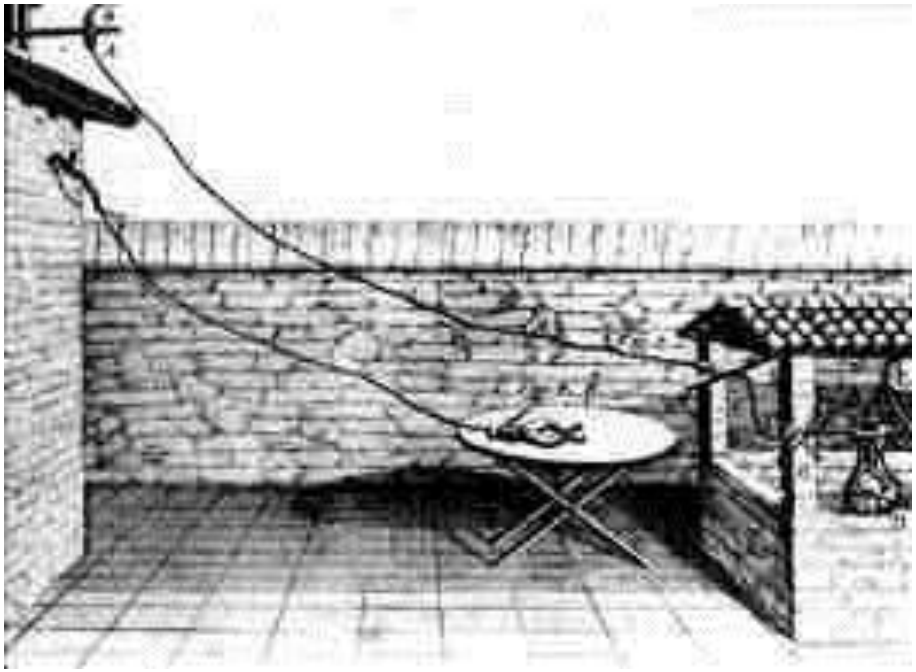
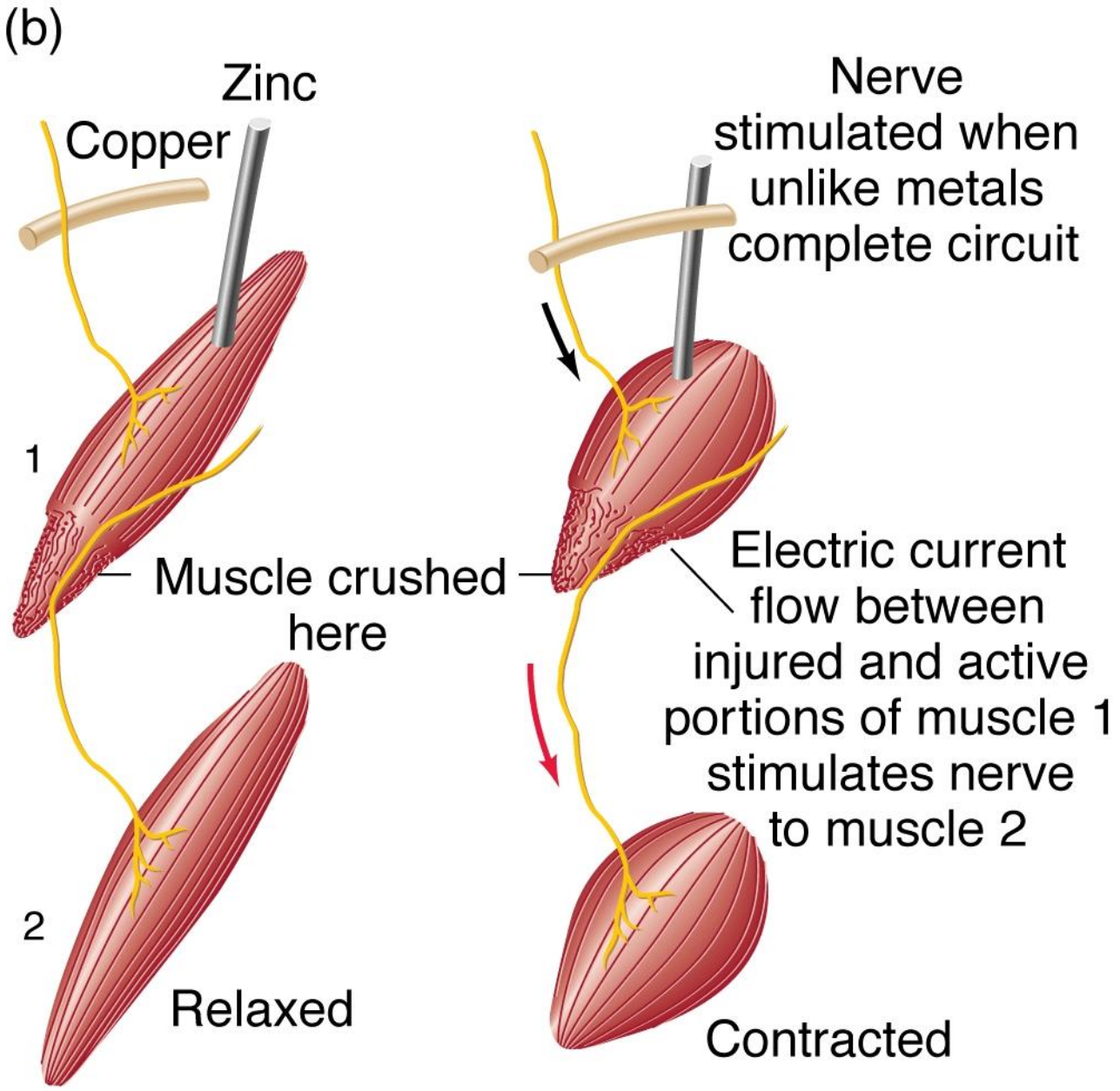
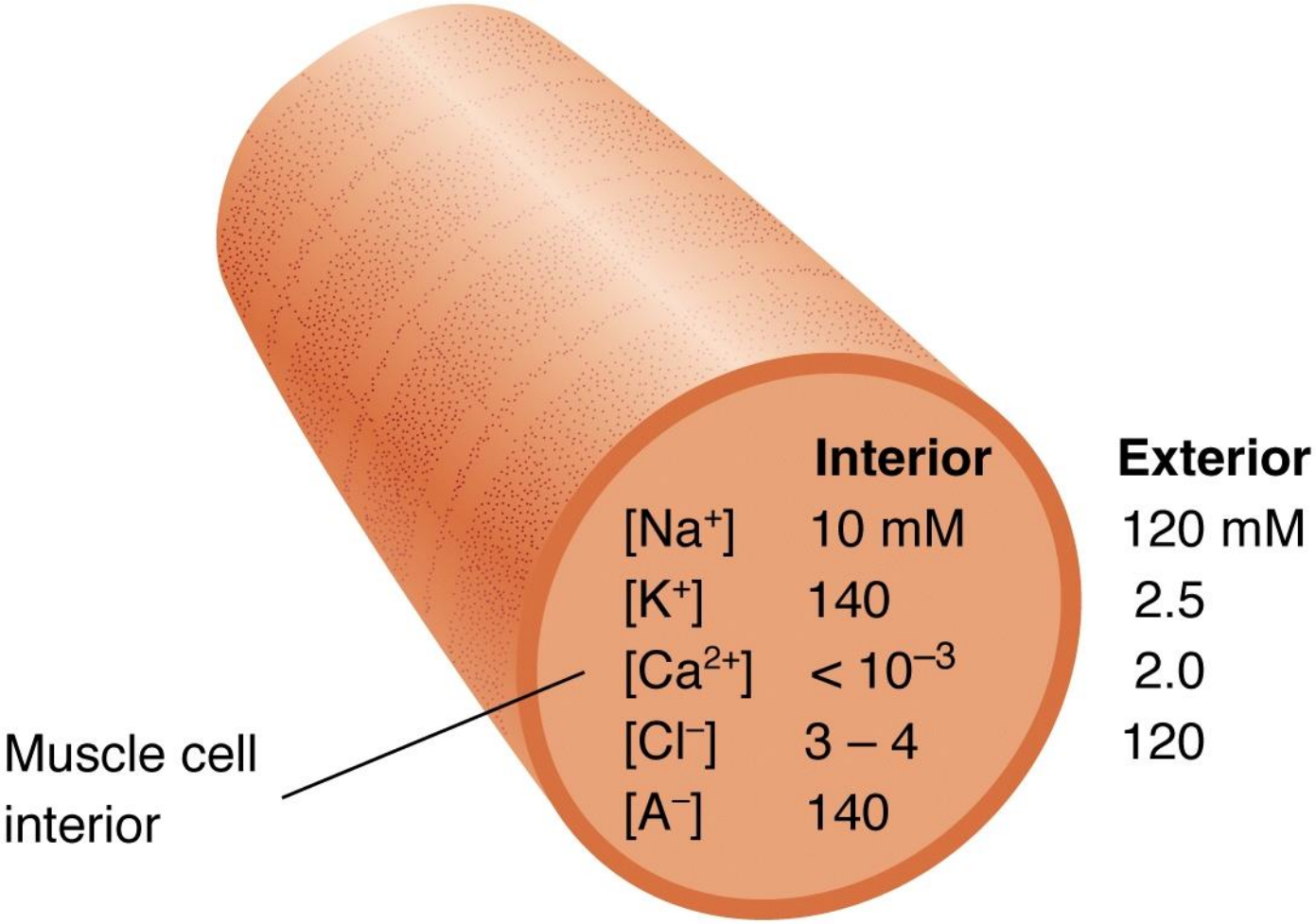
Trying to prove that lightning was an electrical spark, as Benjamin Franklin had proposed, Galvani suspended the frog's legs with brass hooks from an electrical railing during a thunderstorm. Luigi Galvani (1737-1798)



Italian physicist Alessandro Volta (1745-1827) repeated Galvani's experiments at the University of Pavia

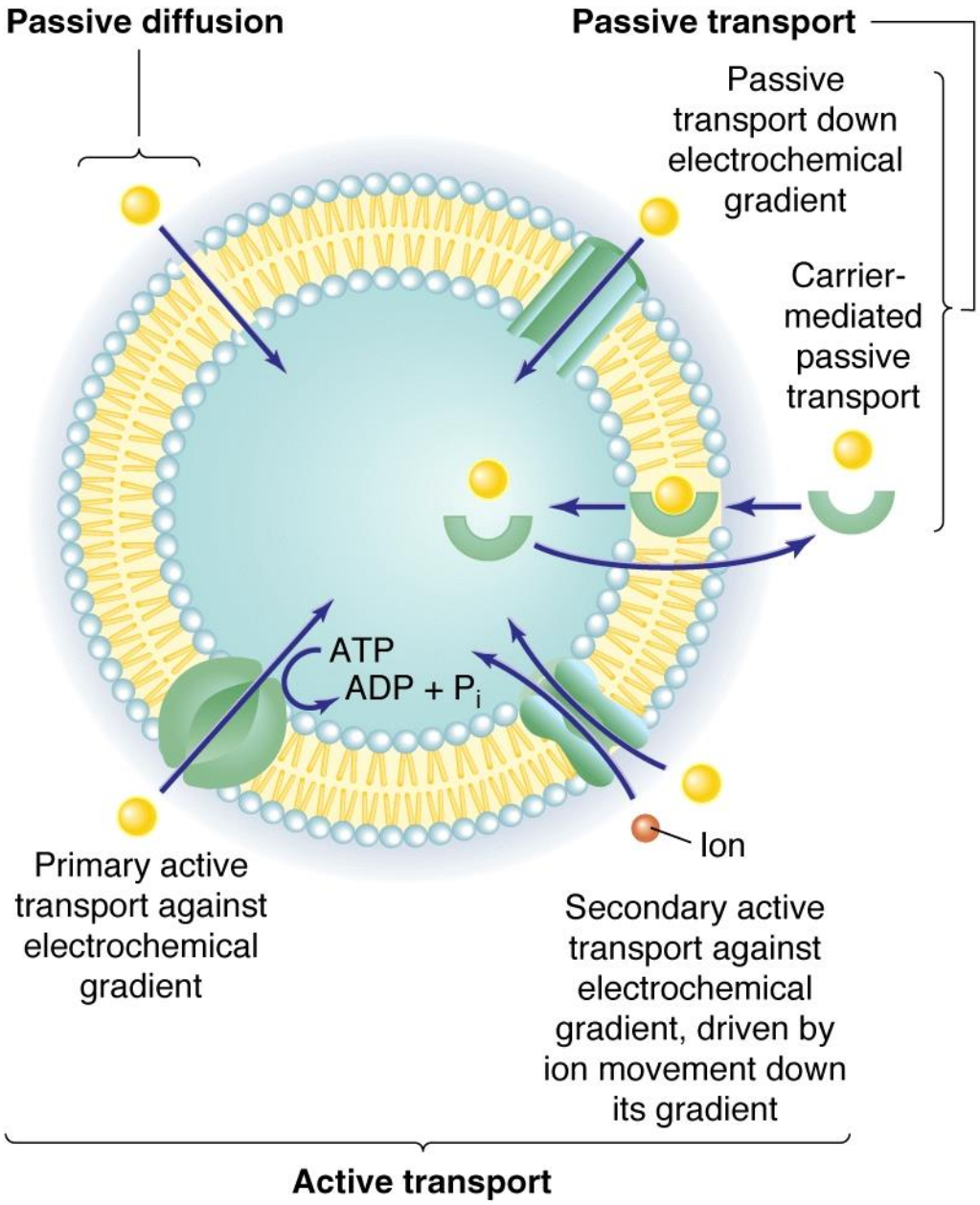

(b)
Zinc
Copper
Nerve stimulated when unlike metals complete circuit
1
Muscle crushed here
Electric current flow between injured and active portions of muscle 1 stimulates nerve to muscle 2
2
Relaxed
Contracted



[A^-] = molar equivalent of negative charges carried by other molecules and ions.

