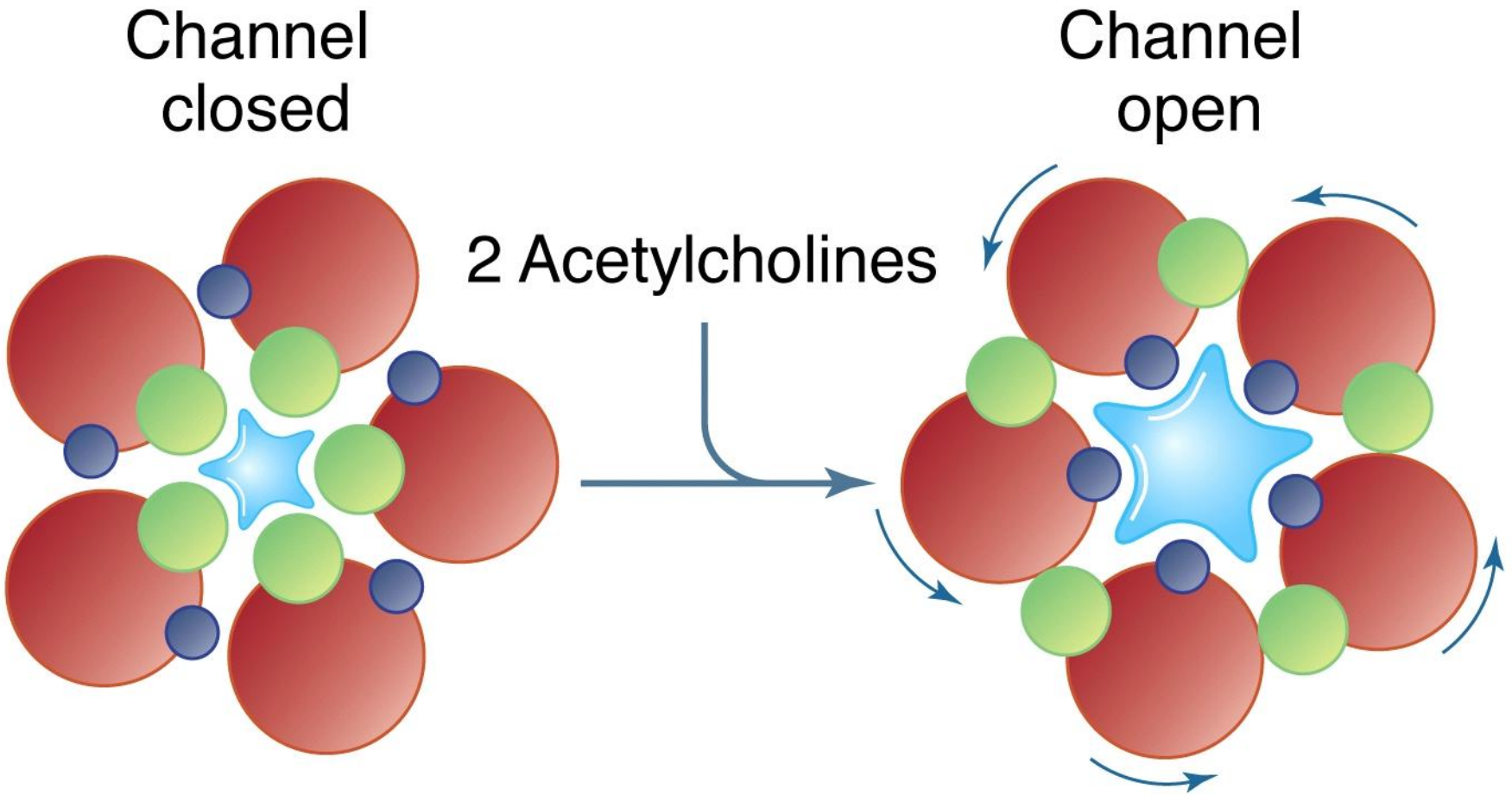
Carbachol, an ACh agonist

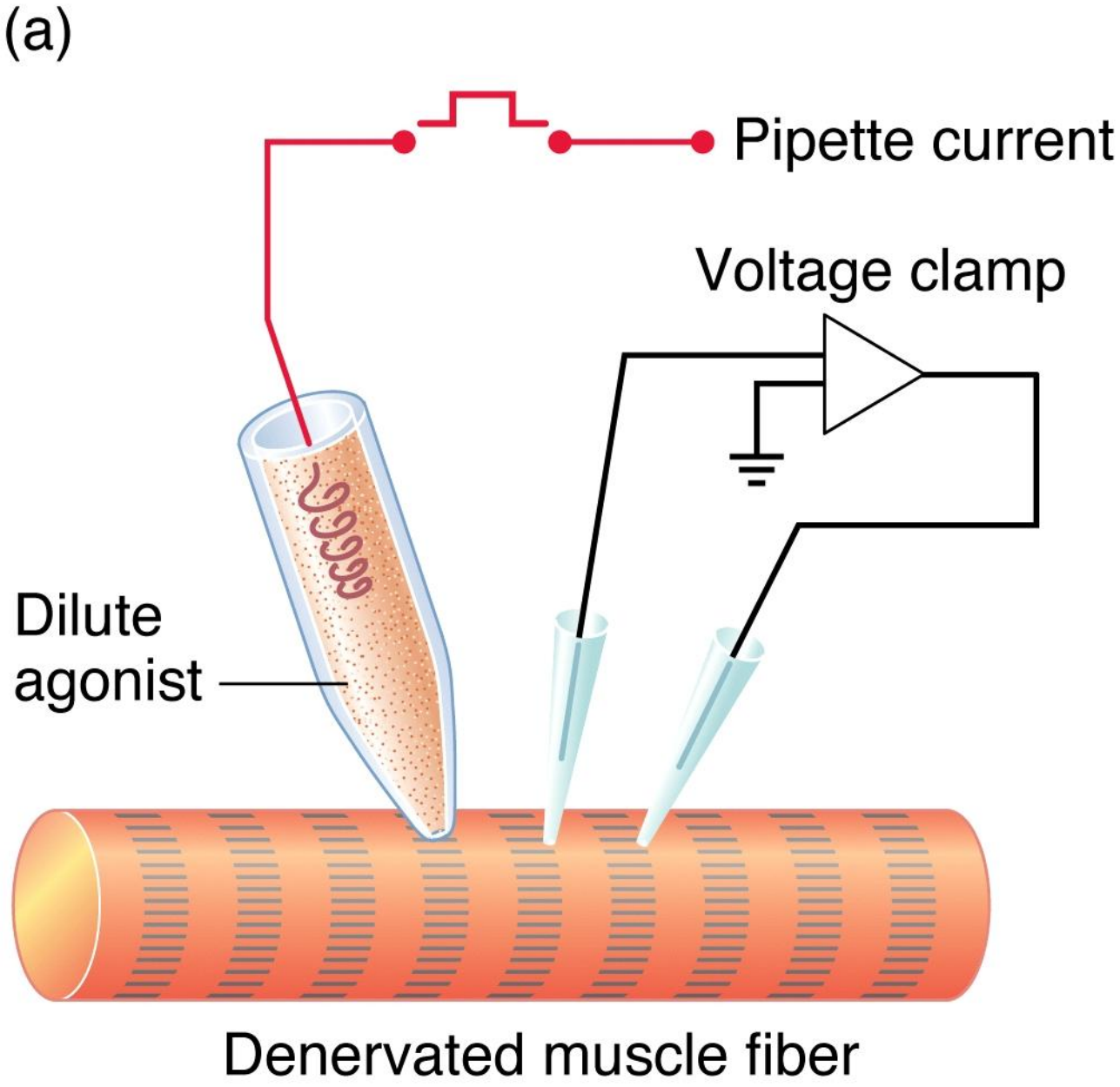


D-Tubocurarine, an ACh antagonist

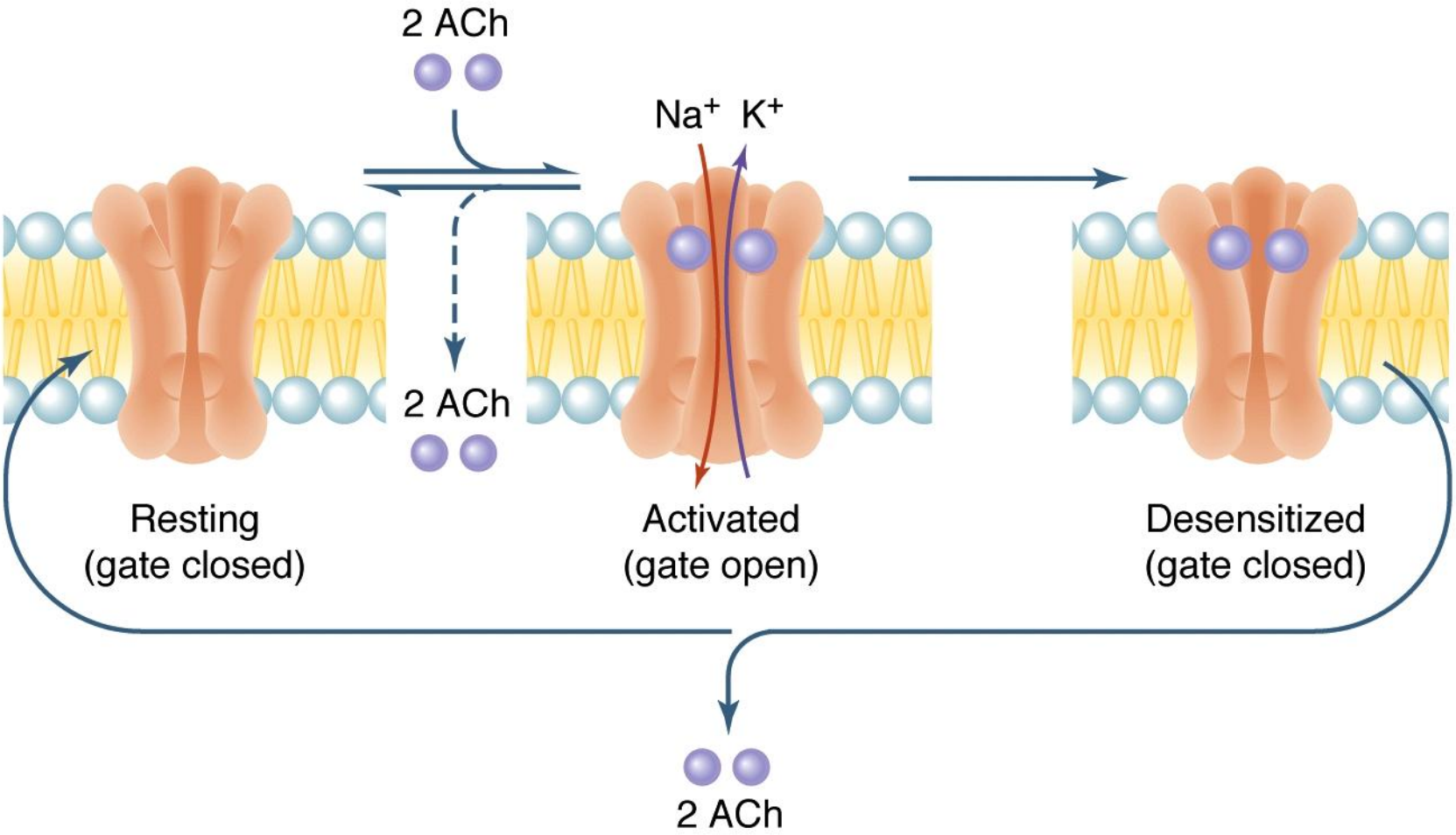

Presynaptic neuron
Postsynaptic cell
Tyrosine
(+OH)
Dopa
(–COOH)
Dopamine
Synaptic vesicle
Dopamine
(+OH)
NE
Mitochondrion
MAO
NE
Adrenergic receptors
Deactivation by methylation
Circulation
(b)

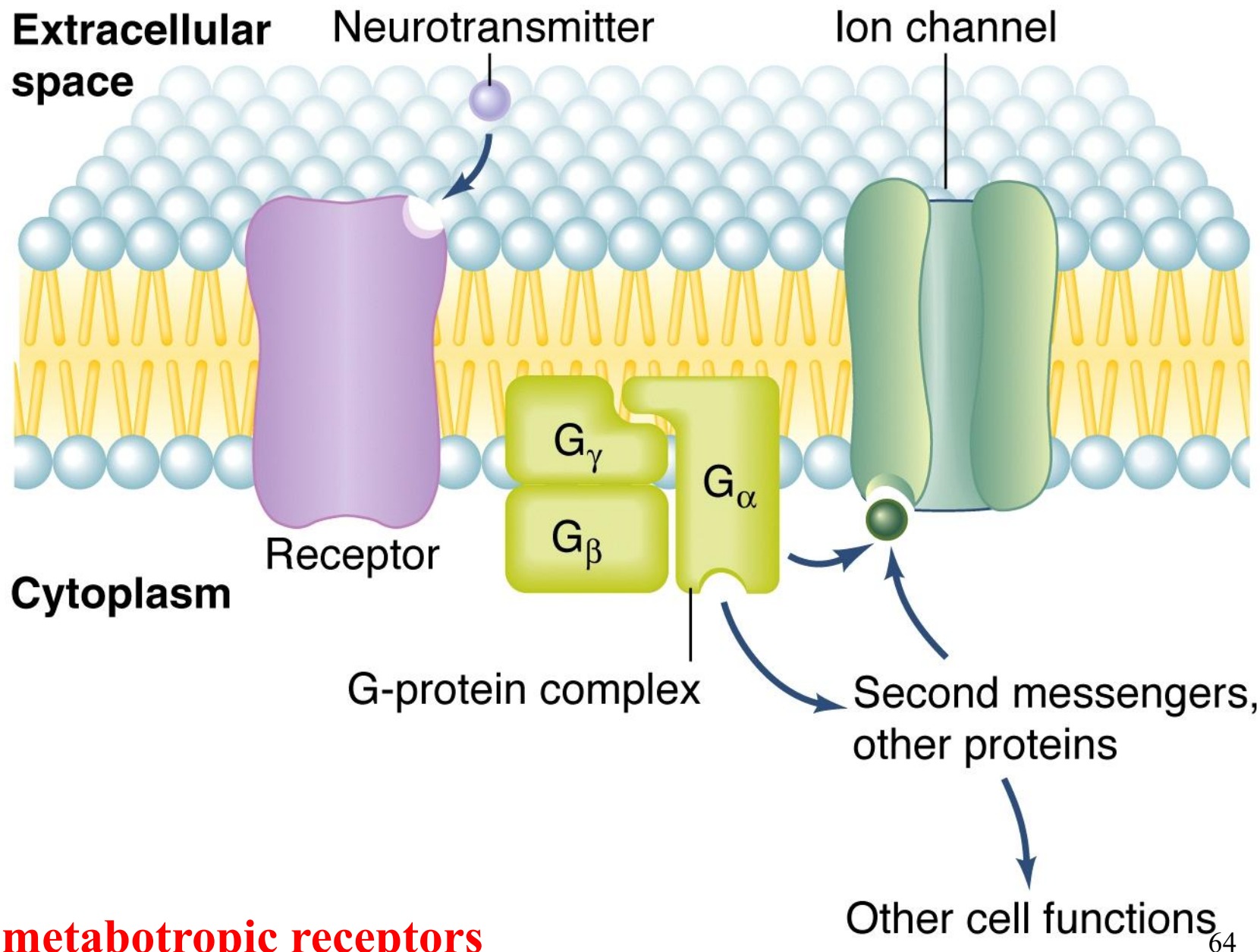
(c)