Table 4-2 Internal and external concentrations of some electrolytes in specific nerve and muscle tissues

Tissue	Internal concentrations (mM)			External concentrations (mM)			Ratios, inside/outside		
	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-
Squid nerve	49	410	40–100	440	22	560	1/9	19/1	1/14–1/6
Crab leg nerve	52	410	26	510	12	540	1/10	34/1	1/21
Frog sartorius muscle	10	140	4	120	2.5	120	1/12	56/1	1/30


Passive diffusion
Passive transport
Passive transport down electrochemical gradient
Carrier-mediated passive transport
ATP
ADP + P_i
Primary active transport against electrochemical gradient
Ion
Secondary active transport against electrochemical gradient, driven by ion movement down its gradient
Active transport

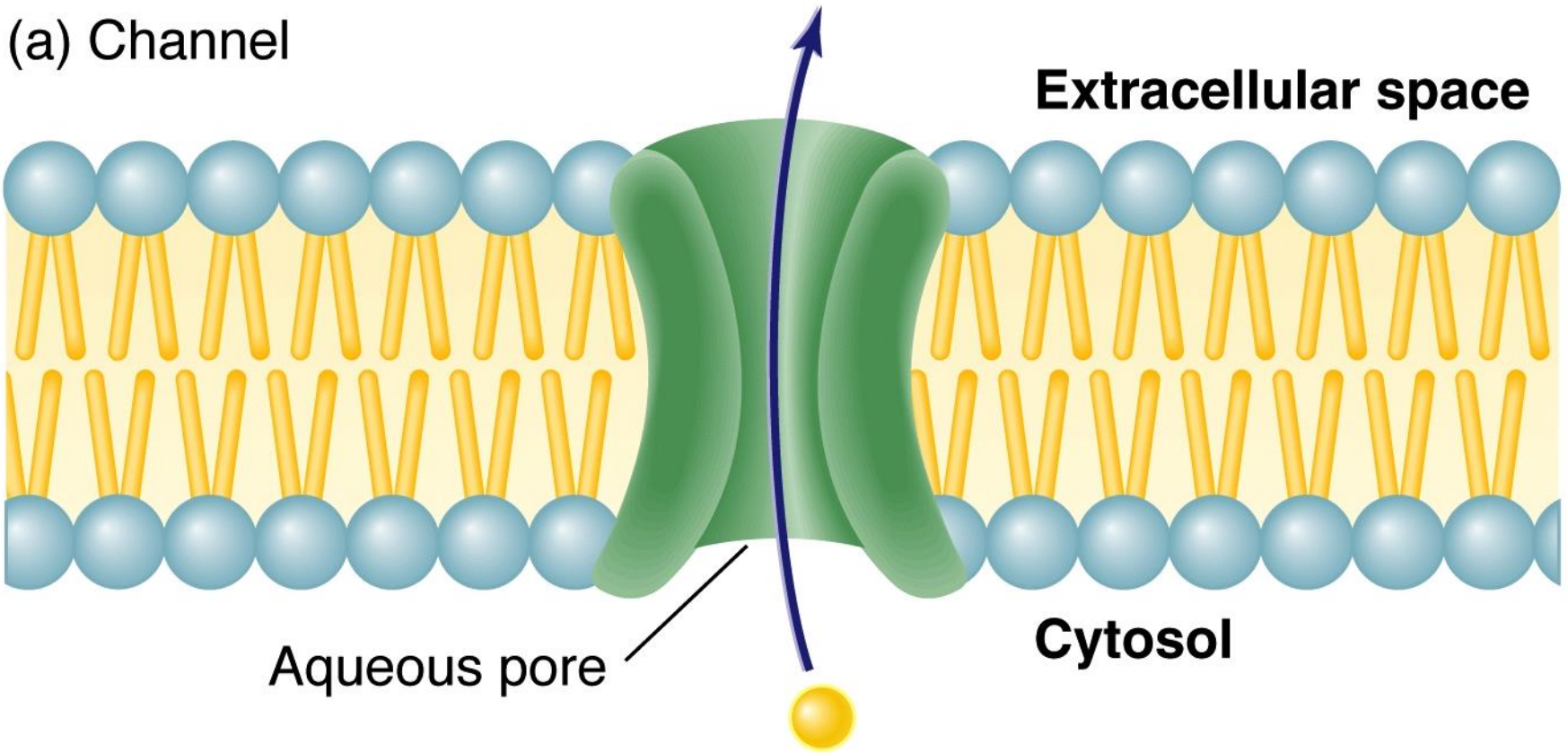
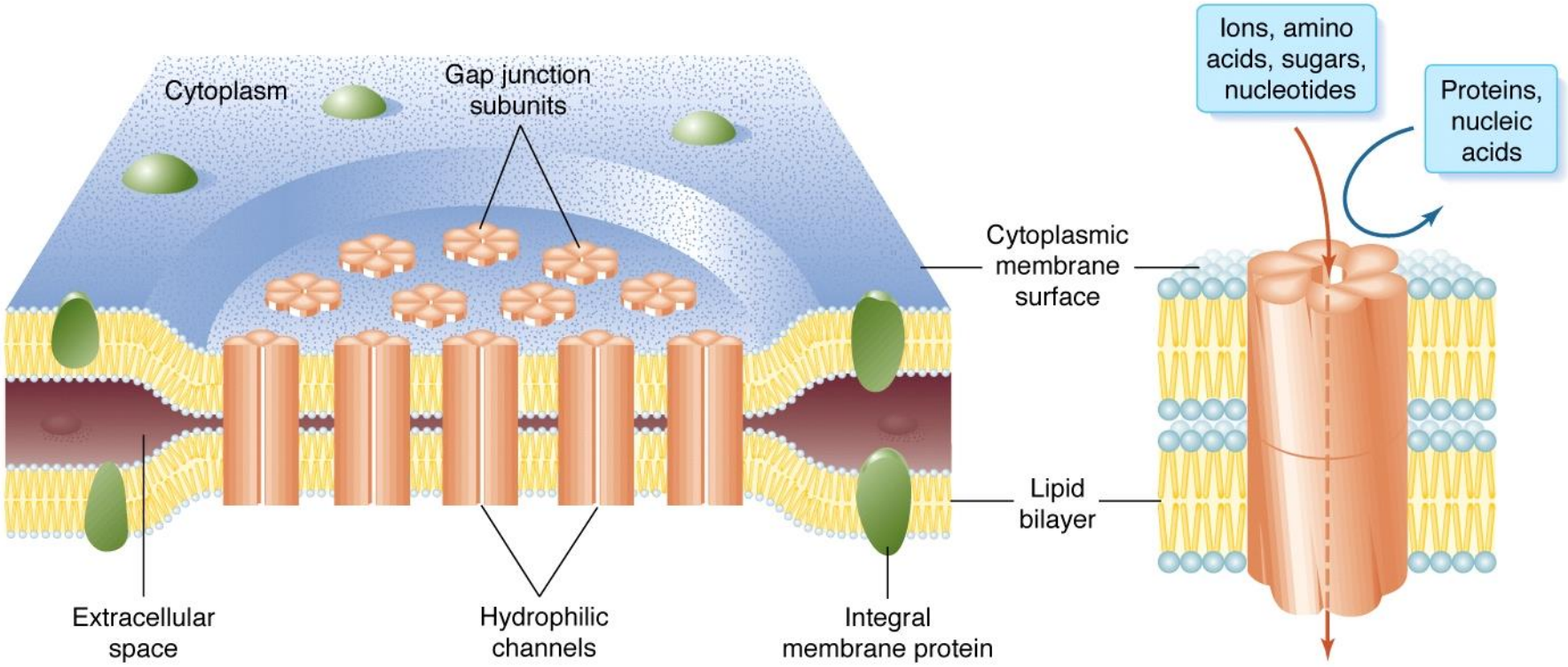
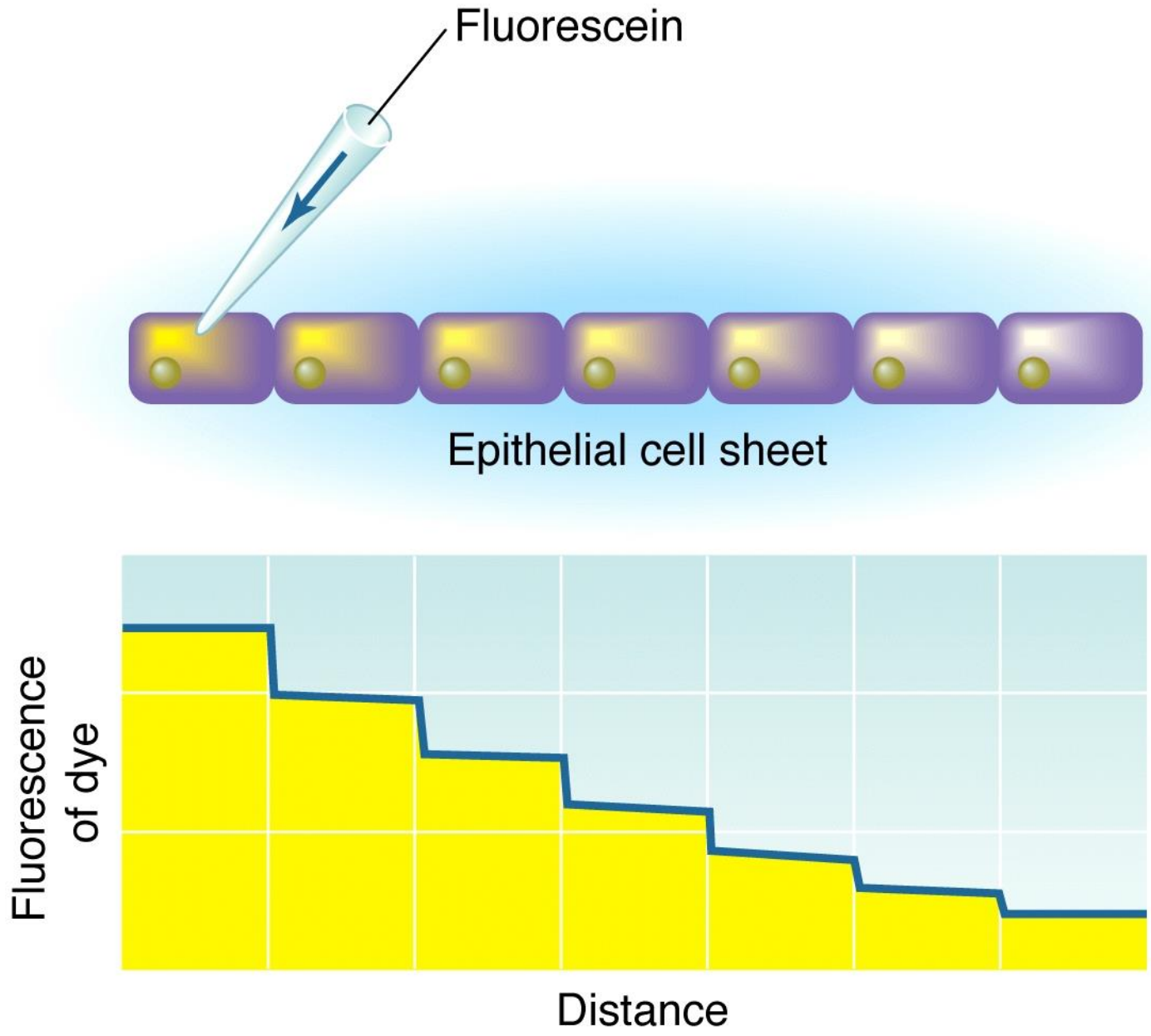
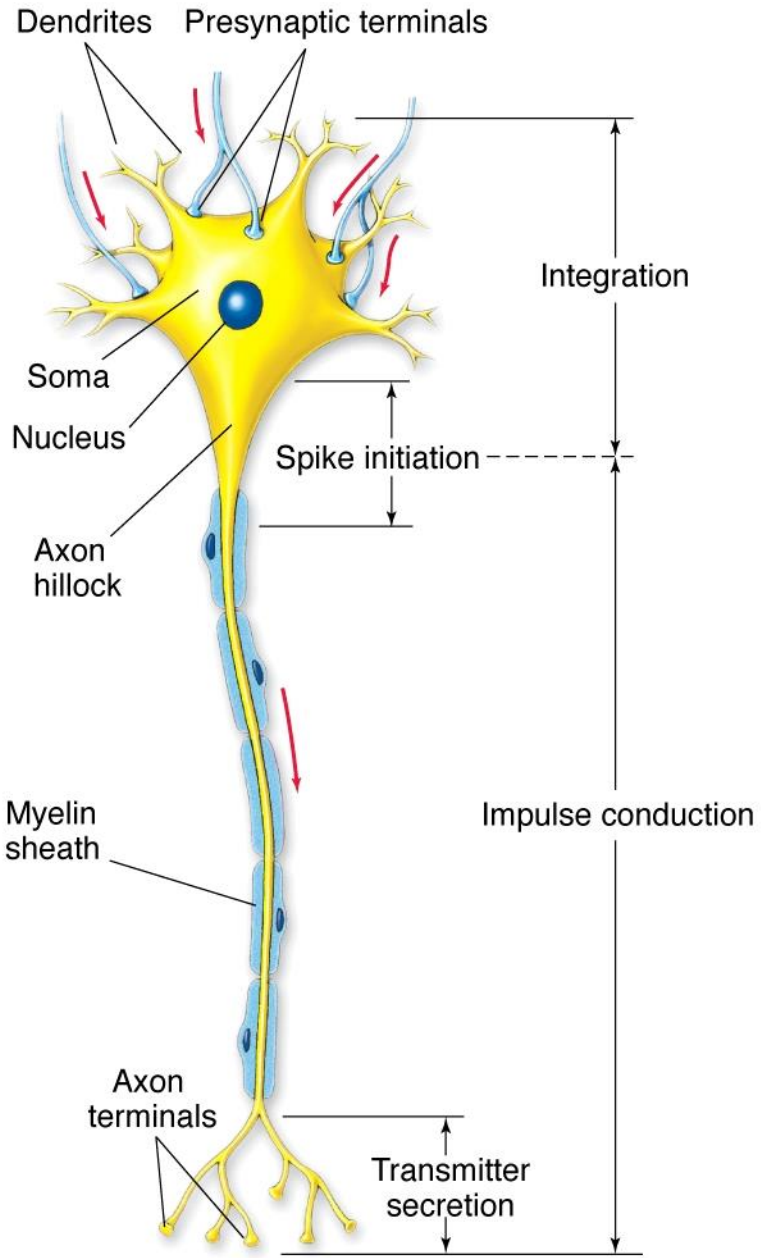