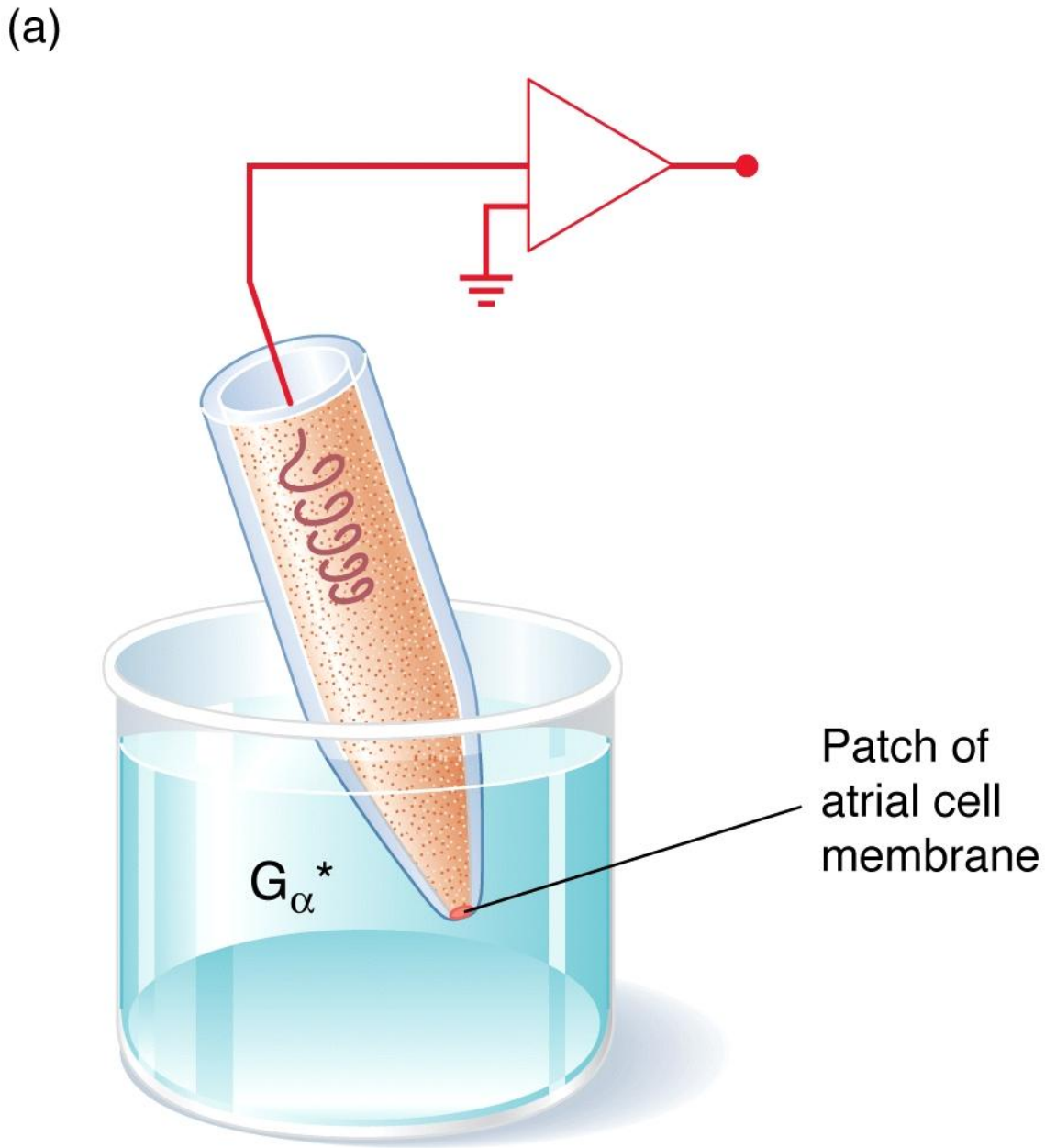

(a)
Pipette current
Voltage clamp
Dilute
agonist
Denervated muscle fiber

(b)

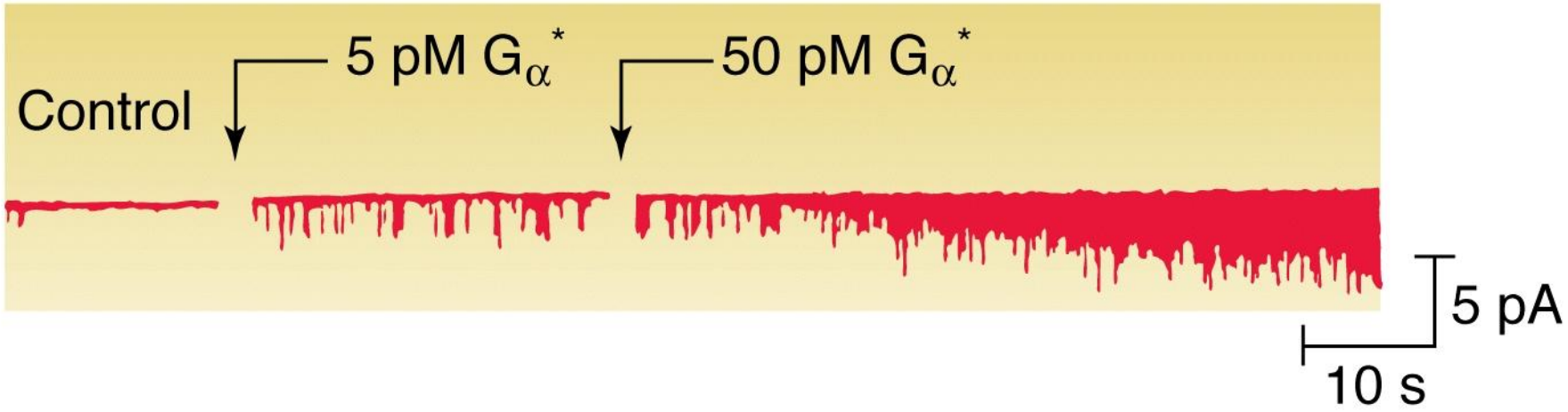

2 ACh
Na+ K+
2 ACh
Resting
(gate closed)
Activated
(gate open)
Desensitized
(gate closed)
2 ACh

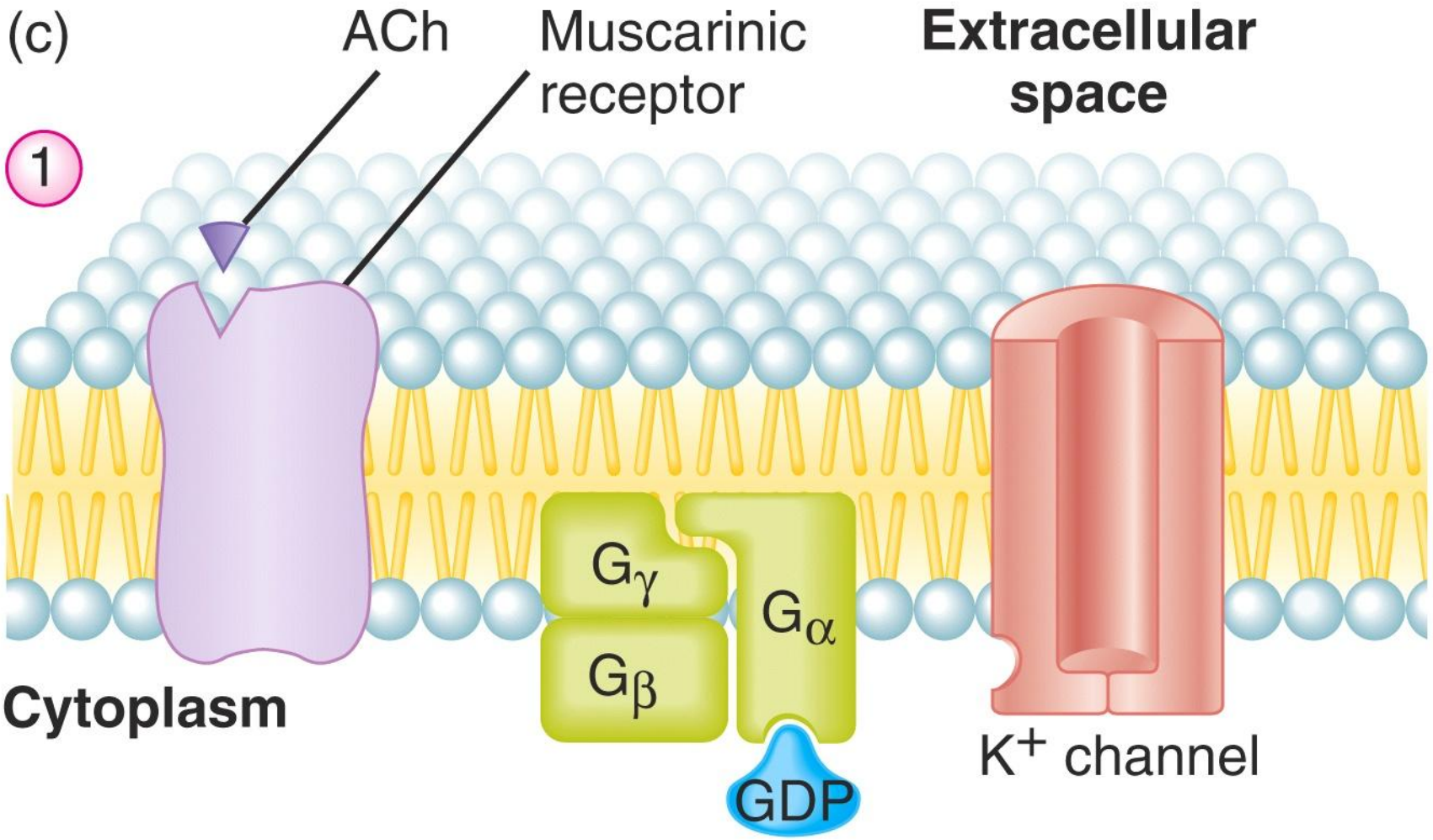


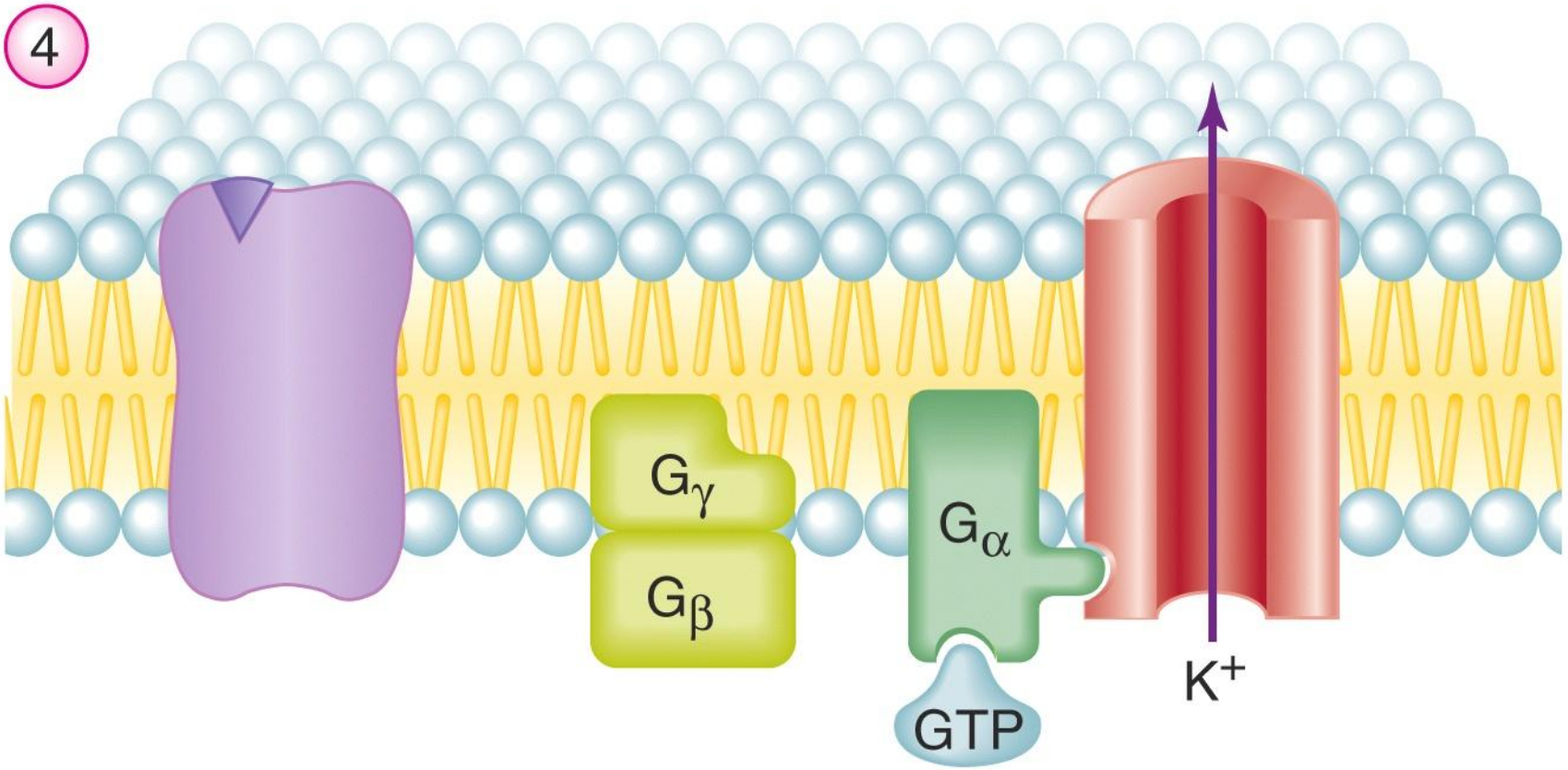
metabotropic receptors

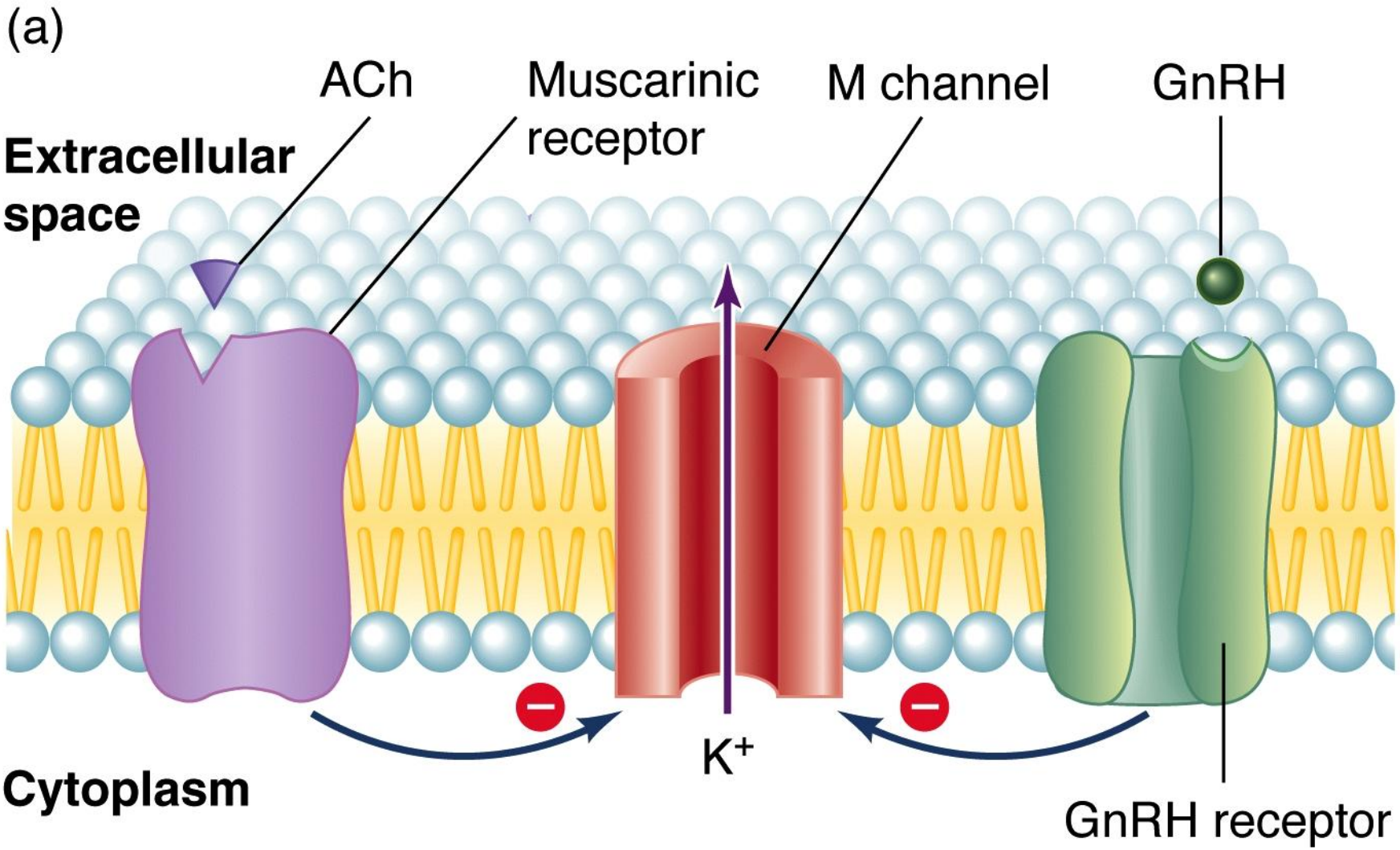

(a)
G_α*
Patch of
atrial cell
membrane

(b)