(a) Channel
Extracellular space
Cytosol
Aqueous pore

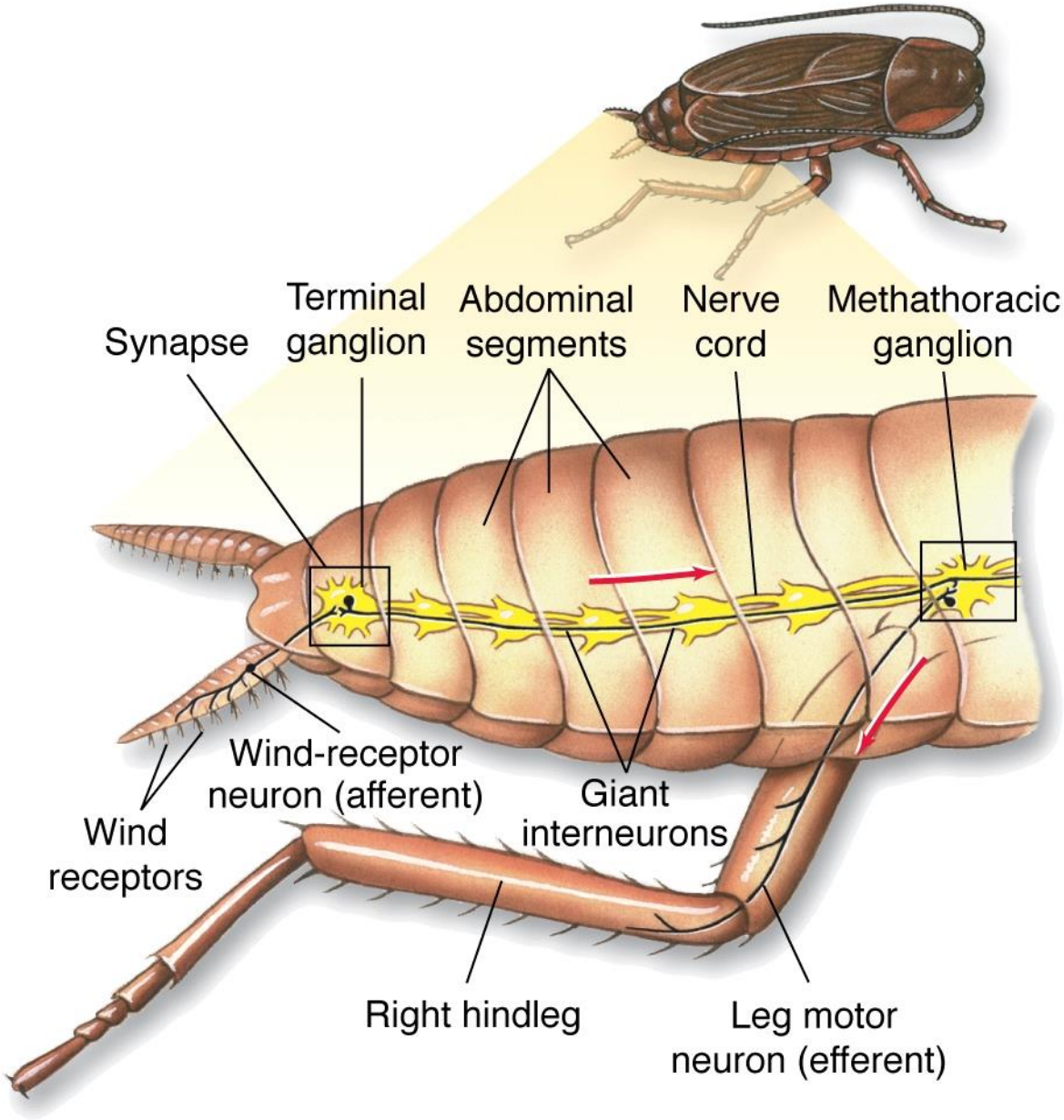
Table 4-3 **Ionic radii and hydration energies of the alkali metal cations**

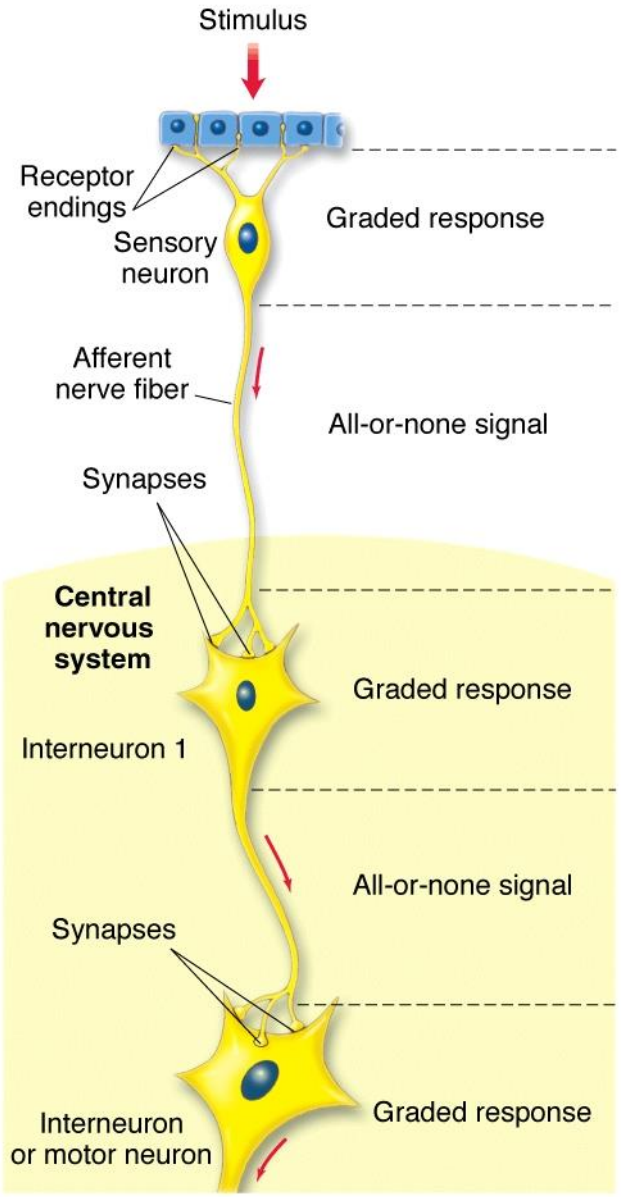
Cation	Ionic radius (Å)		Free energy of hydration ($kcal \cdot mol^{-1}$)
Li^+	0.60		2122
Na^+	0.95		298
K^+	1.33		280
Rb^+	1.48		275
Cs^+	1.69		267

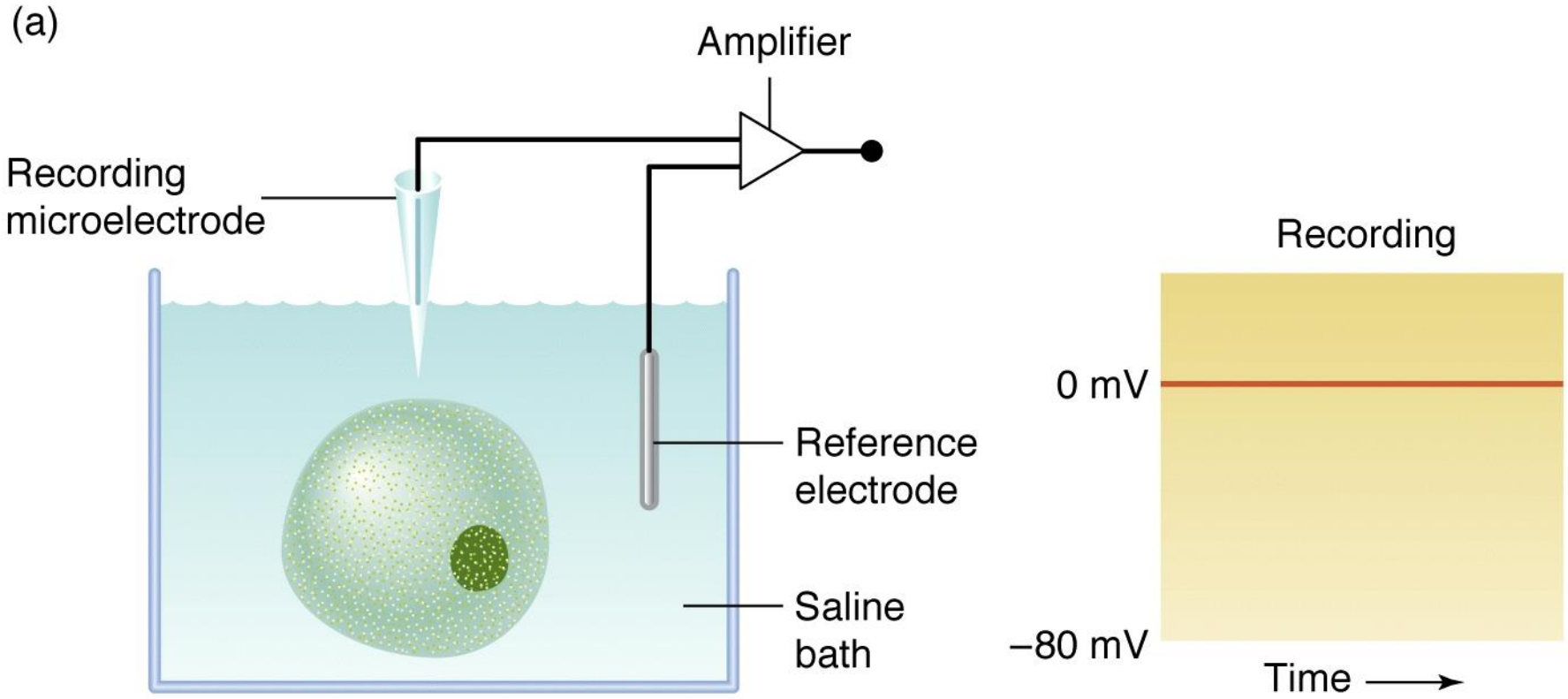

Cytoplasm
Gap junction subunits
Ions, amino acids, sugars, nucleotides
Proteins, nucleic acids
Cytoplasmic membrane surface
Lipid bilayer
Extracellular space
Hydrophilic channels
Integral membrane protein


Fluorescein
Epithelial cell sheet
Fluorescence of dye
Distance

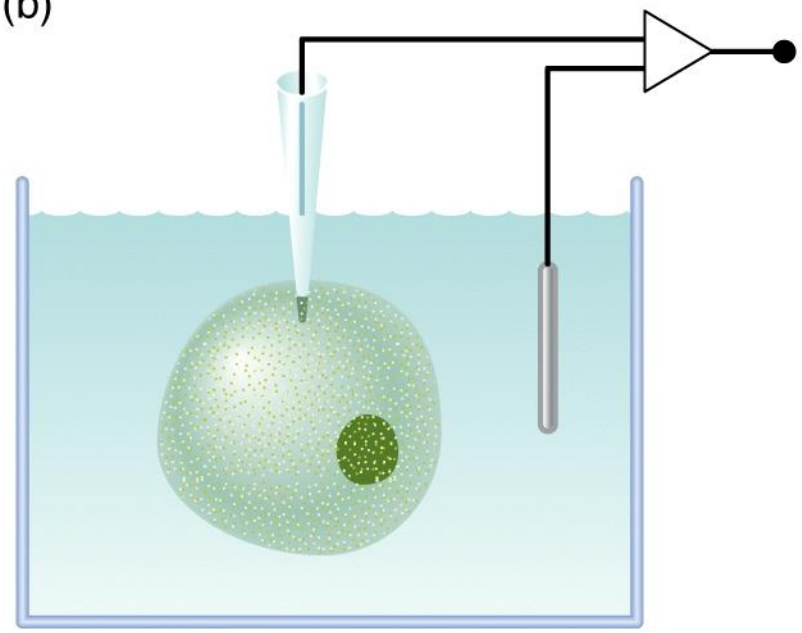

Dendrites
Presynaptic terminals
Integration
Soma
Nucleus
Spike initiation
Axon hillock
Myelin sheath
Impulse conduction
Axon terminals
Transmitter secretion

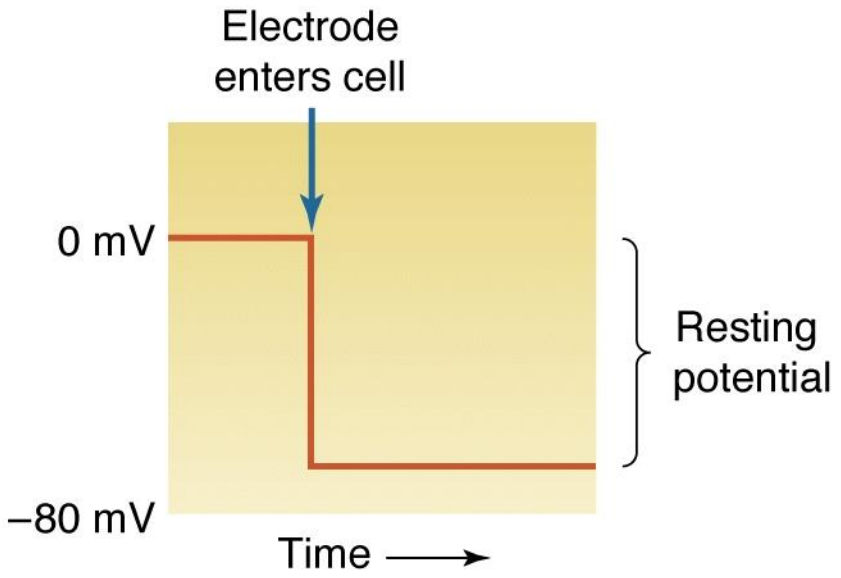

Synapse
Terminal ganglion
Abdominal segments
Nerve cord
Methathoracic ganglion
Wind-receptor neuron (afferent)
Wind receptors
Giant interneurons
Right hindleg
Leg motor neuron (efferent)


Stimulus
Receptor endings
Sensory neuron
Graded response
Afferent nerve fiber
All-or-none signal
Synapses
Central nervous system
Graded response
Interneuron 1
All-or-none signal
Synapses
Interneuron or motor neuron
Graded response


(a)
Amplifier
Recording microelectrode
Reference electrode
Saline bath
Recording
0 mV
−80 mV
Time

(b)





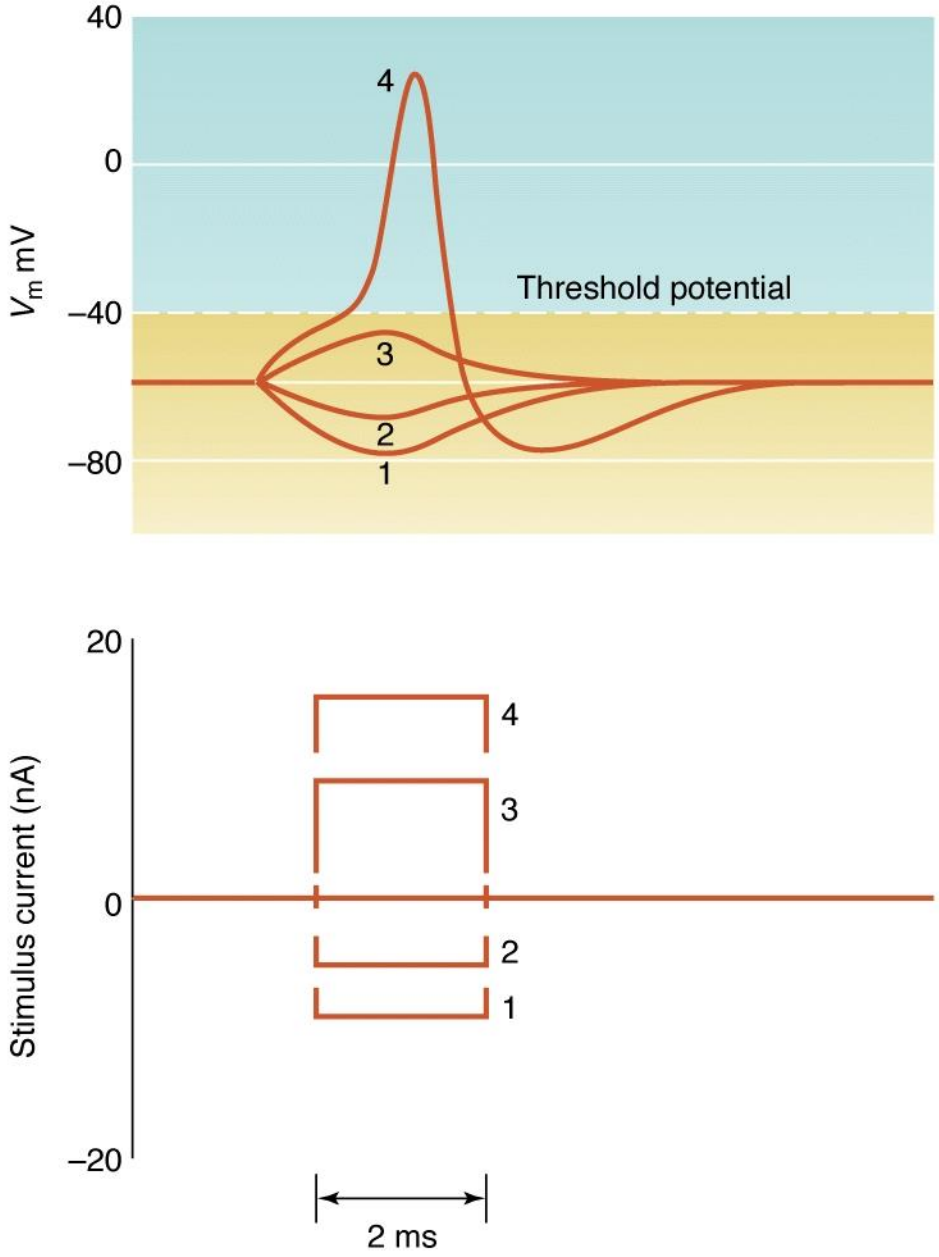
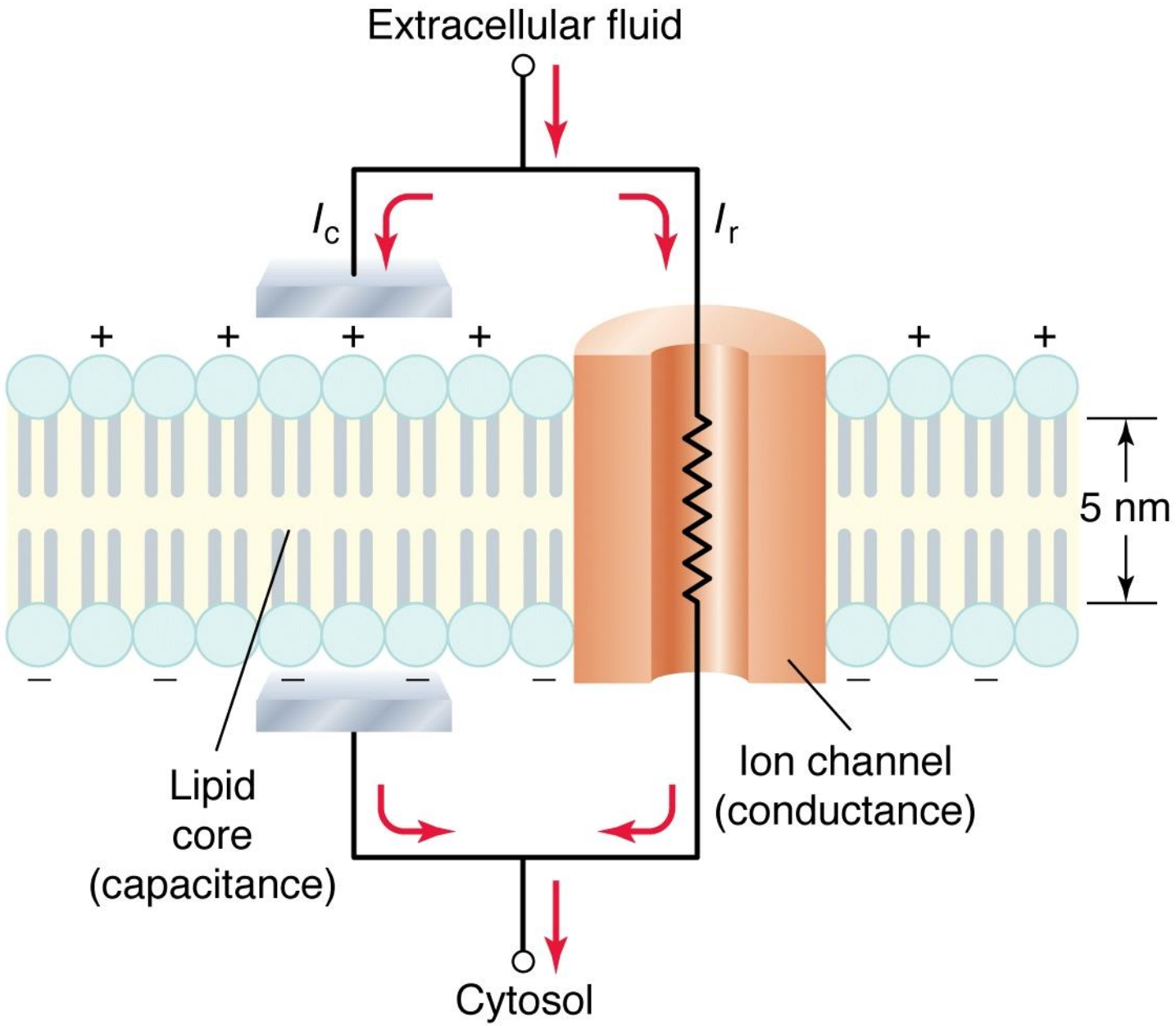
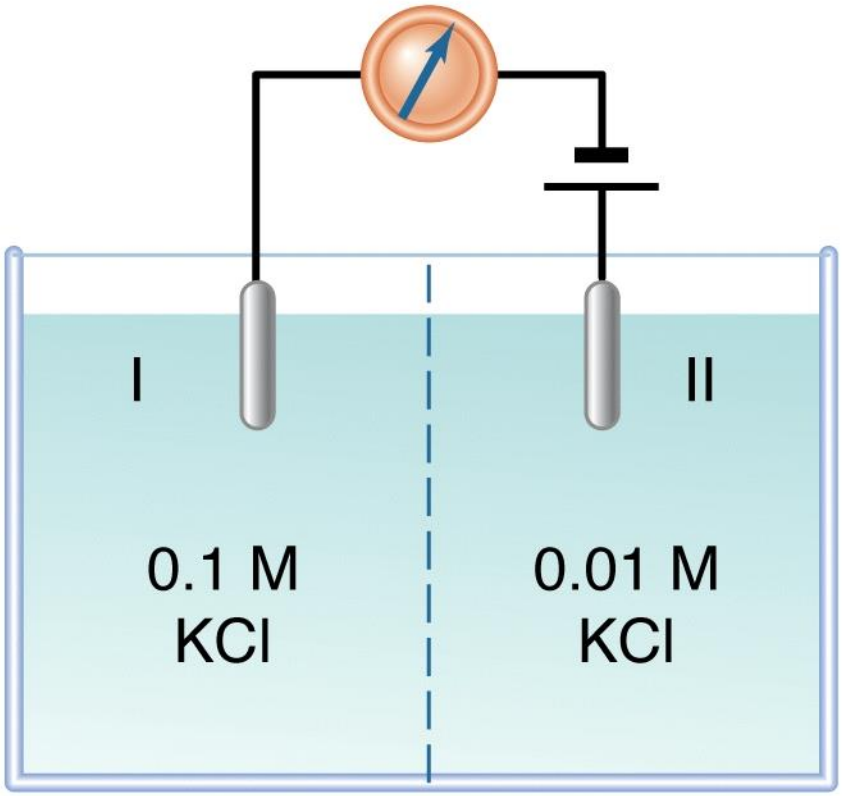