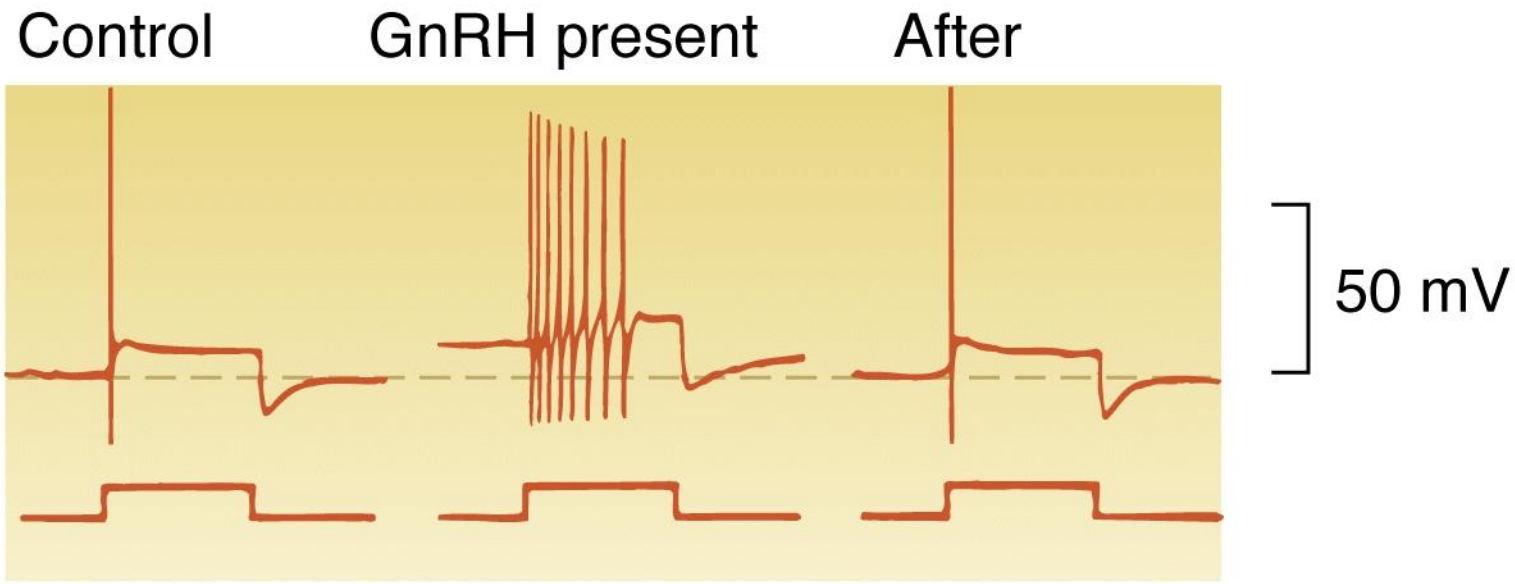


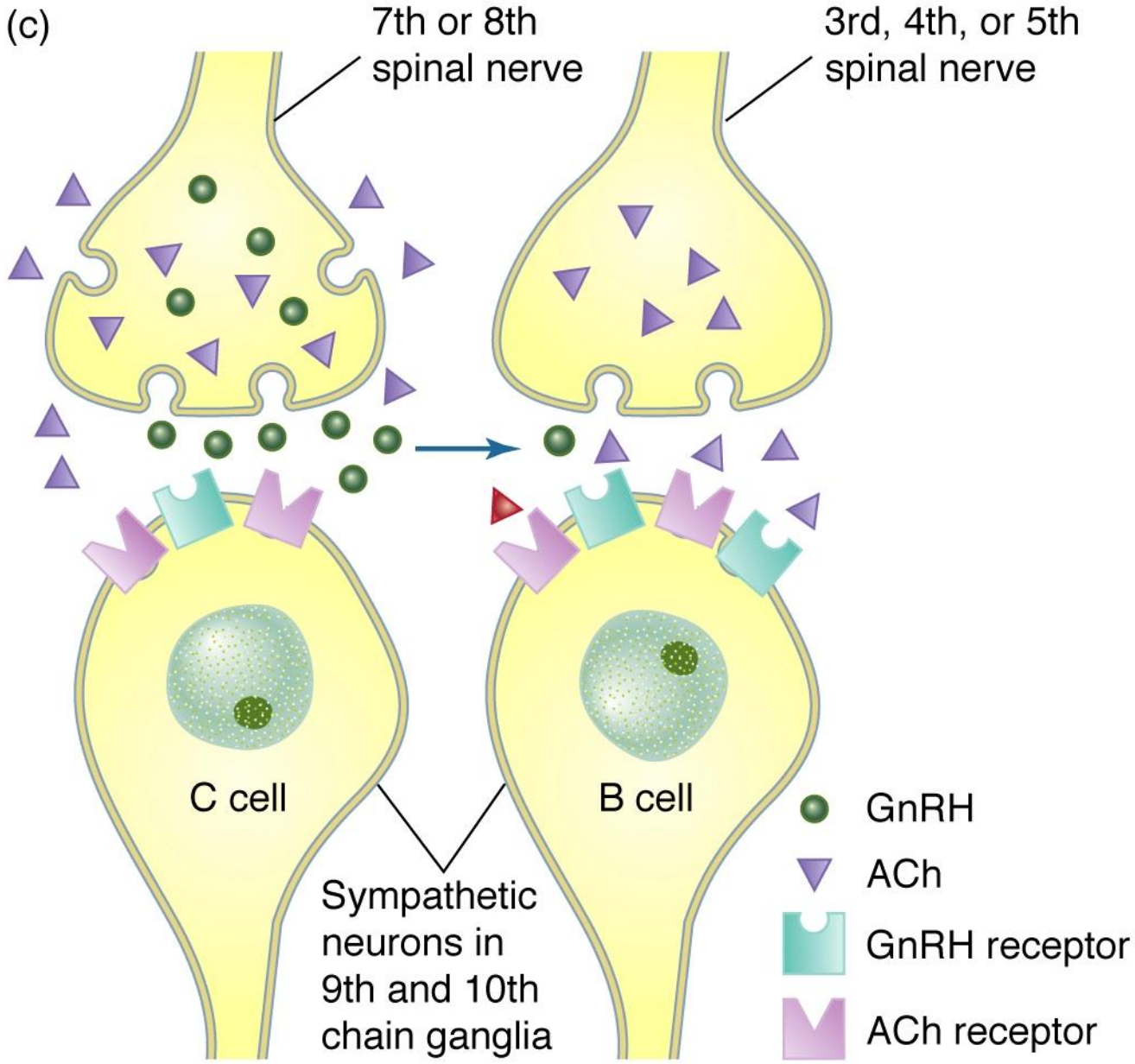

(c)
ACh
Muscarinic receptor
Extracellular space
1
Cytoplasm
Gγ
Gβ
Gα
GDP
K+ channel

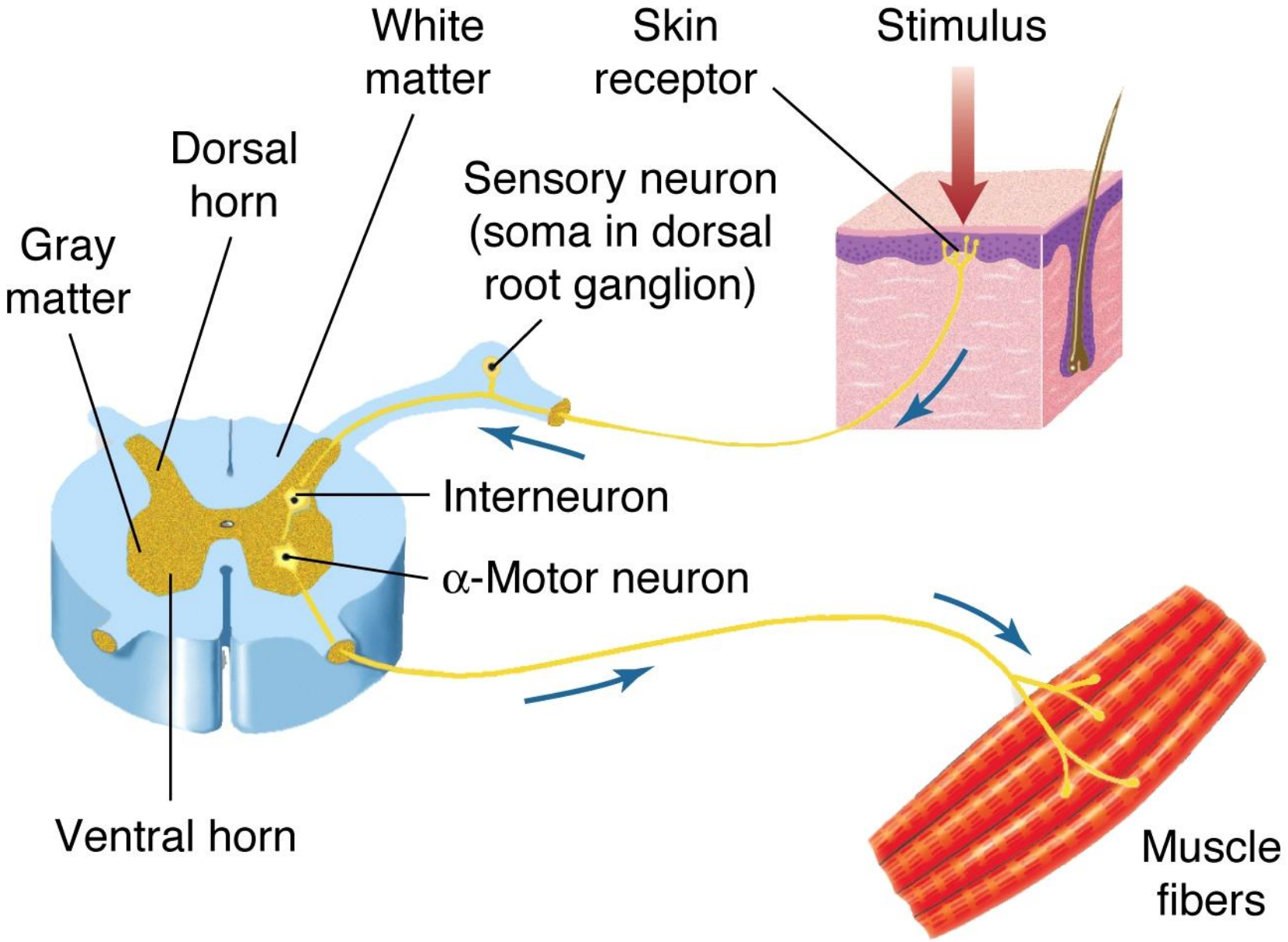

4
Gγ
Gβ
Gα
GTP
K+

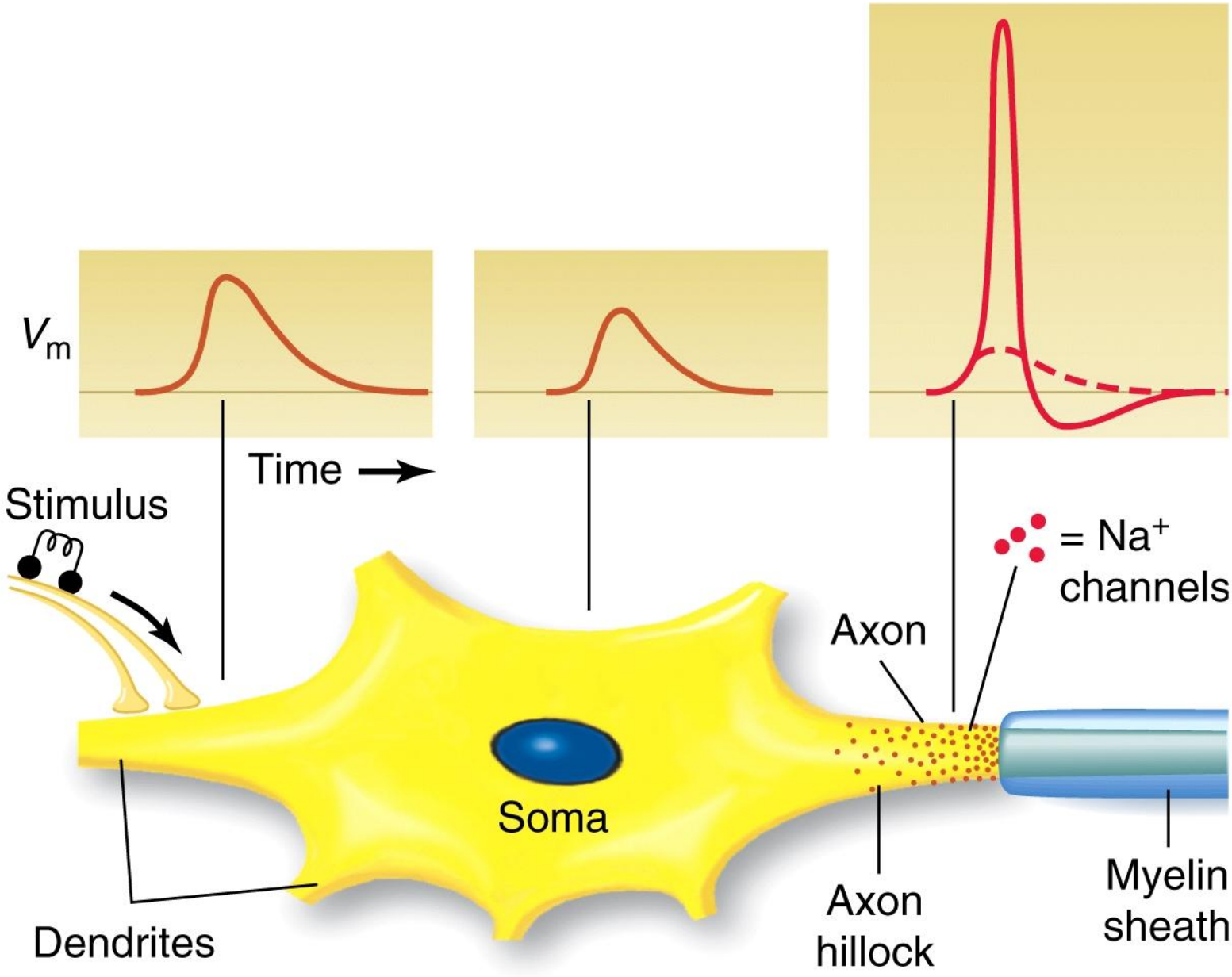

(a)
ACh
Muscarinic receptor
M channel
GnRH
Extracellular space
Cytoplasm
K+
GnRH receptor

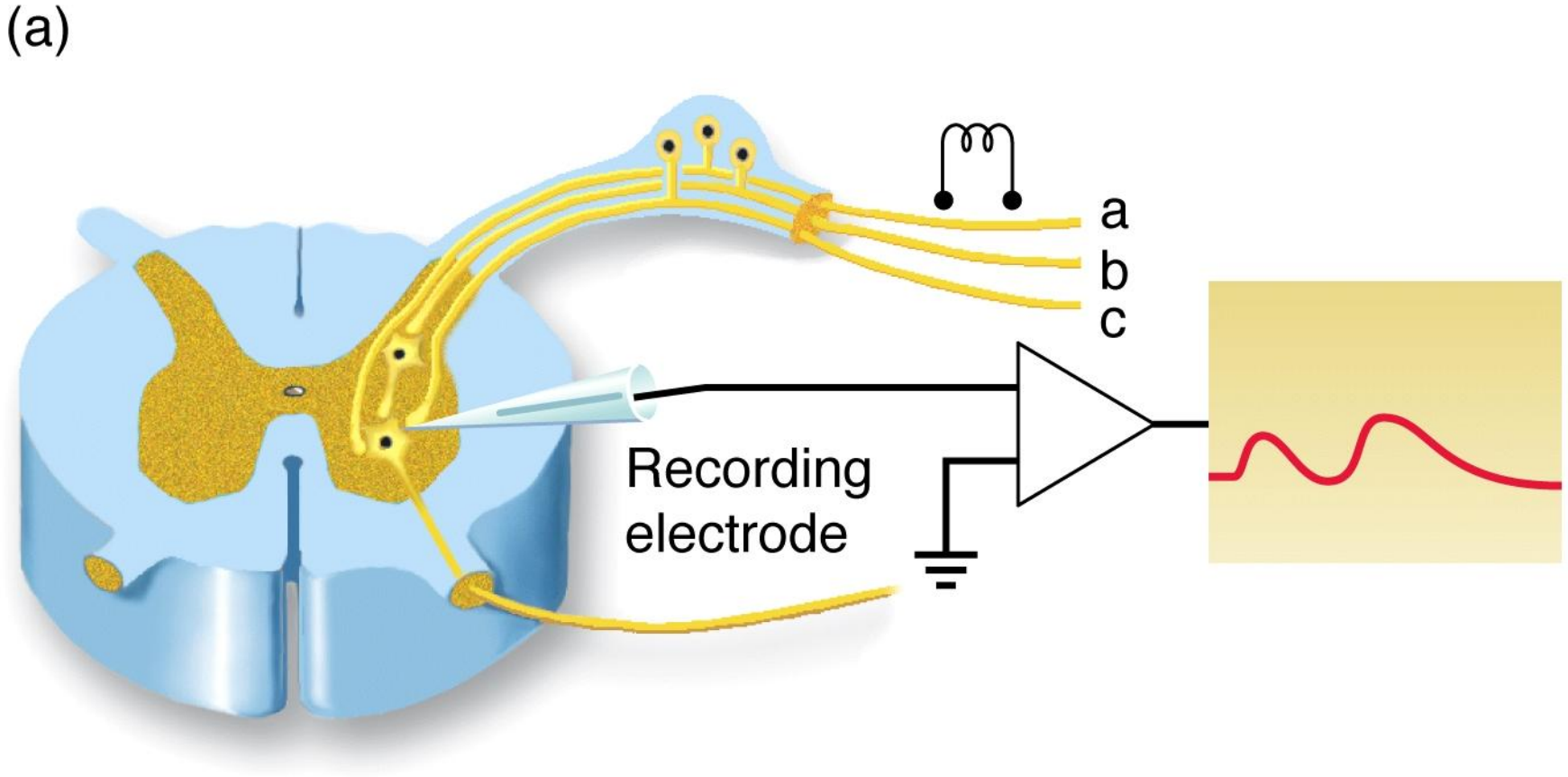
(b)