40
0
−40
−80
V_m mV
Threshold potential
4
3
2
1
20
0
−20
Stimulus current (nA)
4
3
2
1
2 ms

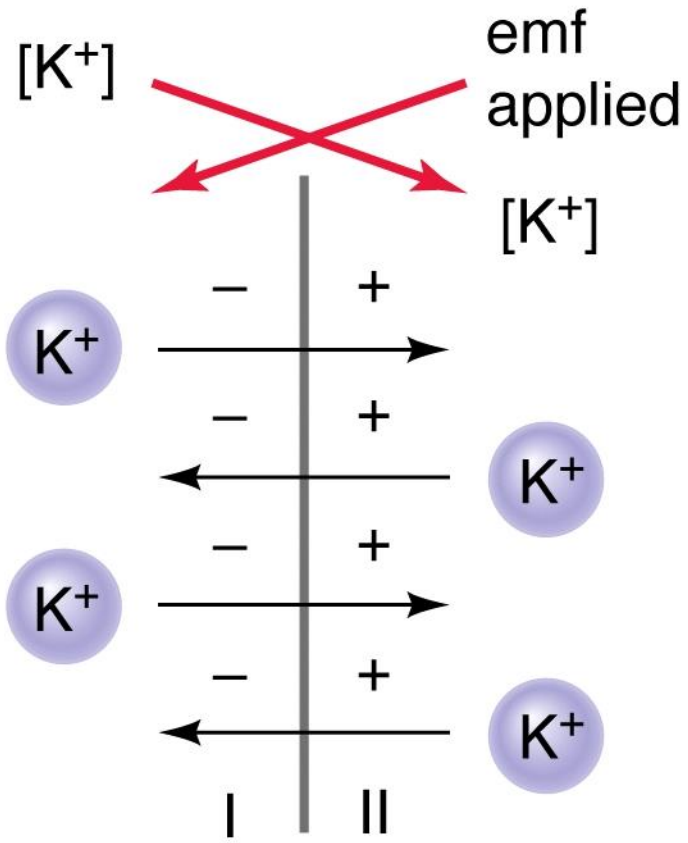
Table 5-1 **Examples of ion channels found in axons**

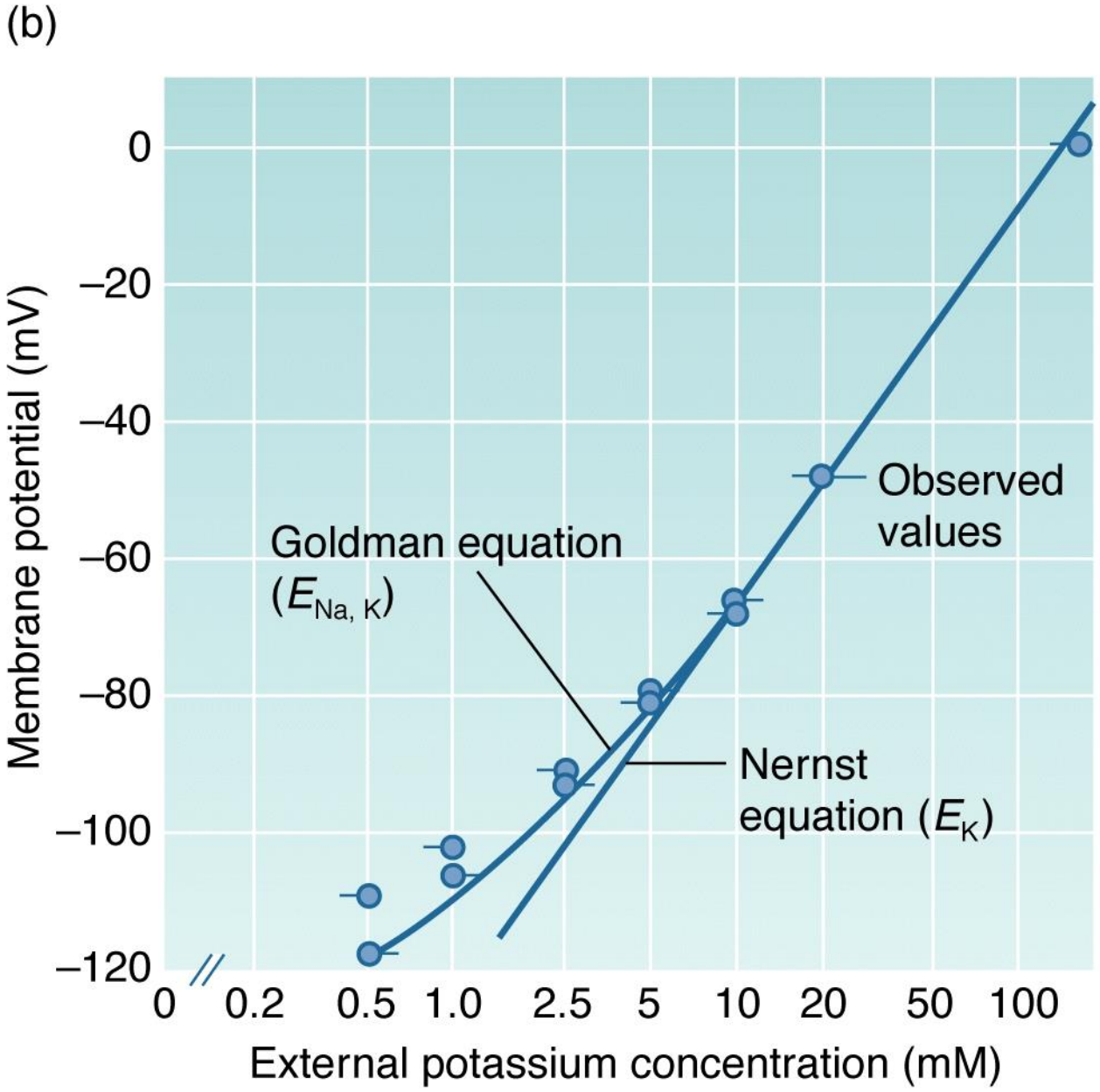
Channel	Current through channel	Characteristics	Selected blockers	Function
Leak channel (open in resting axon)	I_K (leak)	Produces relatively high P_K of resting cell	Partially blocked by tetraethylammonium (TEA)	Largely responsible for V_{rest}
Voltage-gated Na^+ channel	I_{Na}	Rapidly activated by depolarization; becomes inactivated even if V_m remains depolarized	Tetrodotoxin (TTX)	Produces rising phase of AP
Voltage-gated Ca^{2+} channel	I_{Ca}	Activated by depolarization but more slowly than Na^+ channel; inactivated as function of cytoplasmic $[Ca^{2+}]$ or V_m	Verapamil, D600, Co^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, La^{3+}	Produces slow depolarization; allows Ca^{2+} to enter cell, where it can act as second messenger
Voltage-gated K^+ channel ("delayed rectifier")	$I_{K(V)}$	Activated by depolarization but more slowly than Na^+ channel; inactivated slowly and not completely if V_m remains depolarized	Intra- and extracellular TEA, amino pyridines	Carries current that rapidly repolarizes the membrane to terminate an AP
Ca^{2+}-dependent K^+ channel	$I_{K(Ca)}$	Activated by depolarization plus elevated cytoplasmic $[Ca^{2+}]$; remains open as long as cytoplasmic $[Ca^{2+}]$ is higher than normal	Extracellular TEA	Carries current that repolarizes the cell following APs based on either Na^+ or Ca^{2+} and that balances I_{Ca}, thus limiting depolarization by I_{Ca}

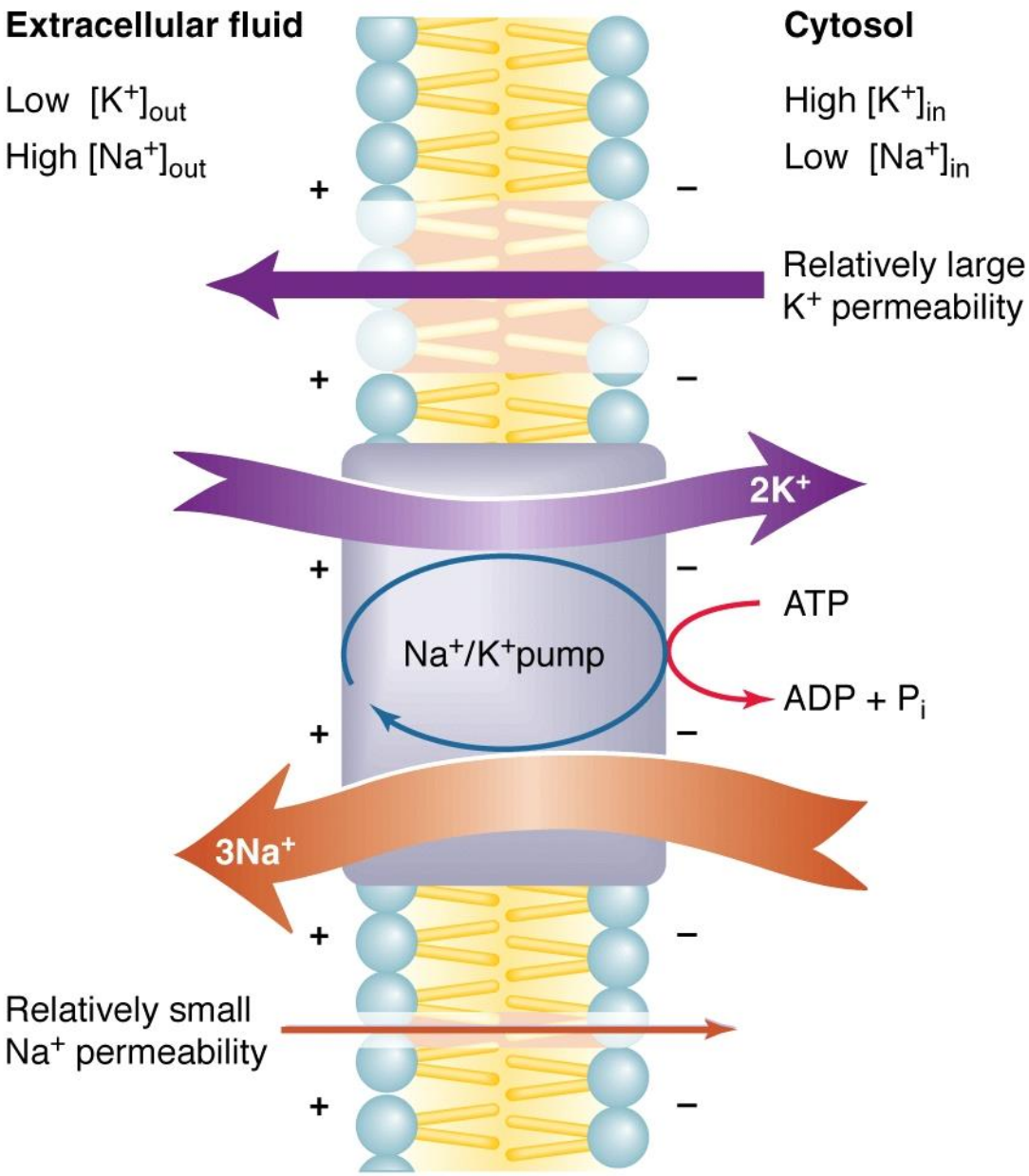

Extracellular fluid
I_c
I_r
+ + + + + +
− − − − − − −
5 nm
Lipid
core
(capacitance)
Ion channel
(conductance)
Cytosol

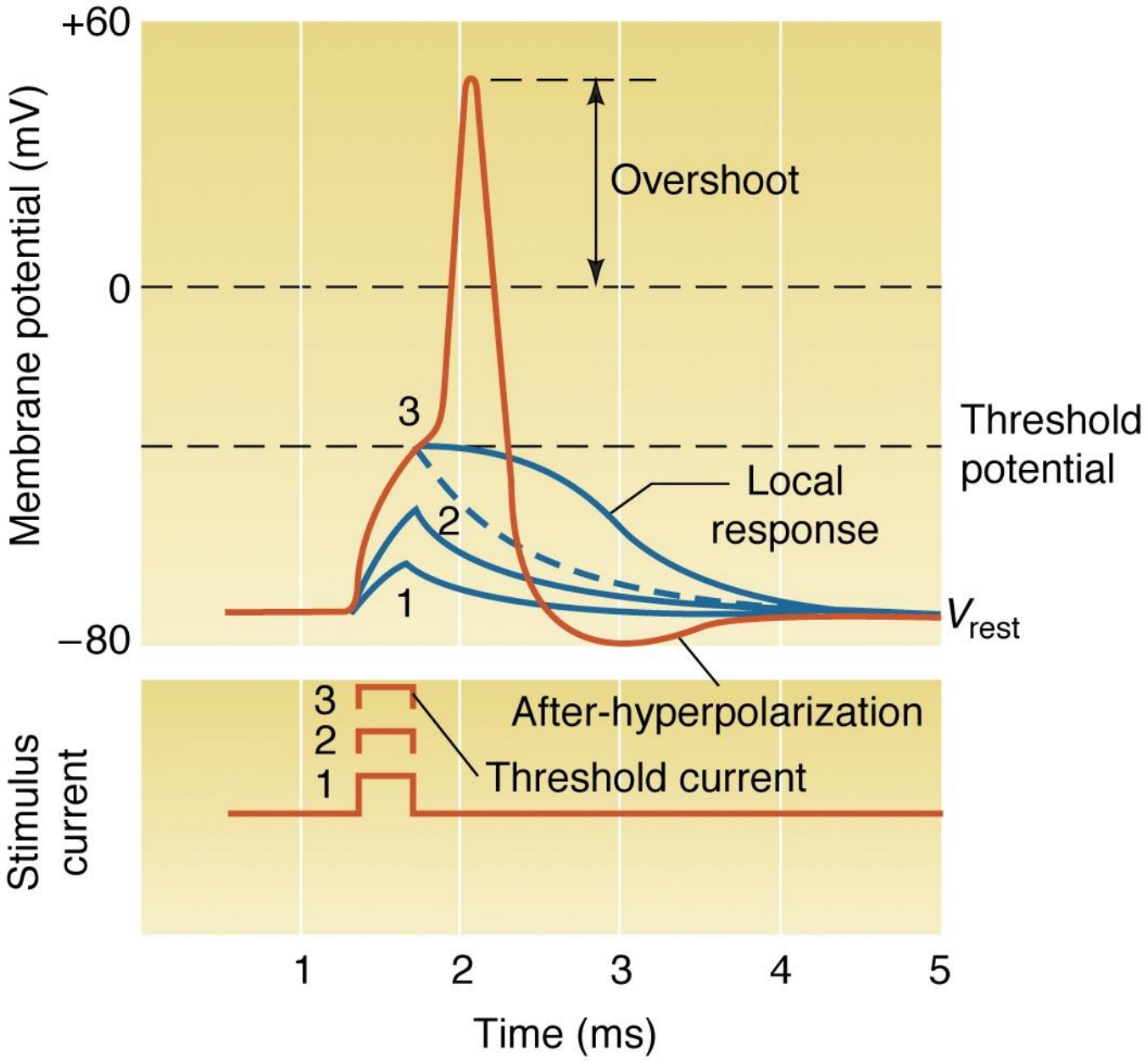
(c)



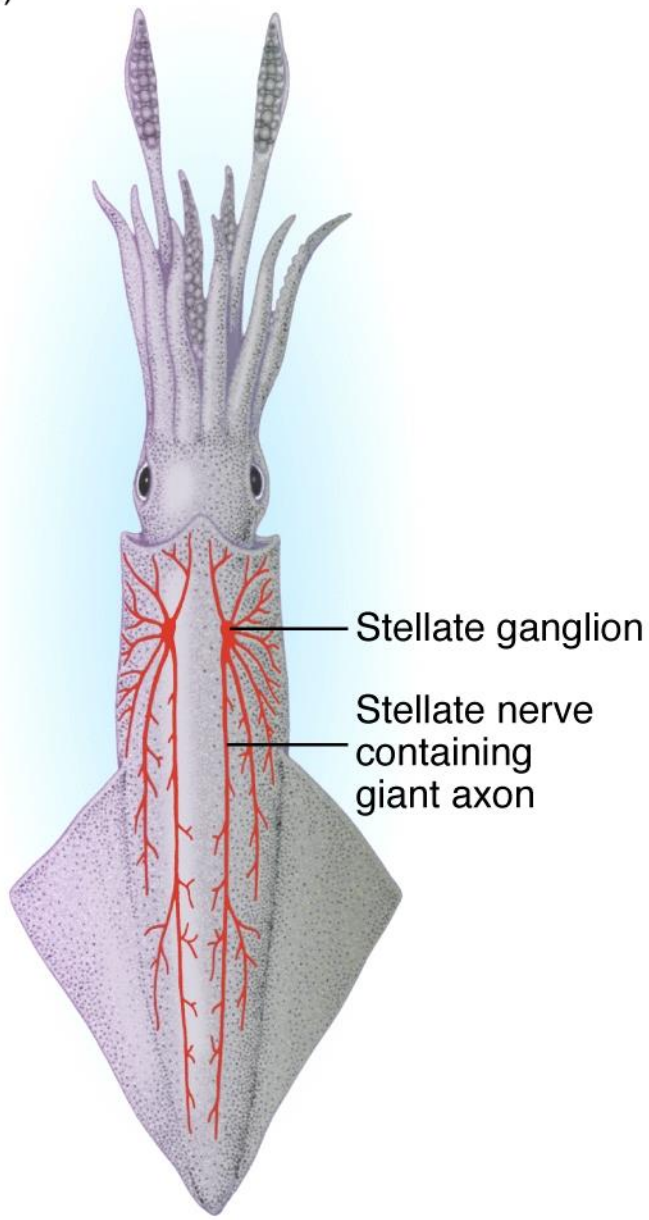


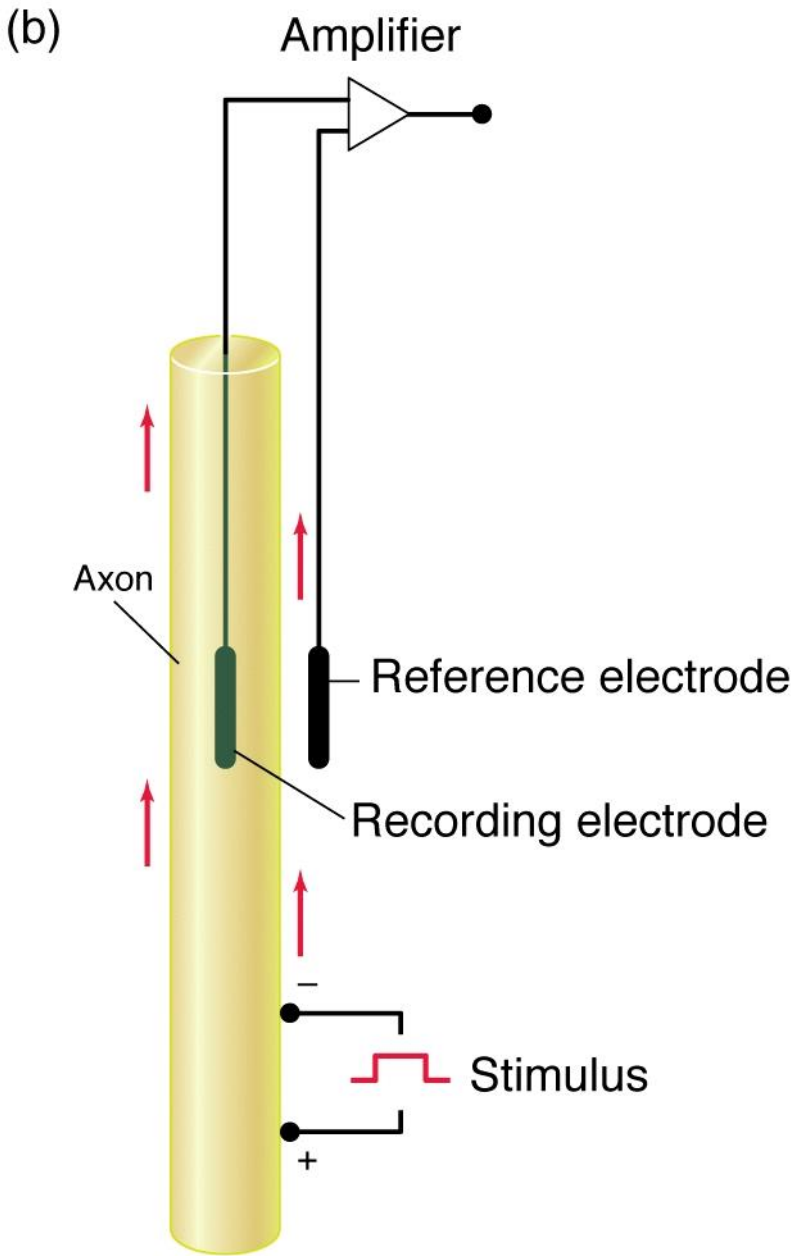

(b)
Membrane potential (mV)
0
–20
–40
–60
–80
–100
–120
0
0.2
0.5
1.0
2.5
5
10
20
50
100
External potassium concentration (mM)
Goldman equation
($E_{Na, K}$)
Nernst
equation (E_K)
Observed
values

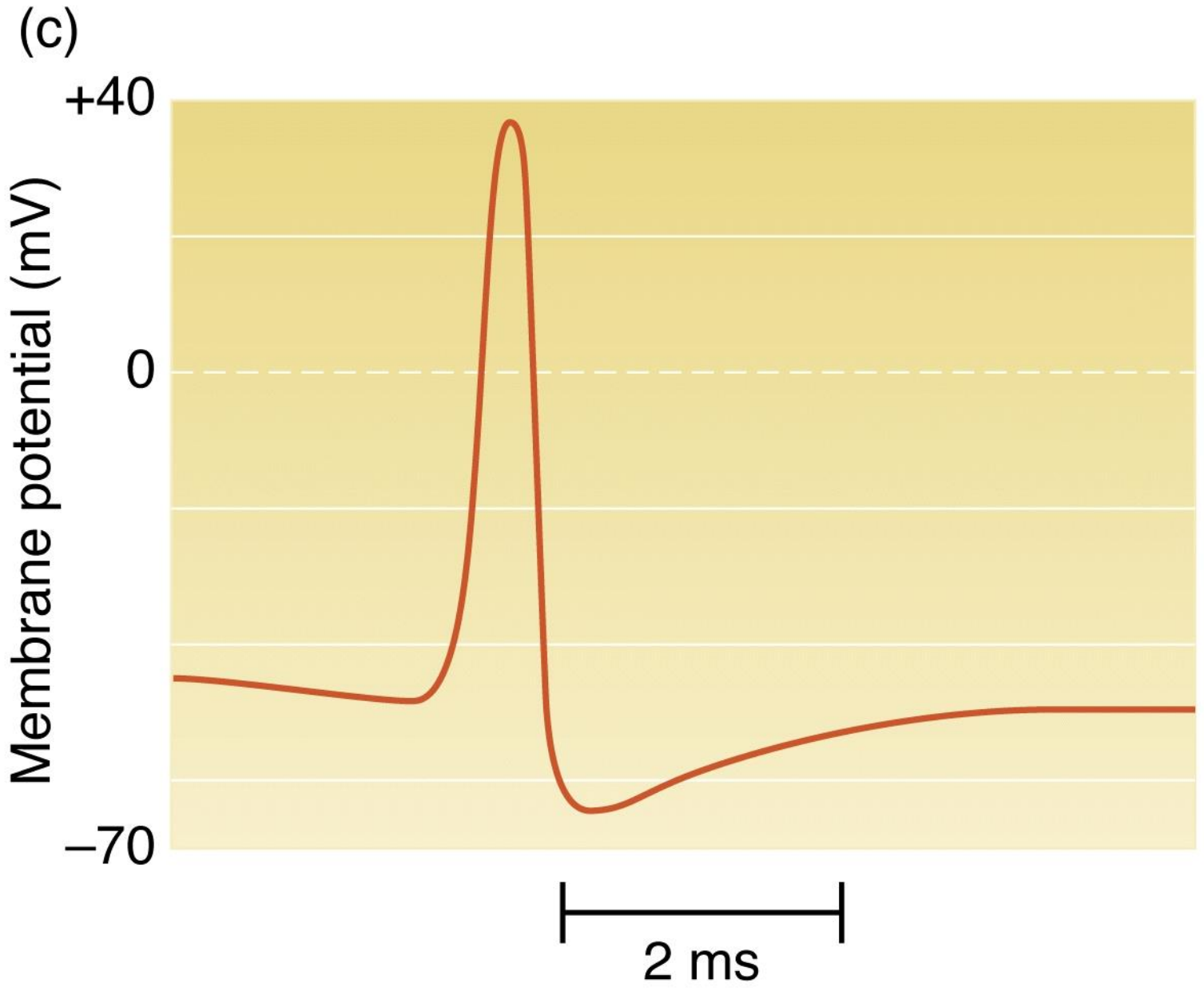

Extracellular fluid
Low $[K^+]_{out}$
High $[Na^+]_{out}$
Cytosol
High $[K^+]_{in}$
Low $[Na^+]_{in}$
Relatively large K^+ permeability
$2K^+$
Na^+/K^+pump
ATP
ADP + P_i
$3Na^+$
Relatively small Na^+ permeability
+
−