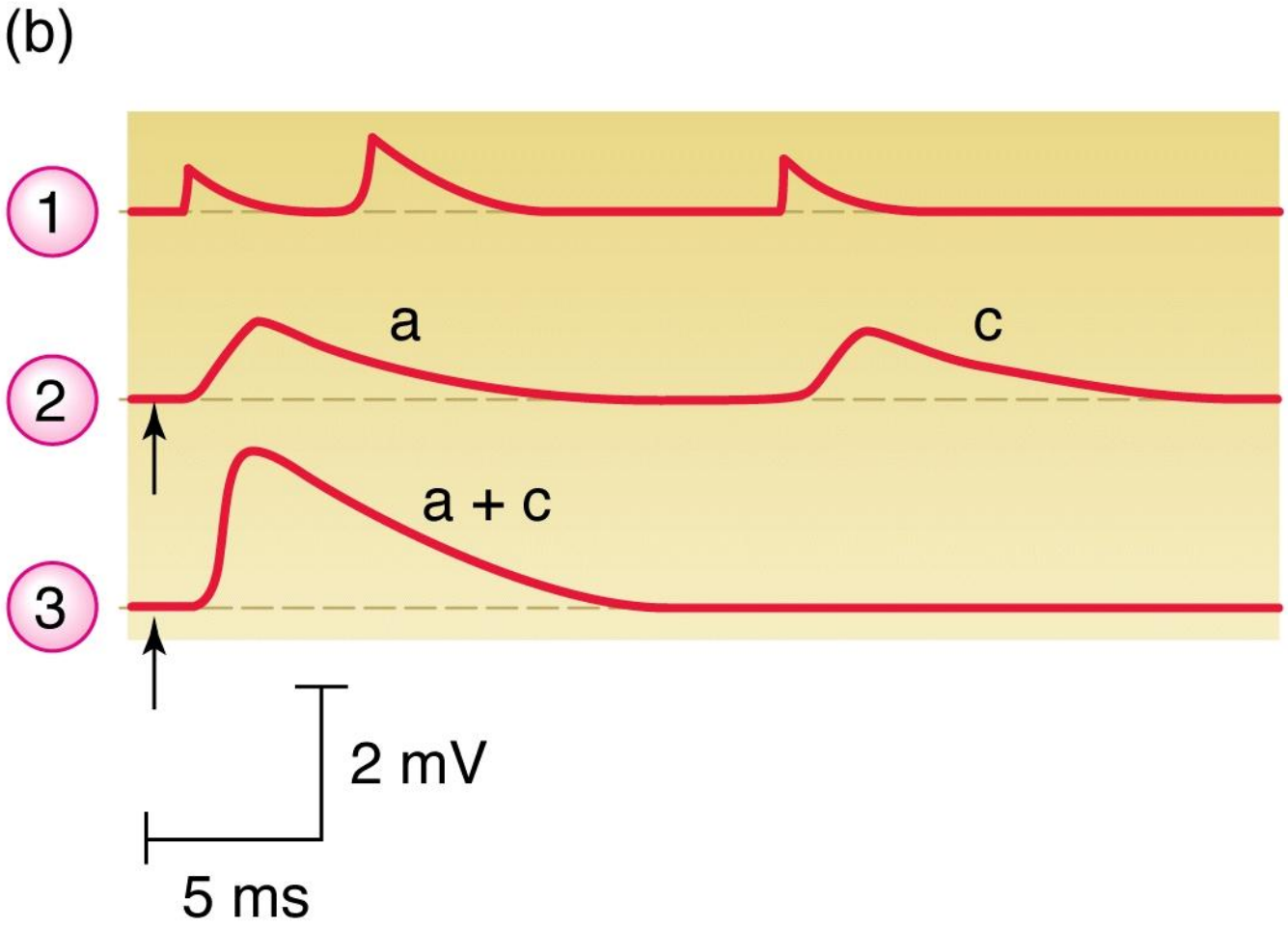


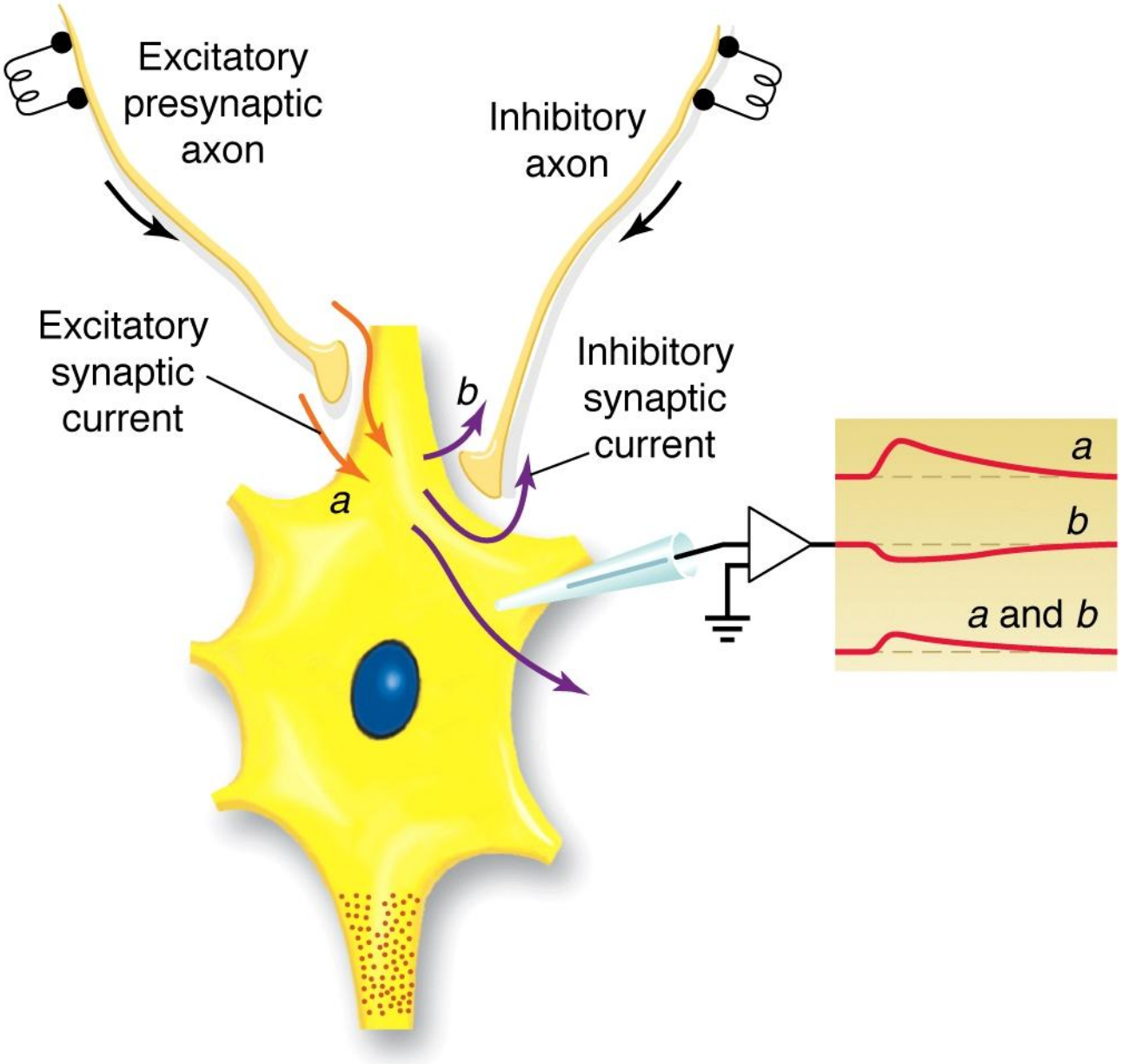

(c)
7th or 8th spinal nerve
3rd, 4th, or 5th spinal nerve
C cell
B cell
Sympathetic neurons in 9th and 10th chain ganglia
GnRH
ACh
GnRH receptor
ACh receptor

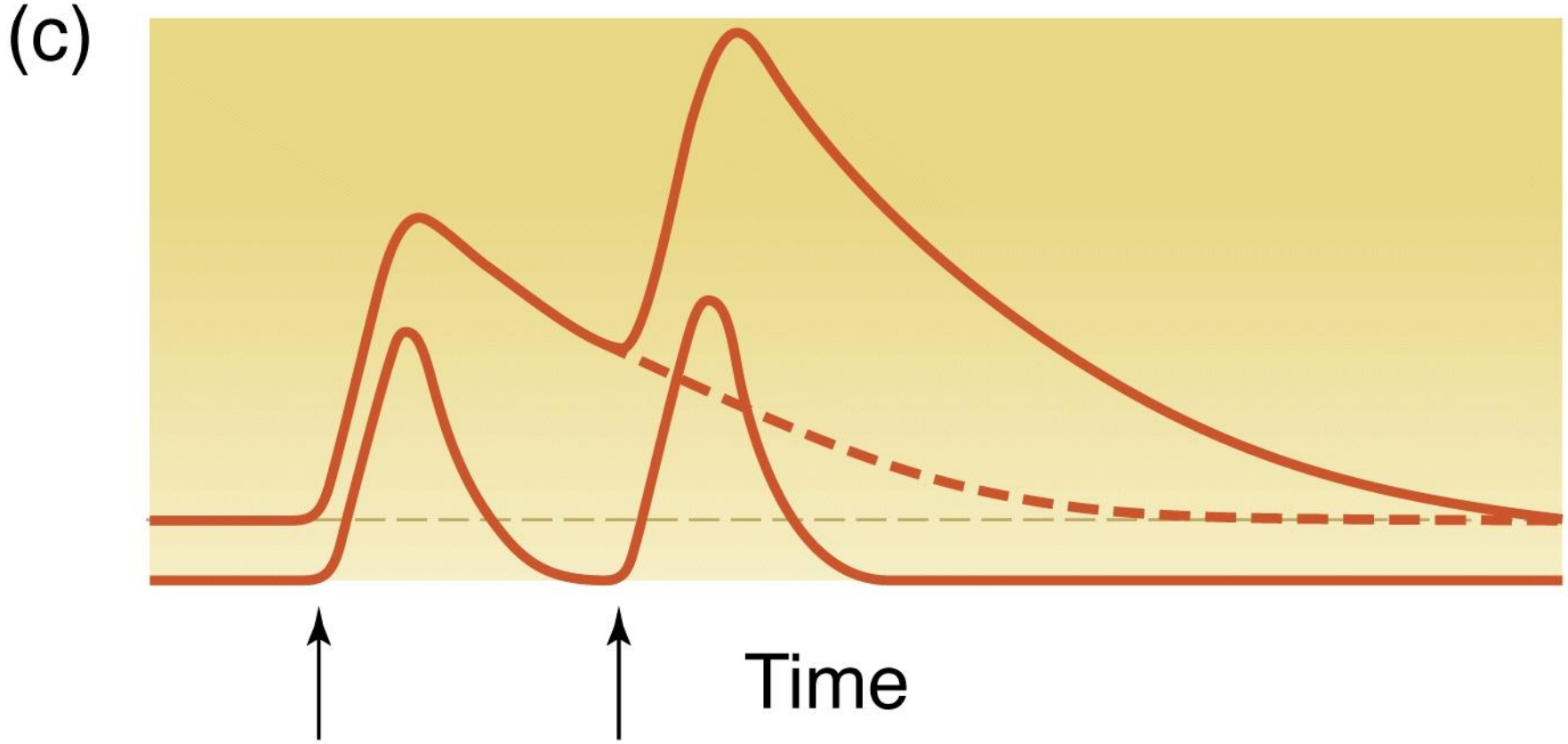

White matter
Skin receptor
Stimulus
Dorsal horn
Sensory neuron (soma in dorsal root ganglion)
Gray matter
Interneuron
α-Motor neuron
Ventral horn
Muscle fibers

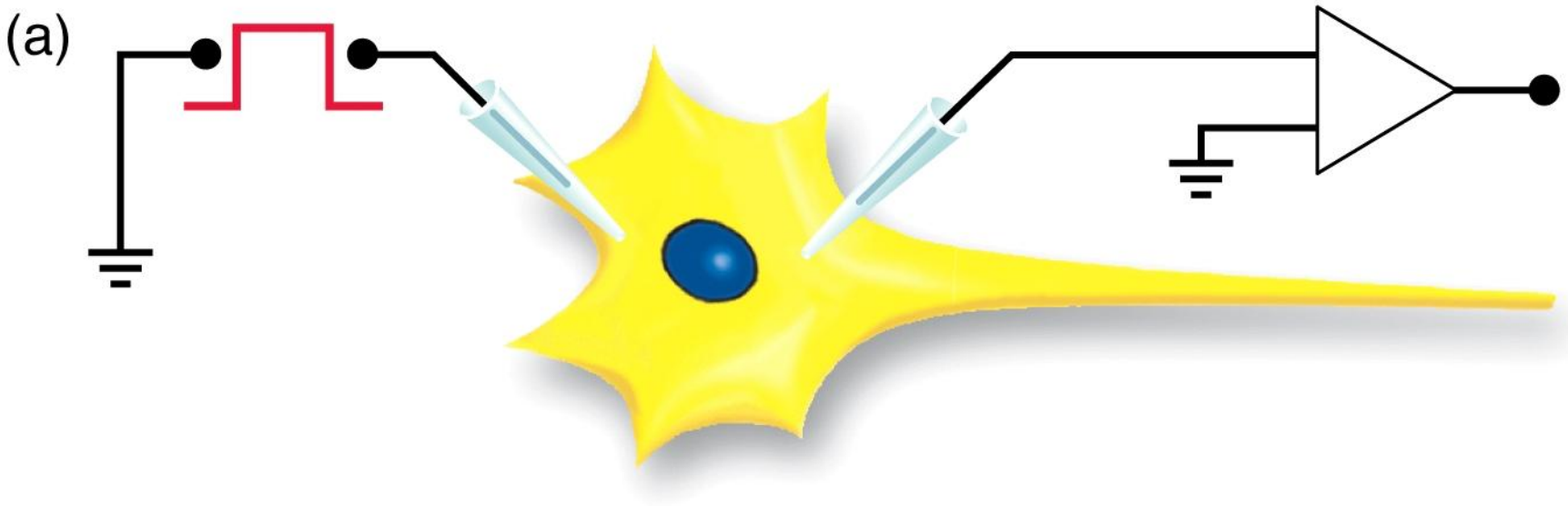

V_m
Time
Stimulus
= Na^+ channels
Axon
Soma
Dendrites
Axon hillock
Myelin sheath

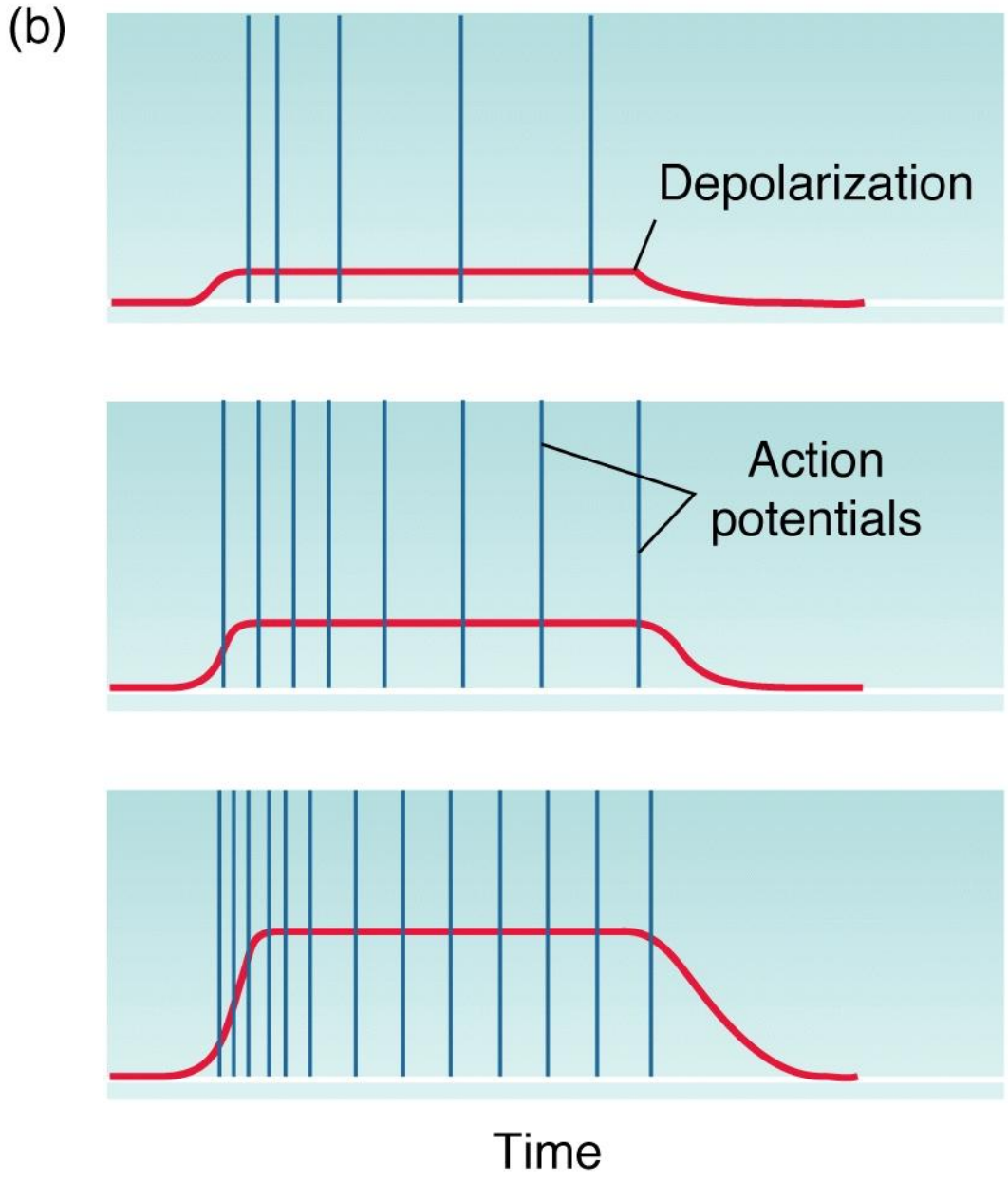

(a)
a
b
c
Recording
electrode

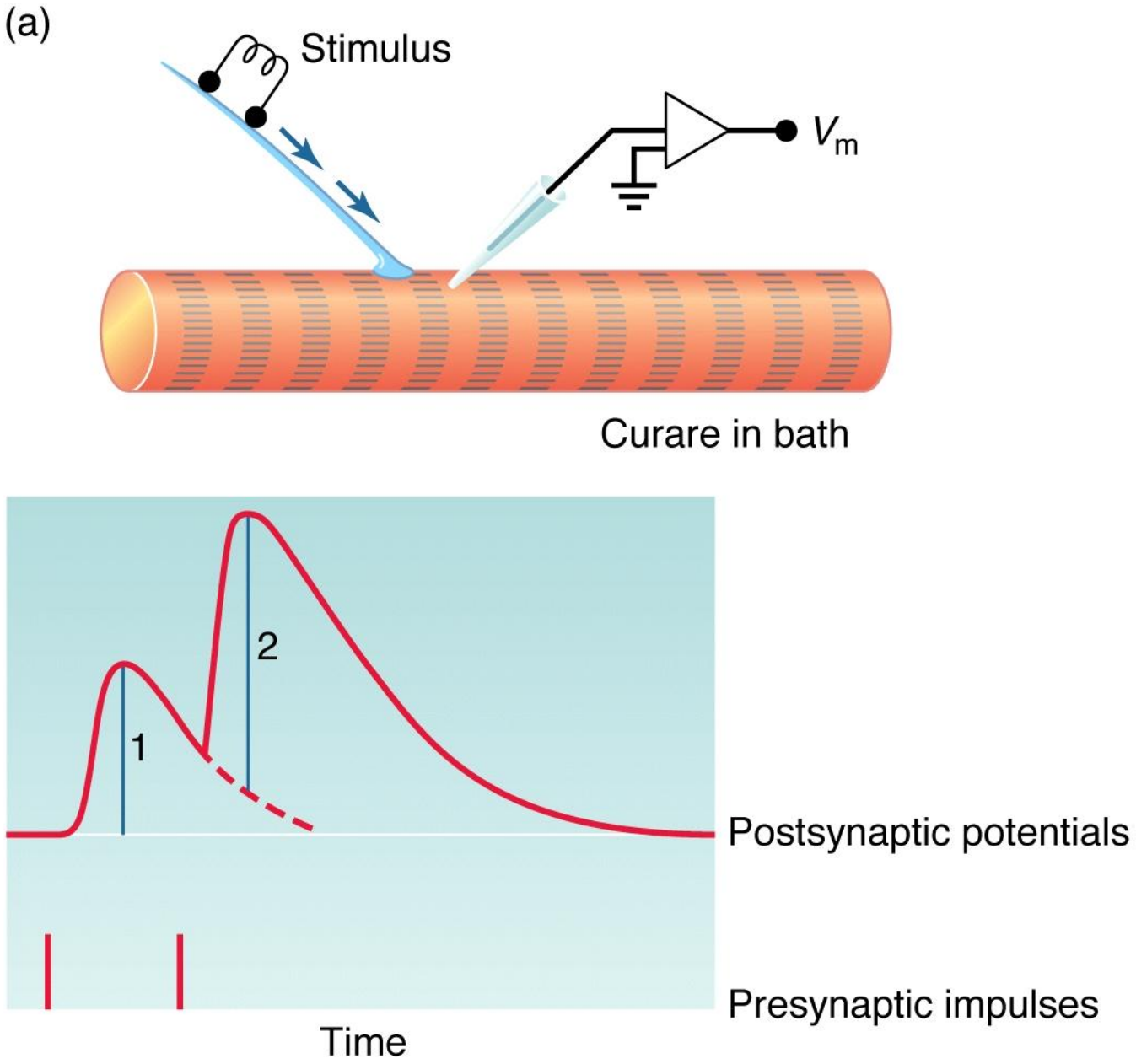

(b)
1
2
3
a
c
a + c
2 mV
5 ms
No sensory nerve stimulation
Stimulate axon a, then axon c
Stimulate axons a + c simultaneously

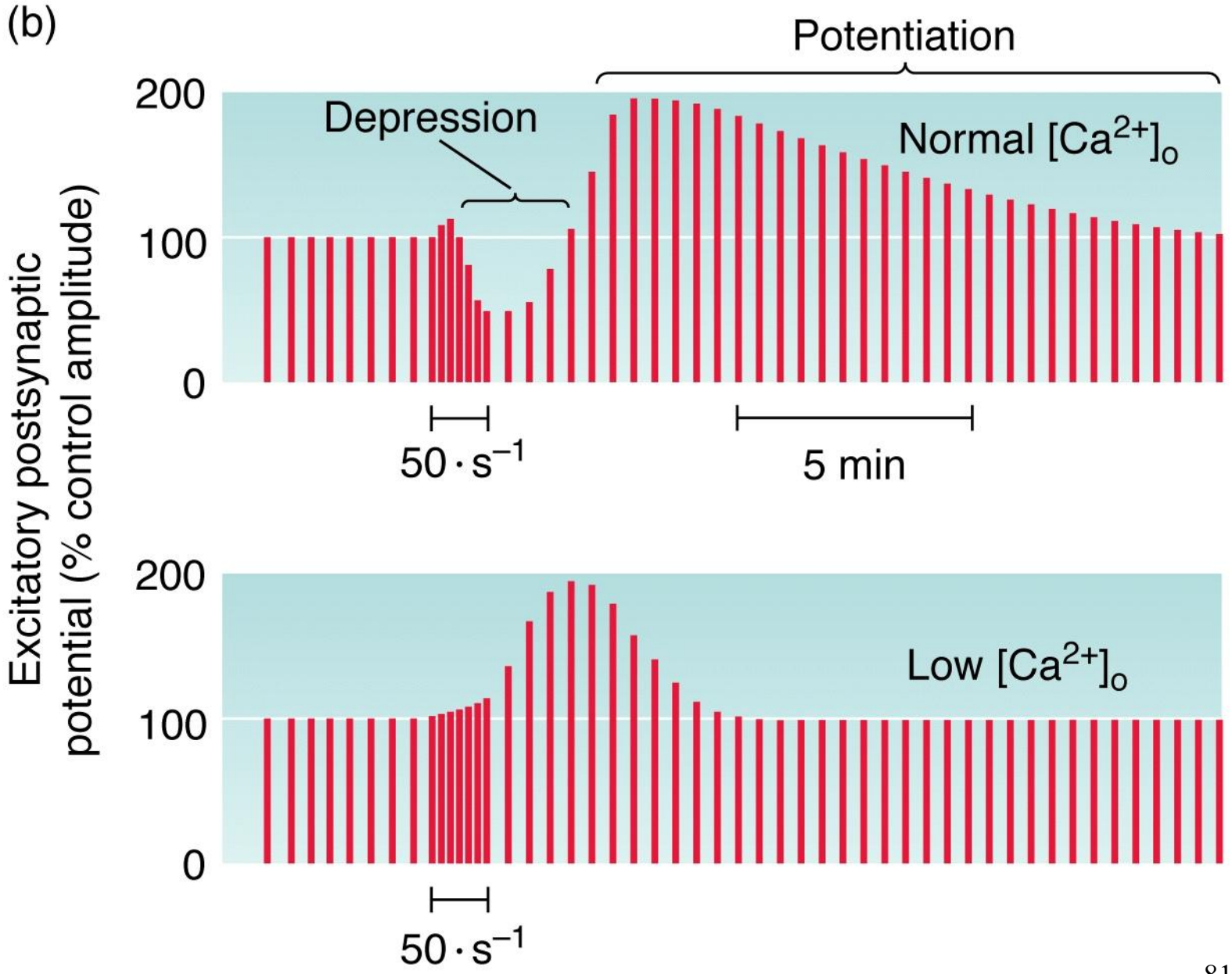

Excitatory presynaptic axon
Inhibitory axon
Excitatory synaptic current
Inhibitory synaptic current
a
b
a
b
a and b

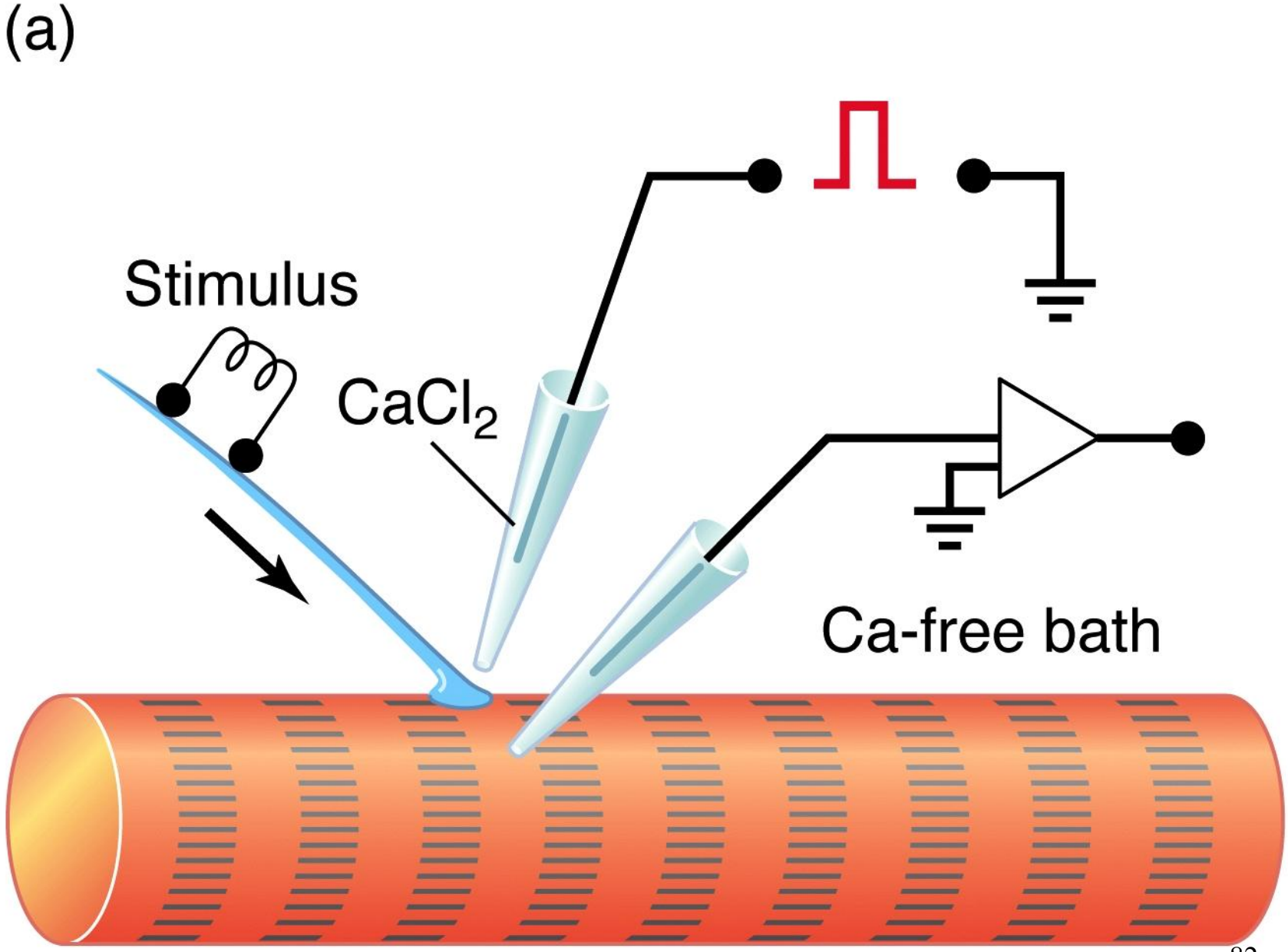

(c)
Time

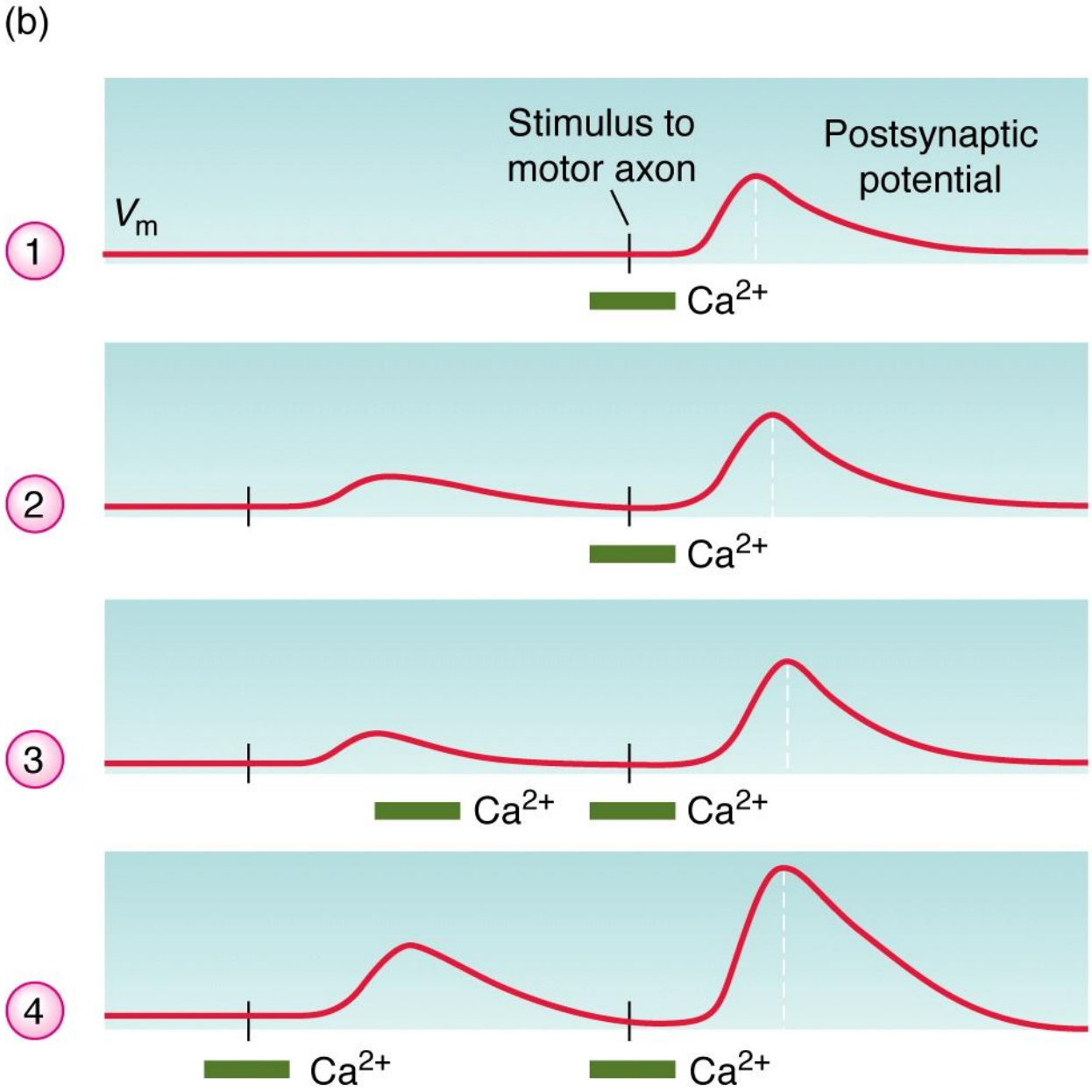

(a)