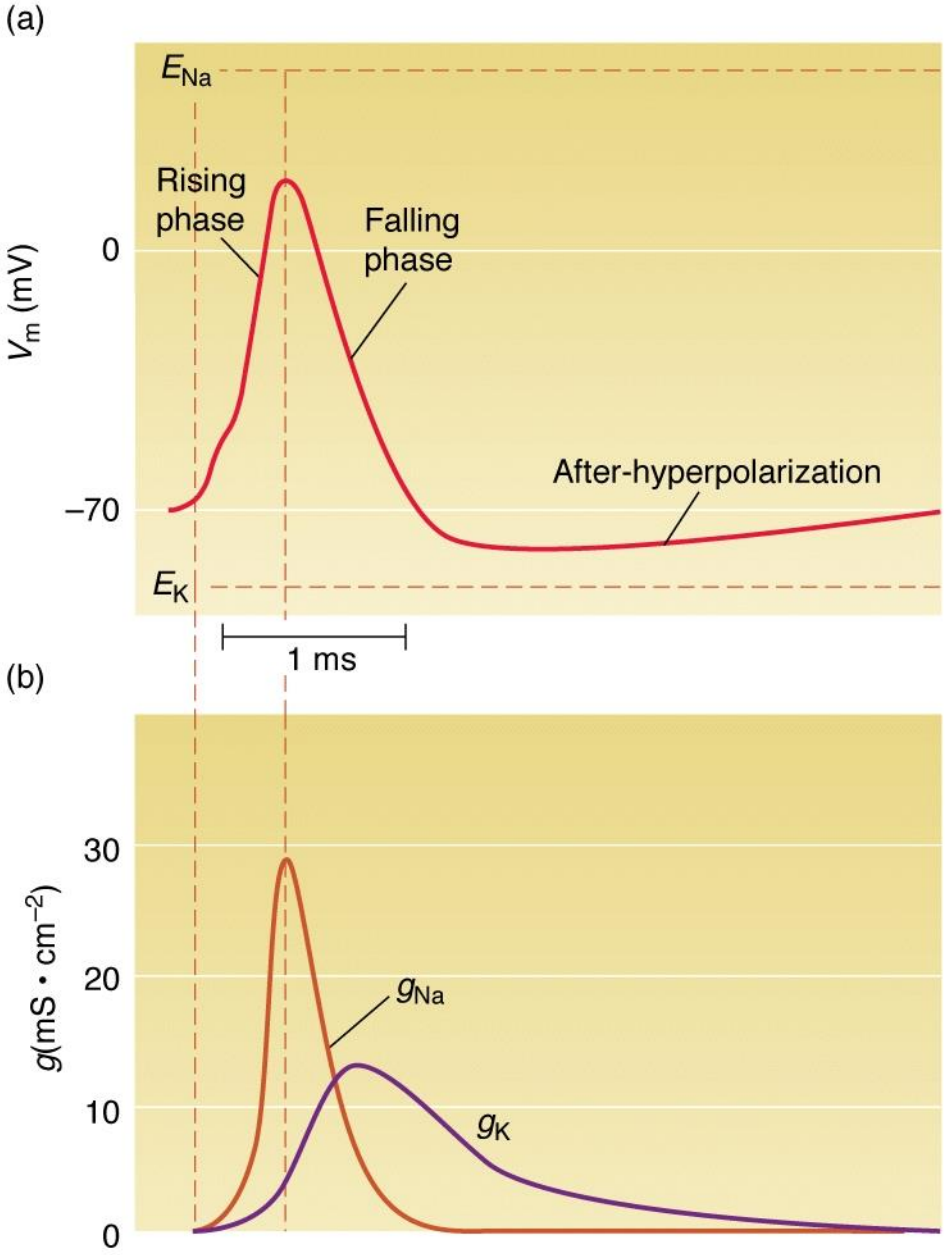

+60
0
−80
Membrane potential (mV)
Overshoot
3
2
1
Threshold potential
Local response
V_{rest}
After-hyperpolarization
Threshold current
Stimulus current
1
2
3
4
5
Time (ms)

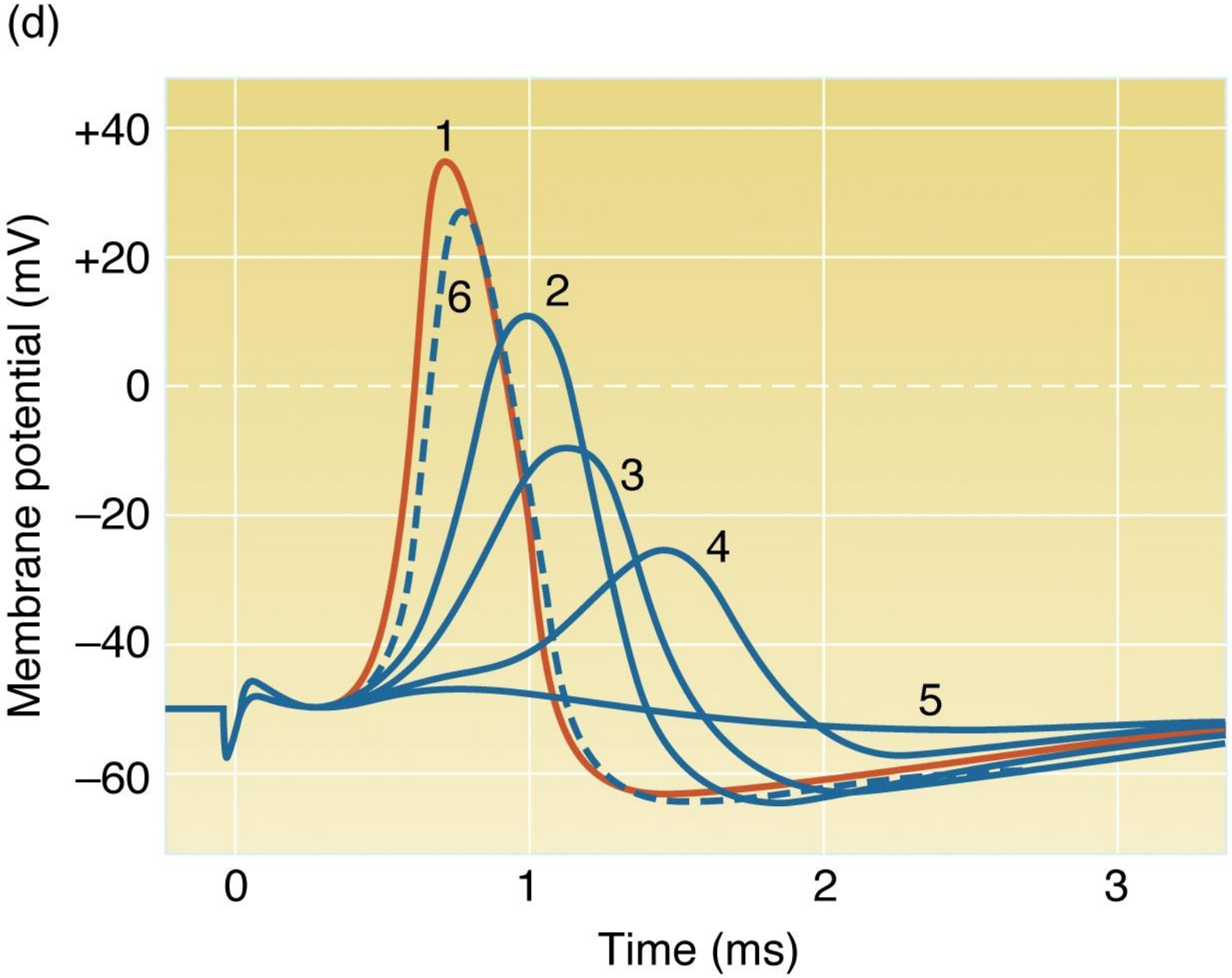
(a)