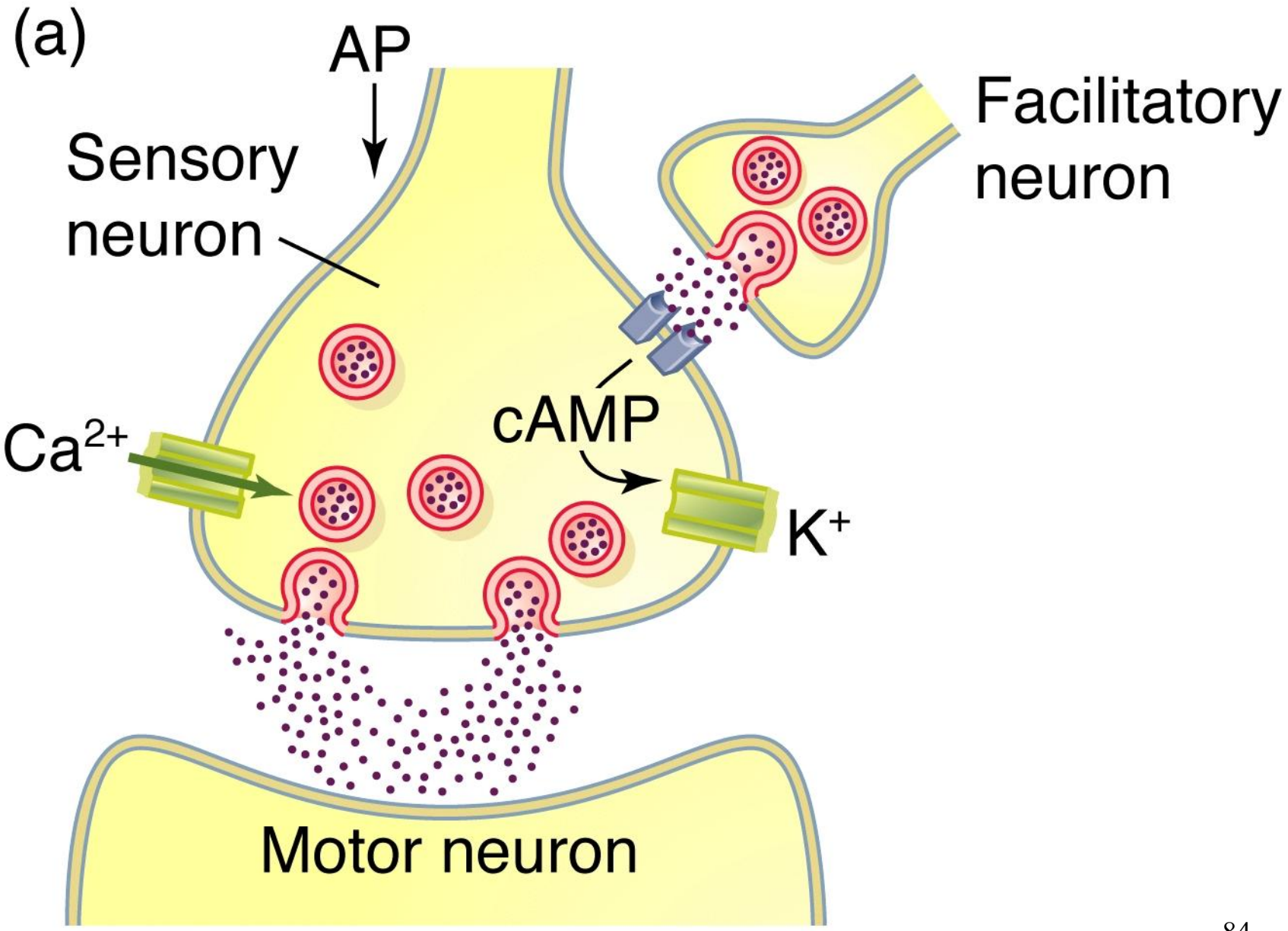

(b)
Depolarization
Action potentials
Time

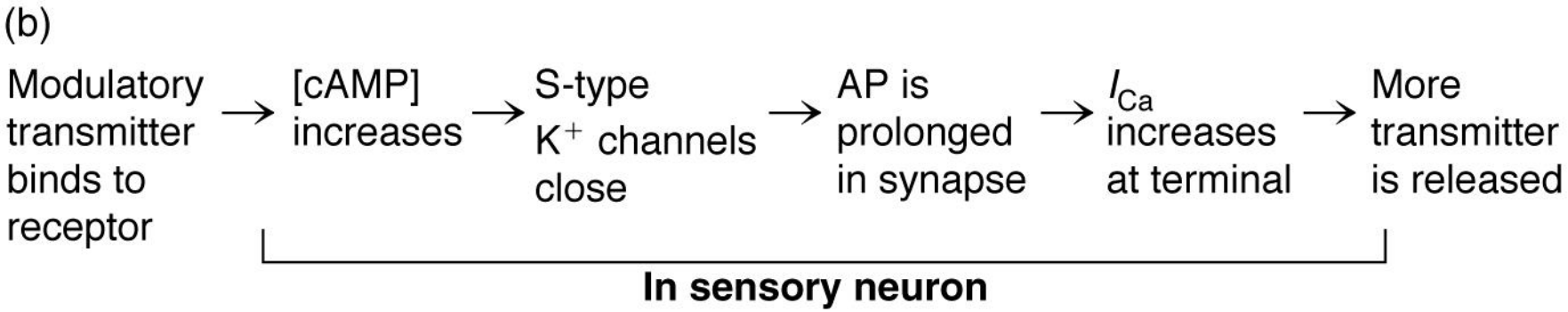

(a)
Stimulus
V_m
Curare in bath
2
1
Postsynaptic potentials
Presynaptic impulses
Time

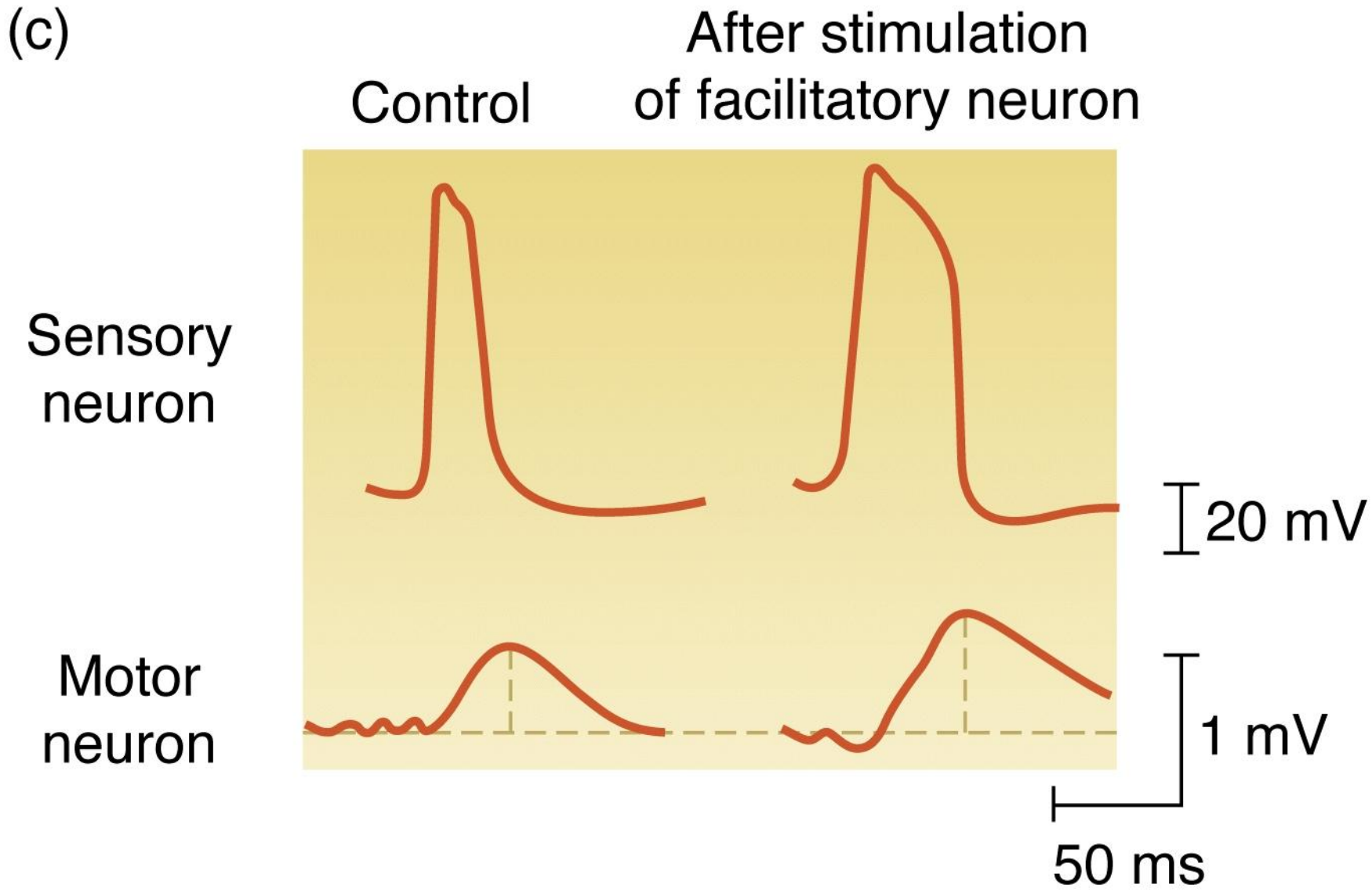

(b)
Potentiation
Depression
Normal $[Ca^{2+}]_o$
Excitatory postsynaptic potential (% control amplitude)
200
100
0
$50 \cdot s^{-1}$
5 min
200
100
0
Low $[Ca^{2+}]_o$
$50 \cdot s^{-1}$

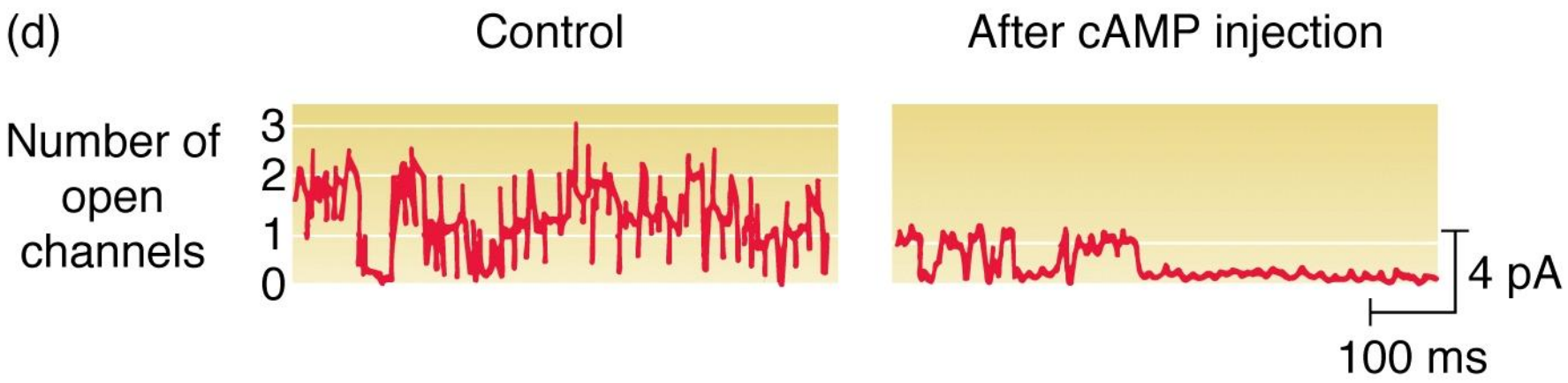

(a)
Stimulus
$CaCl_2$
Ca-free bath


(b)
Stimulus to motor axon
Postsynaptic potential
V_m
1
Ca^{2+}
2
Ca^{2+}
3
Ca^{2+}
Ca^{2+}
4
Ca^{2+}
Ca^{2+}

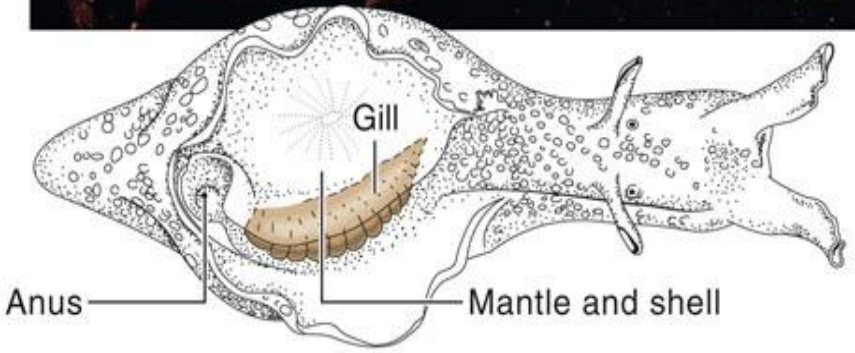

(a)
AP
Sensory neuron
Facilitatory neuron
cAMP
Ca^{2+}
K^+
Motor neuron


(b)
Modulatory transmitter binds to receptor
[cAMP] increases
S-type K^+ channels close
AP is prolonged in synapse
I_{Ca} increases at terminal
More transmitter is released
In sensory neuron

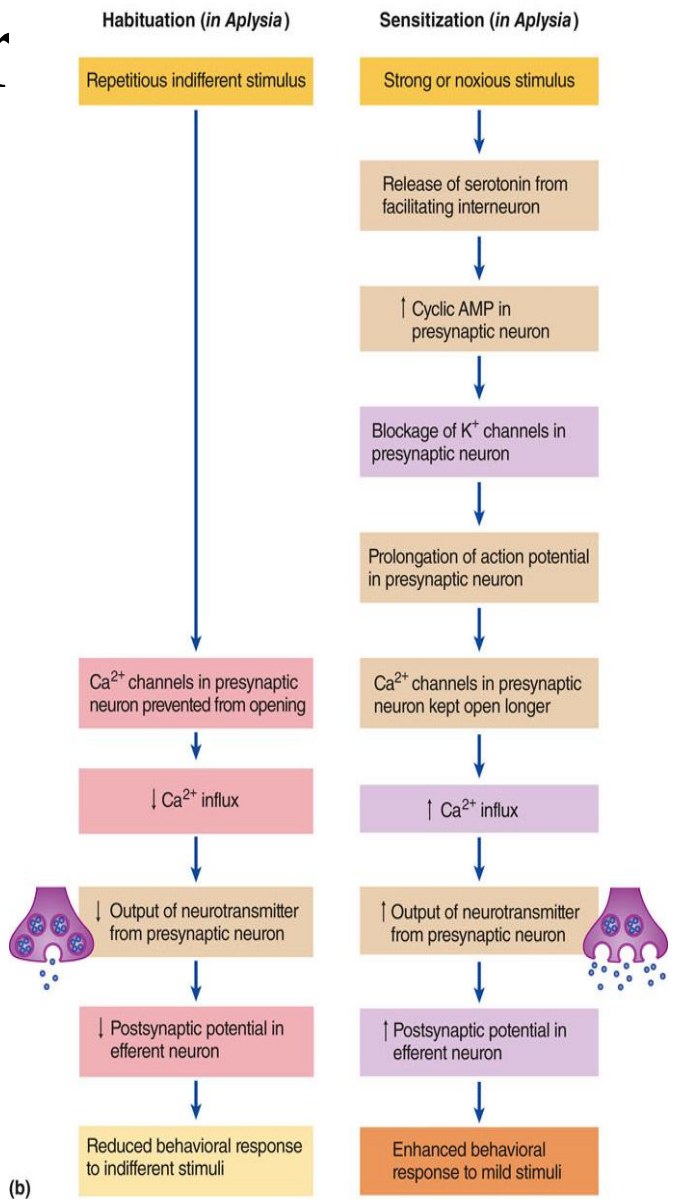

(c)
Control
After stimulation of facilitatory neuron
Sensory neuron
Motor neuron
20 mV
1 mV
50 ms


(d)
Control
After cAMP injection
Number of open channels
3
2
1
0
4 pA
100 ms

5.9 Learning, Memor



(a)

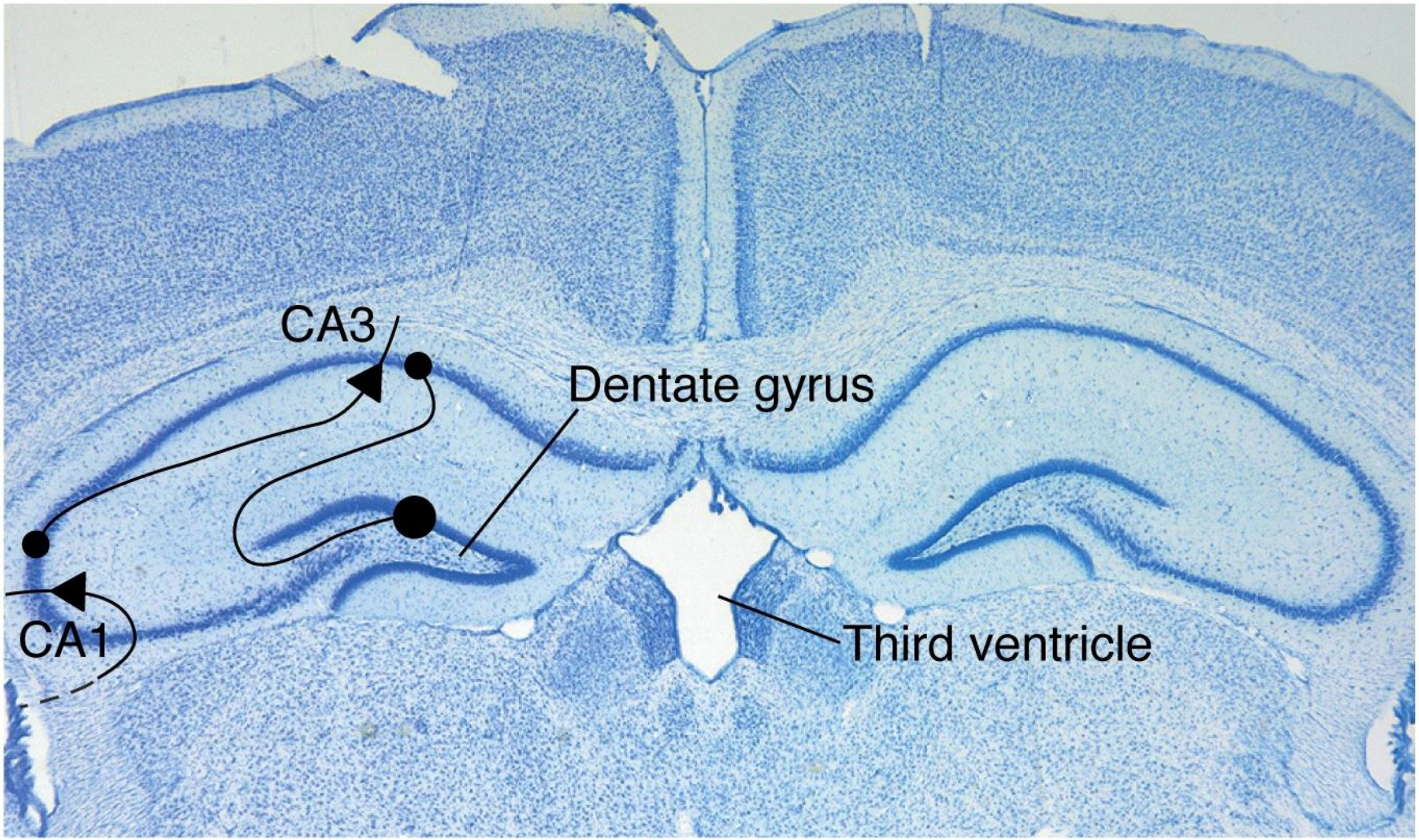


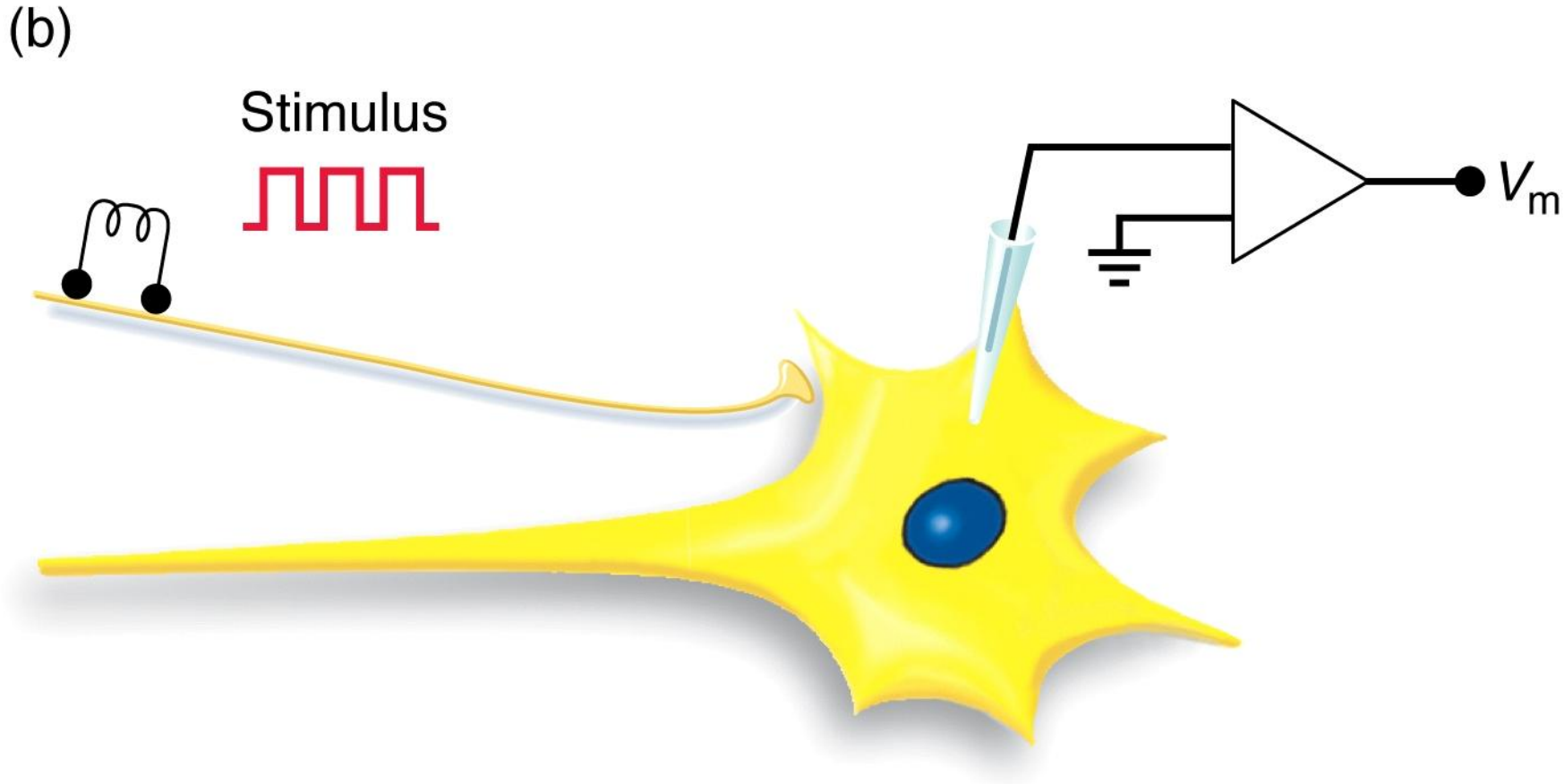
(b)

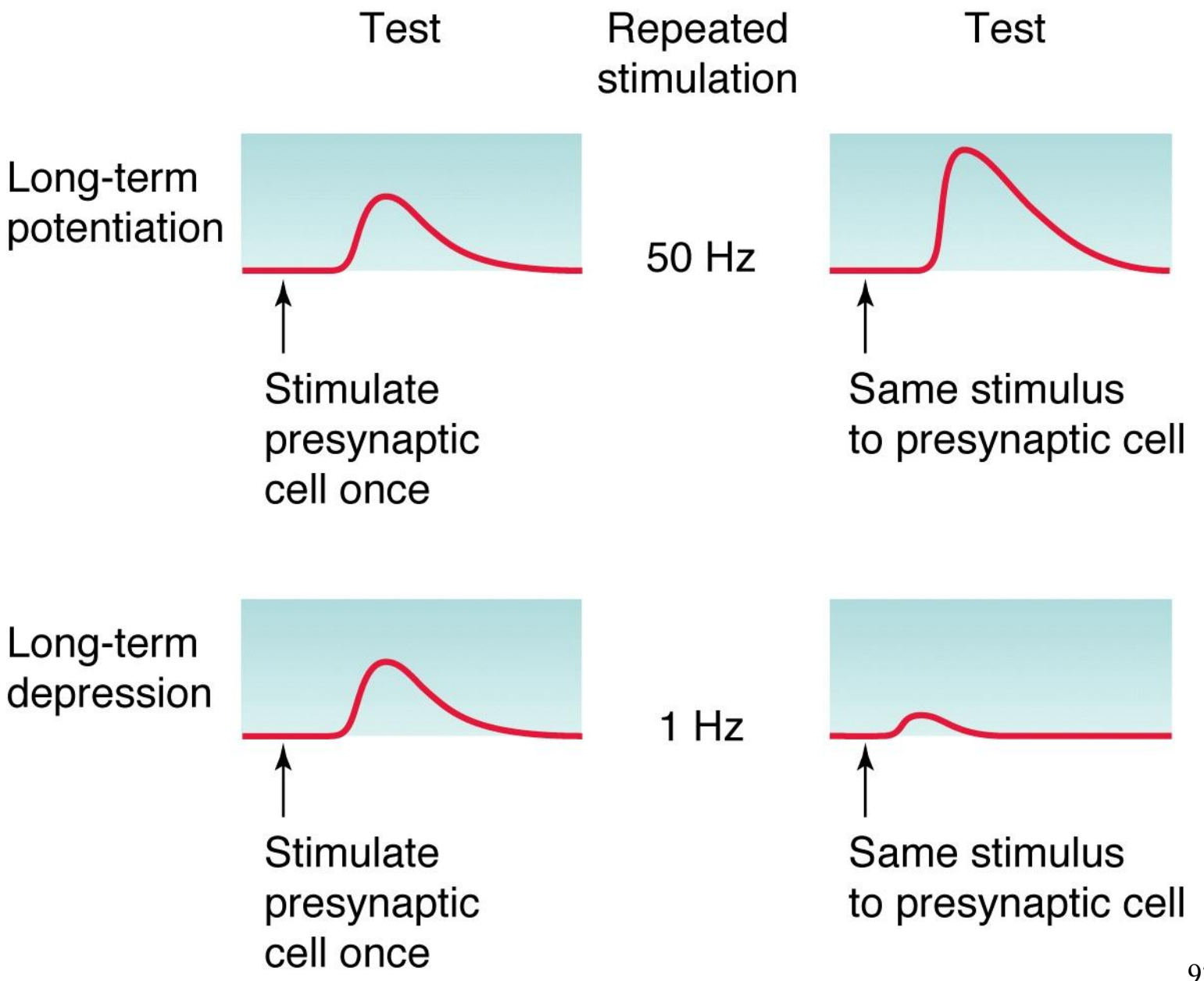
5.9 Learning, Memory, and Sleep

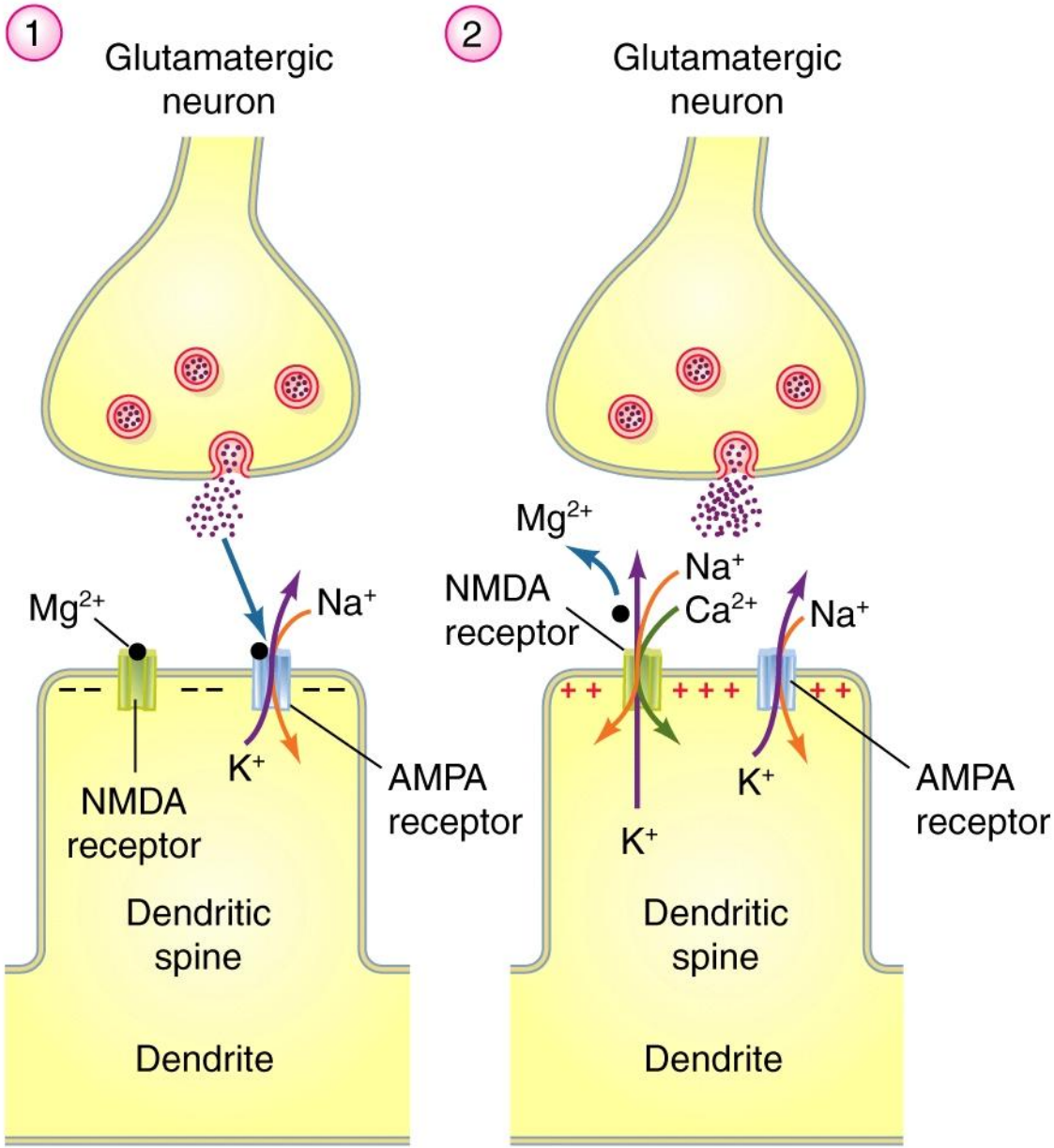
- Mechanisms of memory
  - **Long-term potentiation (LTP)** -- prolonged increase in the strength of existing synaptic connections following repetitive stimulation
  - **Long-term memory** involves formation of new synaptic connections
    - **Immediate early genes (IEGs)** govern synthesis of the proteins that encode long-term memory

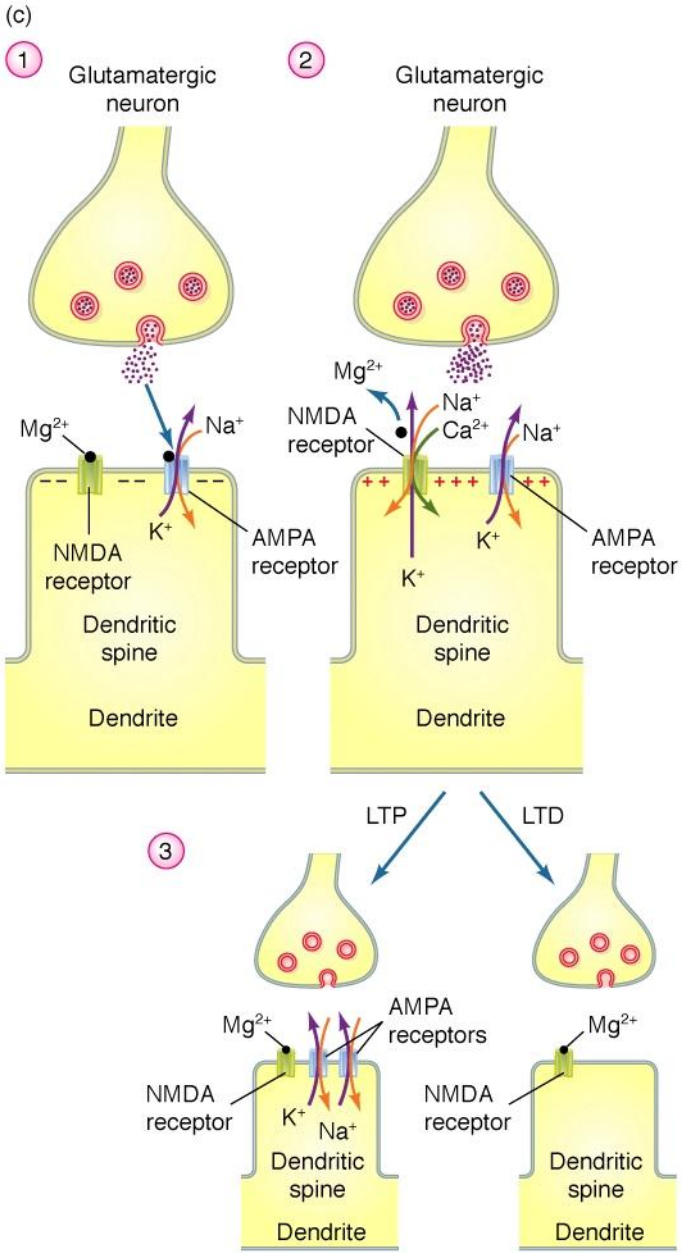
(a)

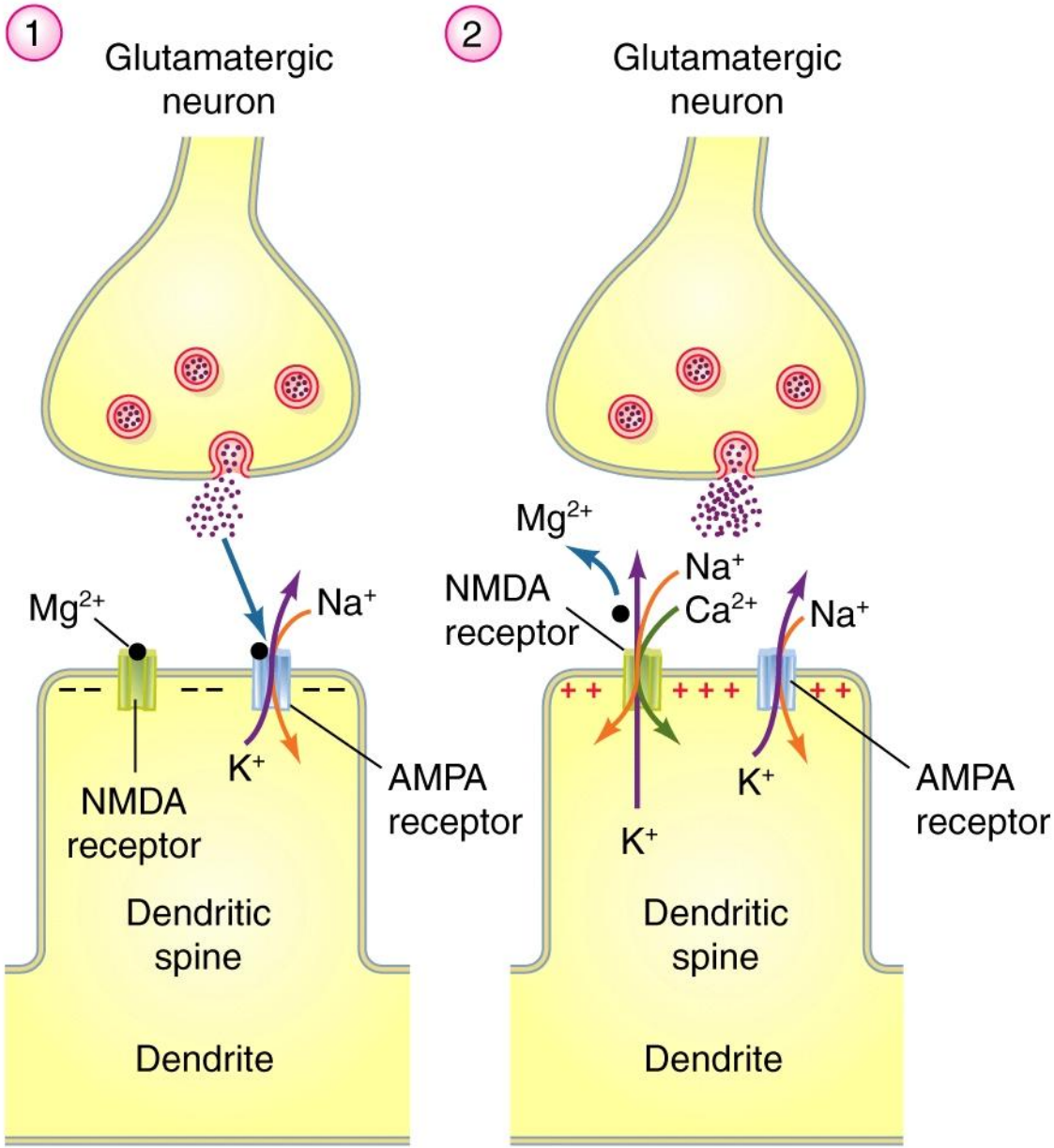


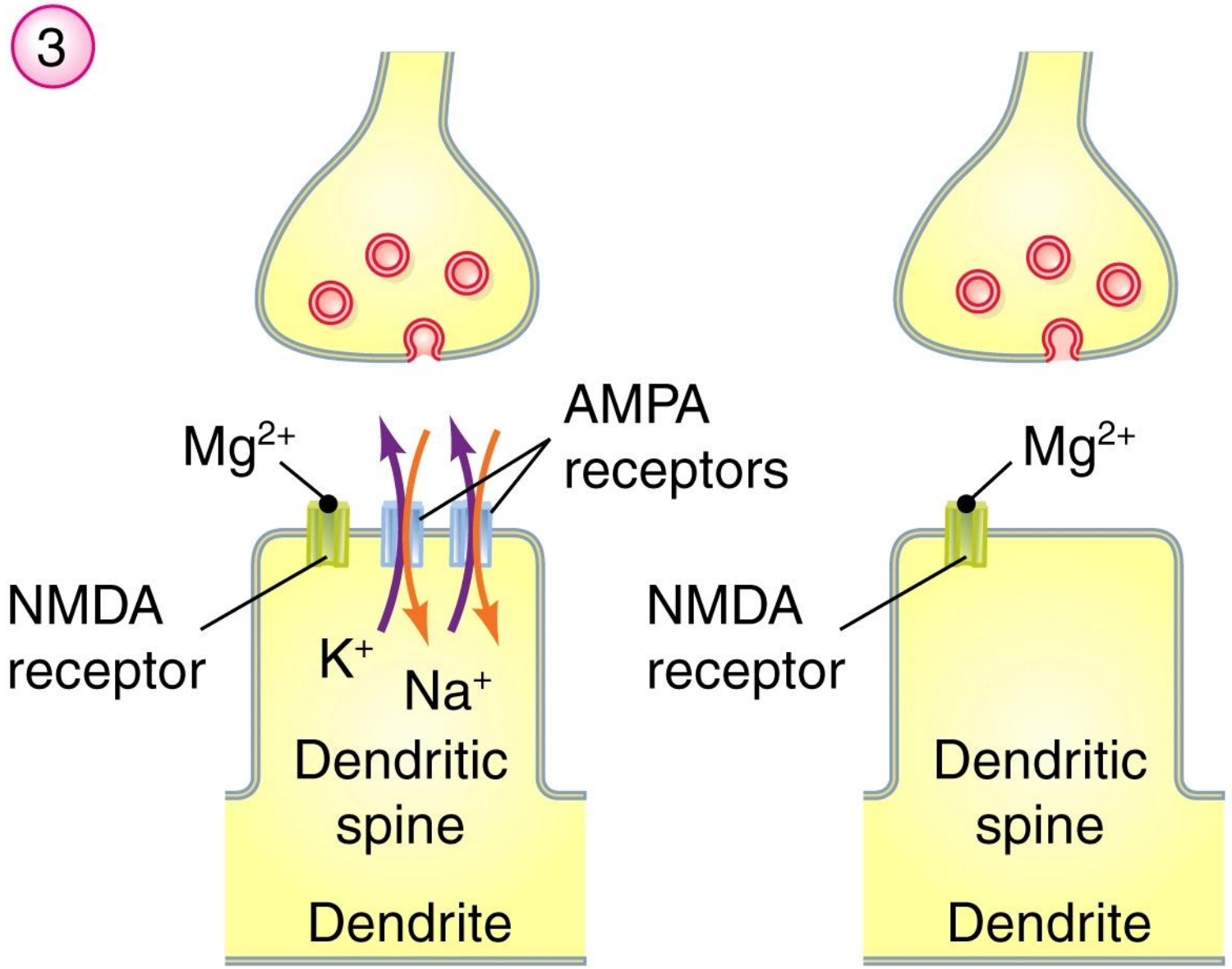

(b)
Stimulus
V_m

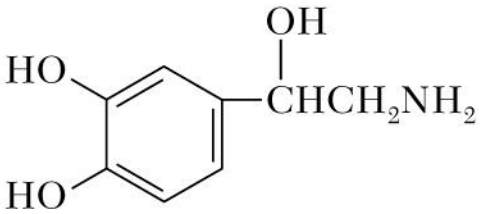
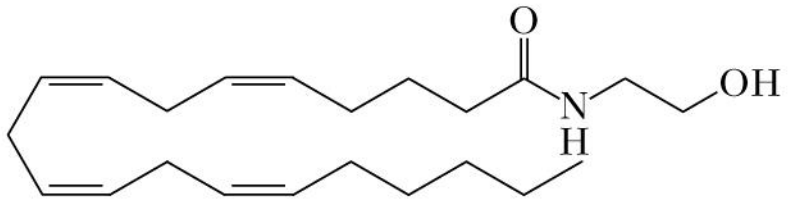
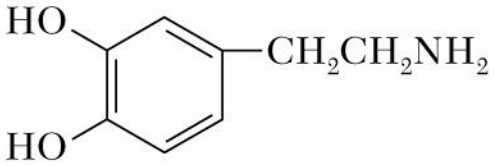
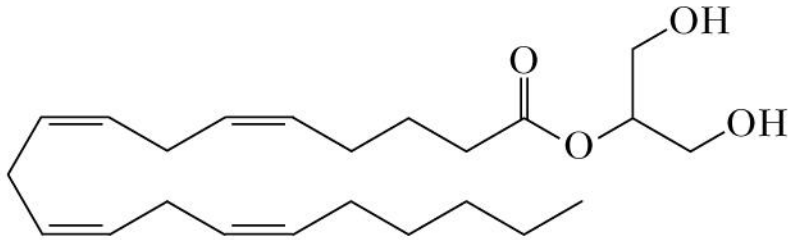
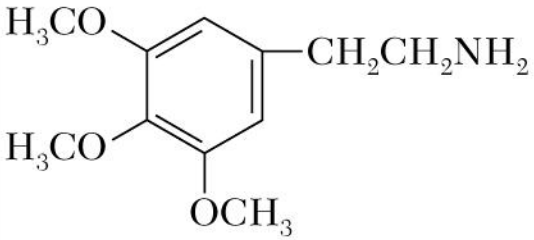
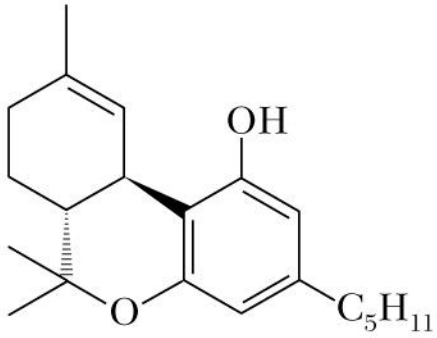

Test
Repeated stimulation
Test
Long-term potentiation
50 Hz
Stimulate presynaptic cell once
Same stimulus to presynaptic cell
Long-term depression
1 Hz
Stimulate presynaptic cell once
Same stimulus to presynaptic cell


1
Glutamatergic neuron
Mg2+
Na+
K+
NMDA receptor
AMPA receptor
Dendritic spine
Dendrite
2
Glutamatergic neuron
Mg2+
NMDA receptor
Na+
Ca2+
Na+
K+
K+
AMPA receptor
Dendritic spine
Dendrite


(c)
1
Glutamatergic neuron
Mg2+
Na+
K+
NMDA receptor
AMPA receptor
Dendritic spine
Dendrite
2
Glutamatergic neuron
Mg2+
NMDA receptor
Na+
Ca2+
Na+
K+
K+
AMPA receptor
Dendritic spine
Dendrite
LTP
LTD
3
Mg2+
AMPA receptors
NMDA receptor
K+
Na+
Dendritic spine
Dendrite
Mg2+
NMDA receptor
Dendritic spine
Dendrite


1
Glutamatergic neuron
Mg2+
Na+
K+
NMDA receptor
AMPA receptor
Dendritic spine
Dendrite
2
Glutamatergic neuron
Mg2+
NMDA receptor
Na+
Ca2+
Na+
K+
K+
AMPA receptor
Dendritic spine
Dendrite


3
Mg2+
AMPA
receptors
NMDA
receptor
K+
Na+
Dendritic
spine
Dendrite
Mg2+
NMDA
receptor
Dendritic
spine
Dendrite

	Biogenic amines	Cannabinoids
Endogenous ligands	 **Norepinephrine (Noradrenaline)**	 **Arachidonylethanolamine**
	 **Dopamine**	 **2-Arachidonylglycerol**
Exogenous ligands	 **Mescaline**	 **Tetrahydrocannabinol**

Neural Signaling and External Agents

- Neurotoxins that alter synaptic transmission
  - **Strychnine** competes with inhibitory neurotransmitter, glycine, at postsynaptic receptors
  - **Tetanus toxin** prevents release of GABA from inhibitory presynaptic axons
  - Both toxins cause unchecked excitation, muscle spasms and death

Neural Signaling and External Agents

- Alteration of the neuromuscular junction
  - **Black widow spider venom** causes explosive release of ACh
  - **Curare** blocks ACh receptors …. **muscle paralysis** and **death**
  - **Myasthenia gravis** is an autoimmune disease in which antibodies attack ACh receptors, leading to muscle weakness
  - **Neostigmine** inhibits acetylcholinesterase, prolonging the activity of ACh in the synapse