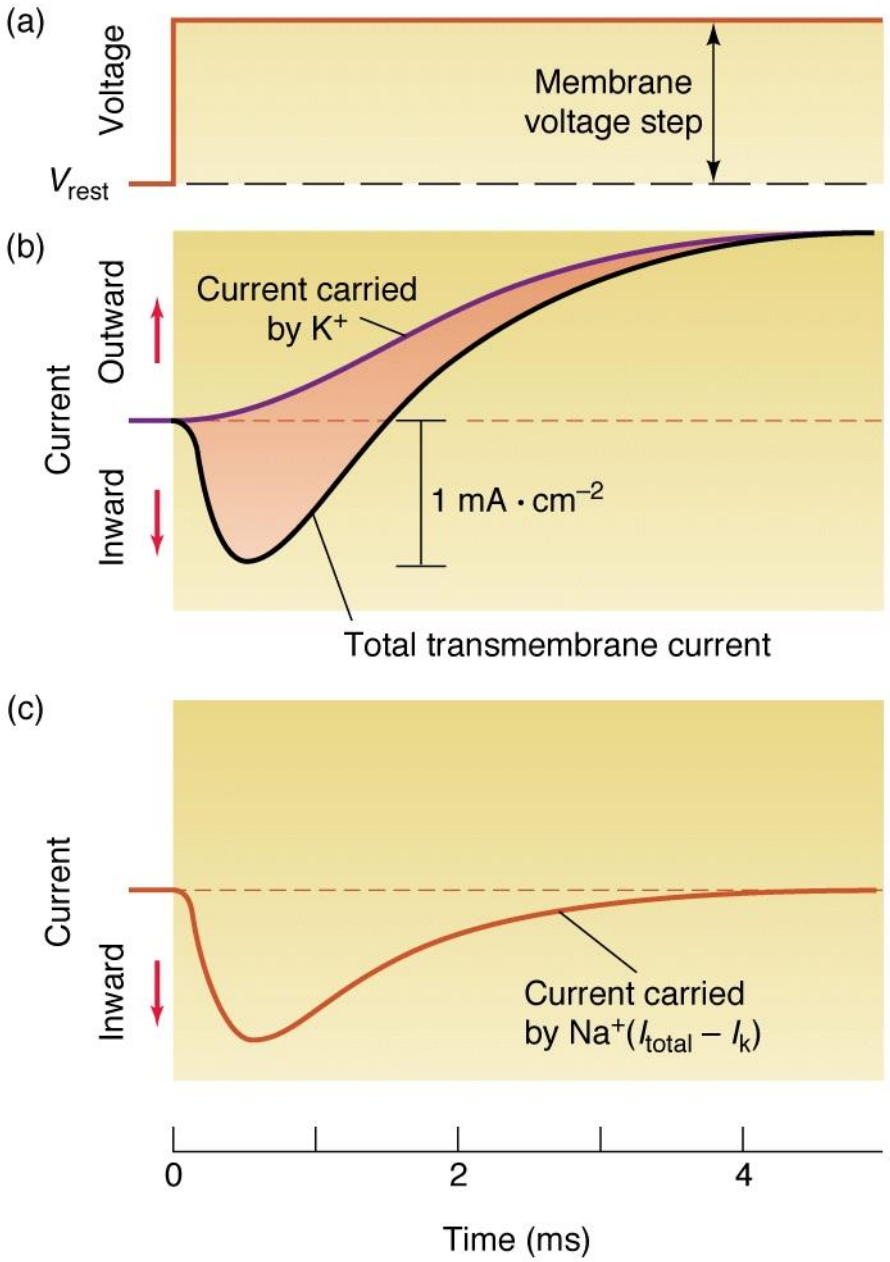



(b)
Amplifier
Axon
Reference electrode
Recording electrode
–
Stimulus
+

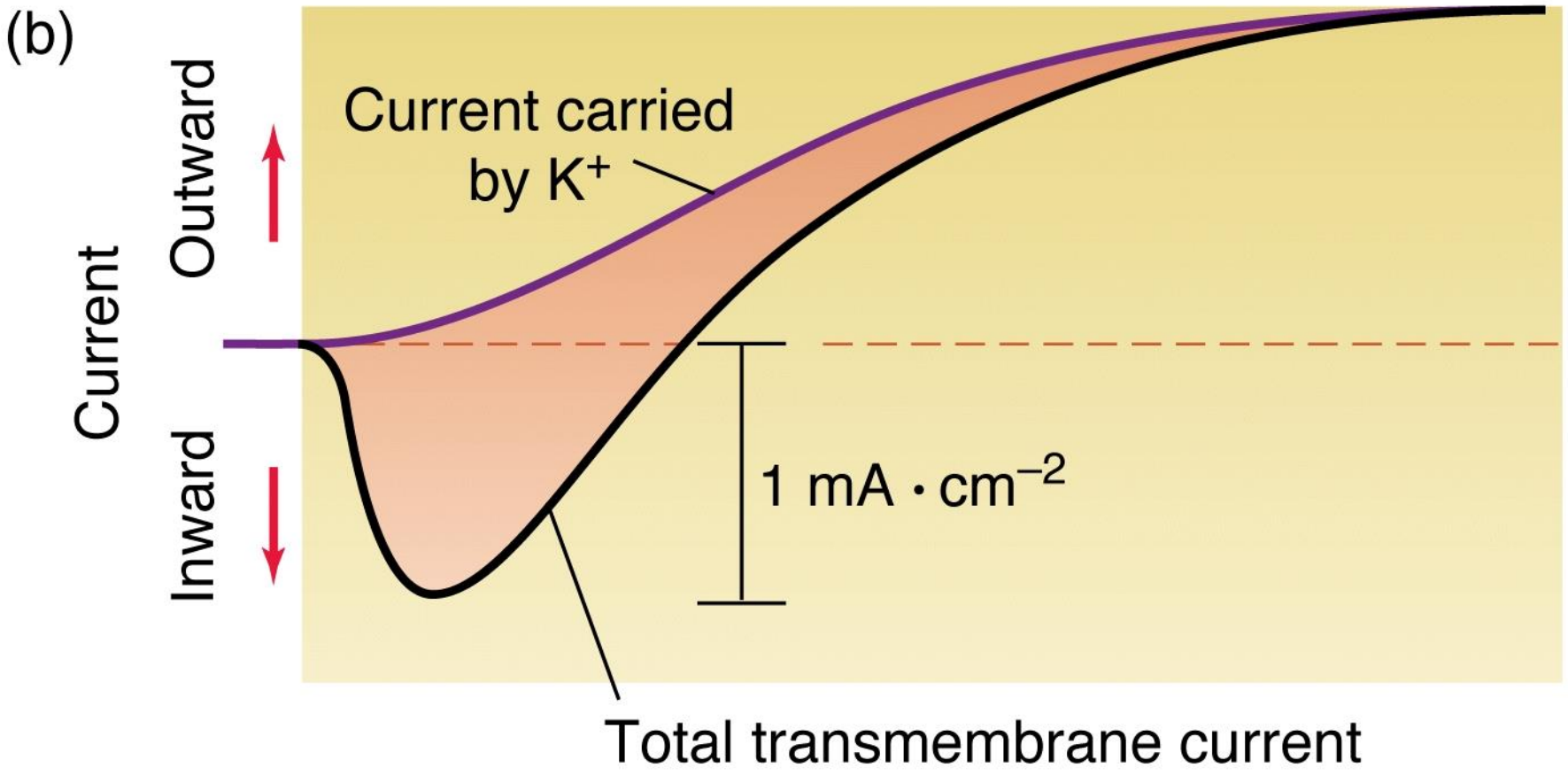

(c)
+40
0
–70
Membrane potential (mV)
2 ms

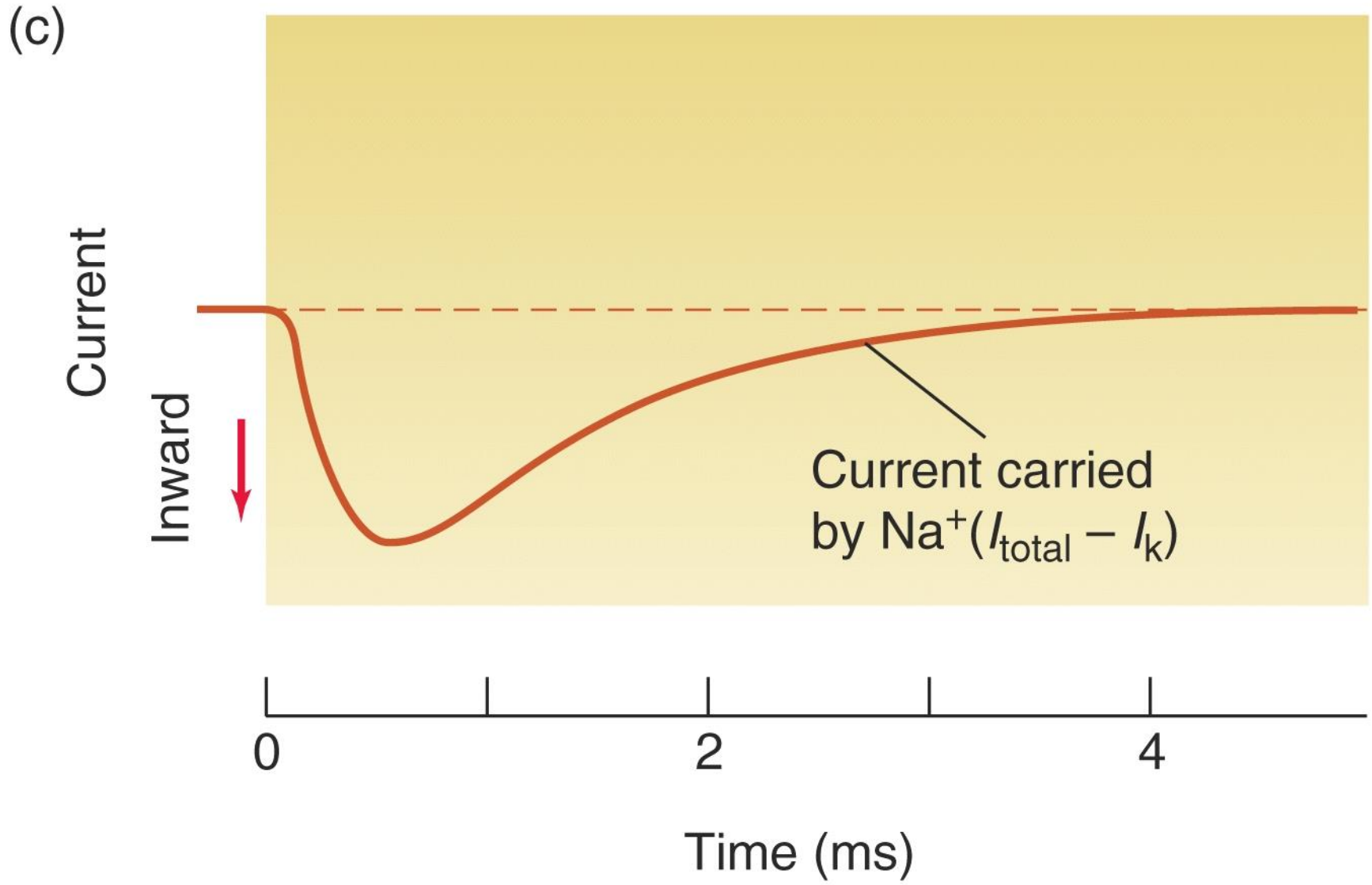

(a)
E_{Na}
Rising phase
Falling phase
0
V_m (mV)
After-hyperpolarization
–70
E_K
1 ms
(b)
30
20
10
0
g(mS • cm^{-2})
g_{Na}
g_K

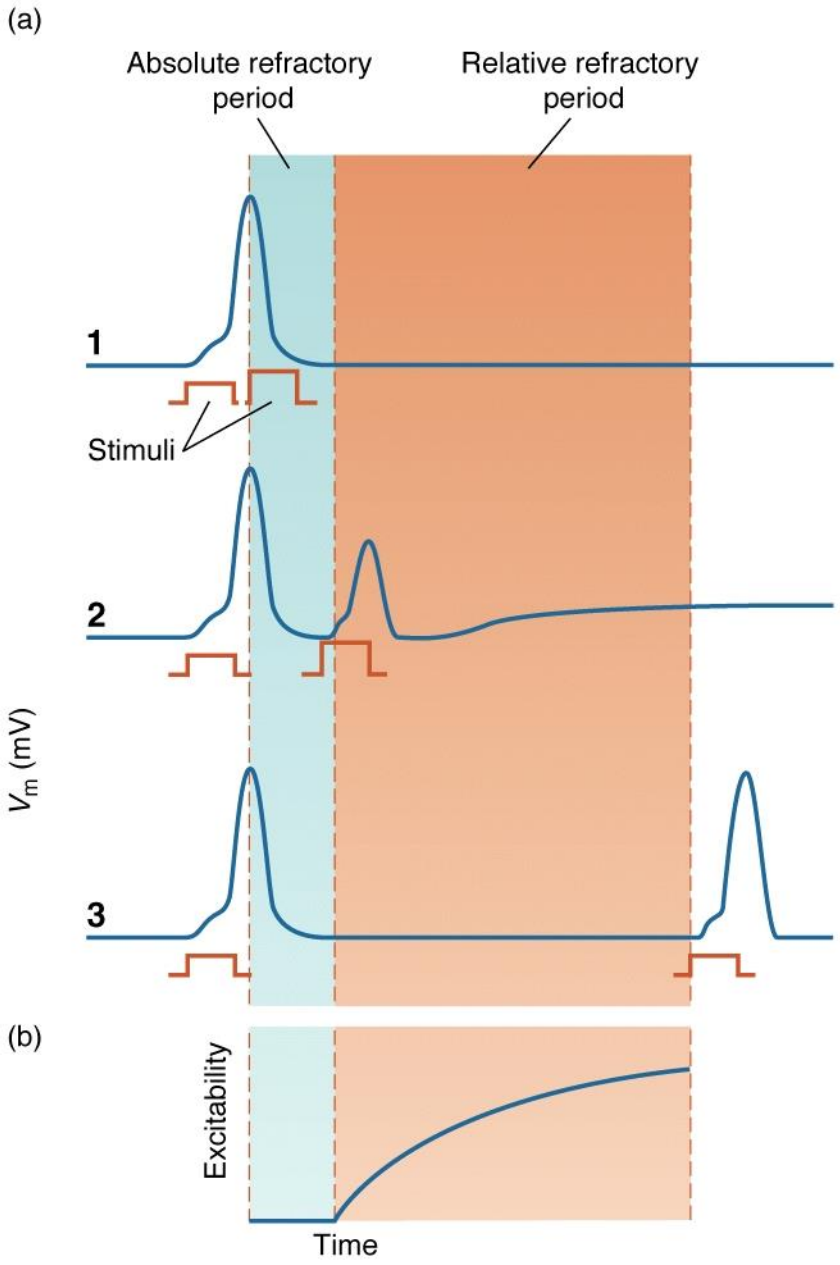

(d)
+40
+20
0
–20
–40
–60
Membrane potential (mV)
1
2
3
4
5
6
0
1
2
3
Time (ms)


(a)
Voltage
Membrane
voltage step
V_{rest}
(b)
Current
Outward
Inward
Current carried
by K^+
1 mA · cm^{-2}
Total transmembrane current
(c)
Current
Inward
Current carried
by $Na^+(I_{total} - I_k)$
0
2
4
Time (ms)

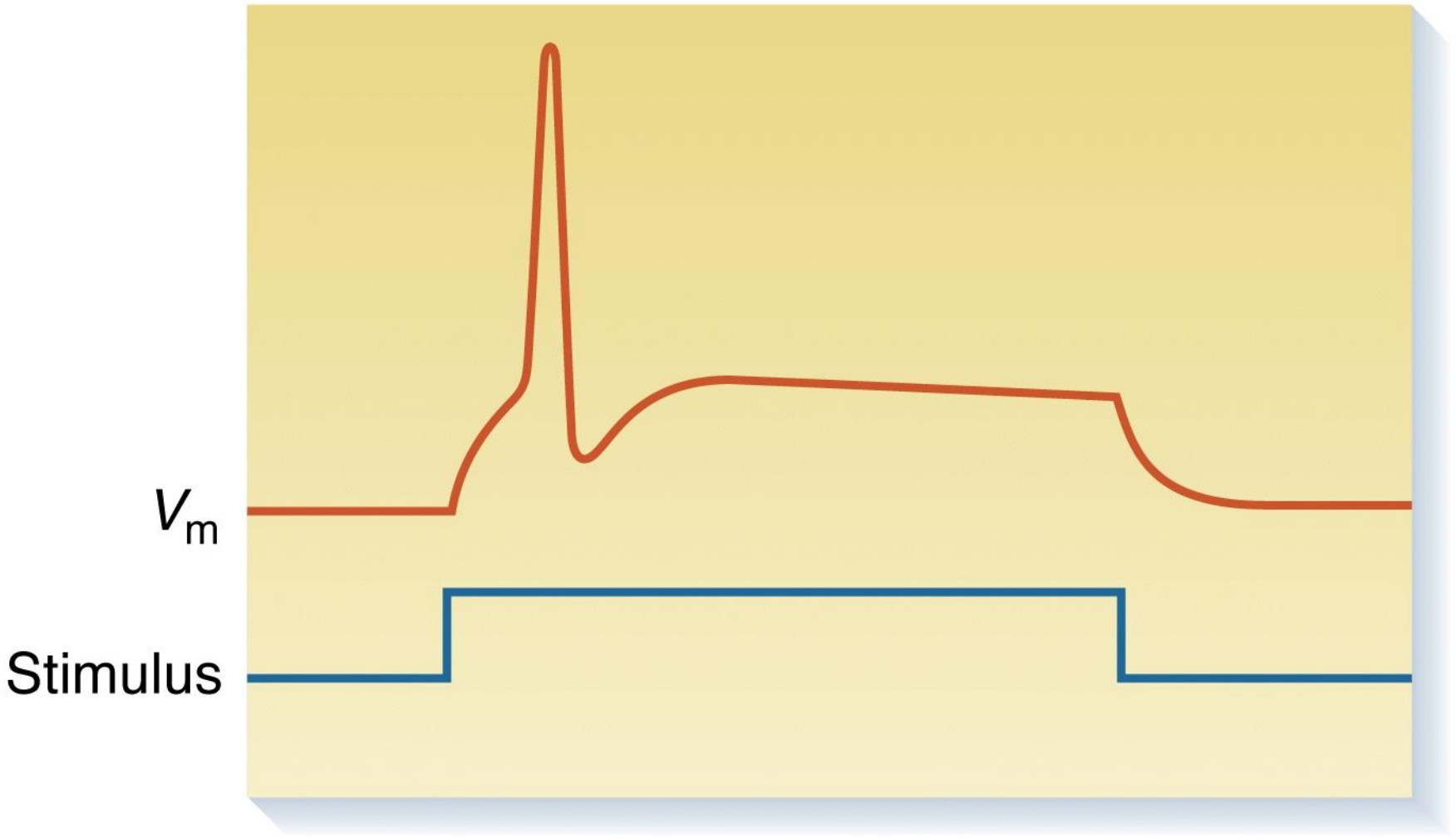

(a)
Voltage
V_{rest}
Membrane
voltage step


(b)
Current
Outward
Inward
Current carried
by K+
1 mA · cm−2
Total transmembrane current

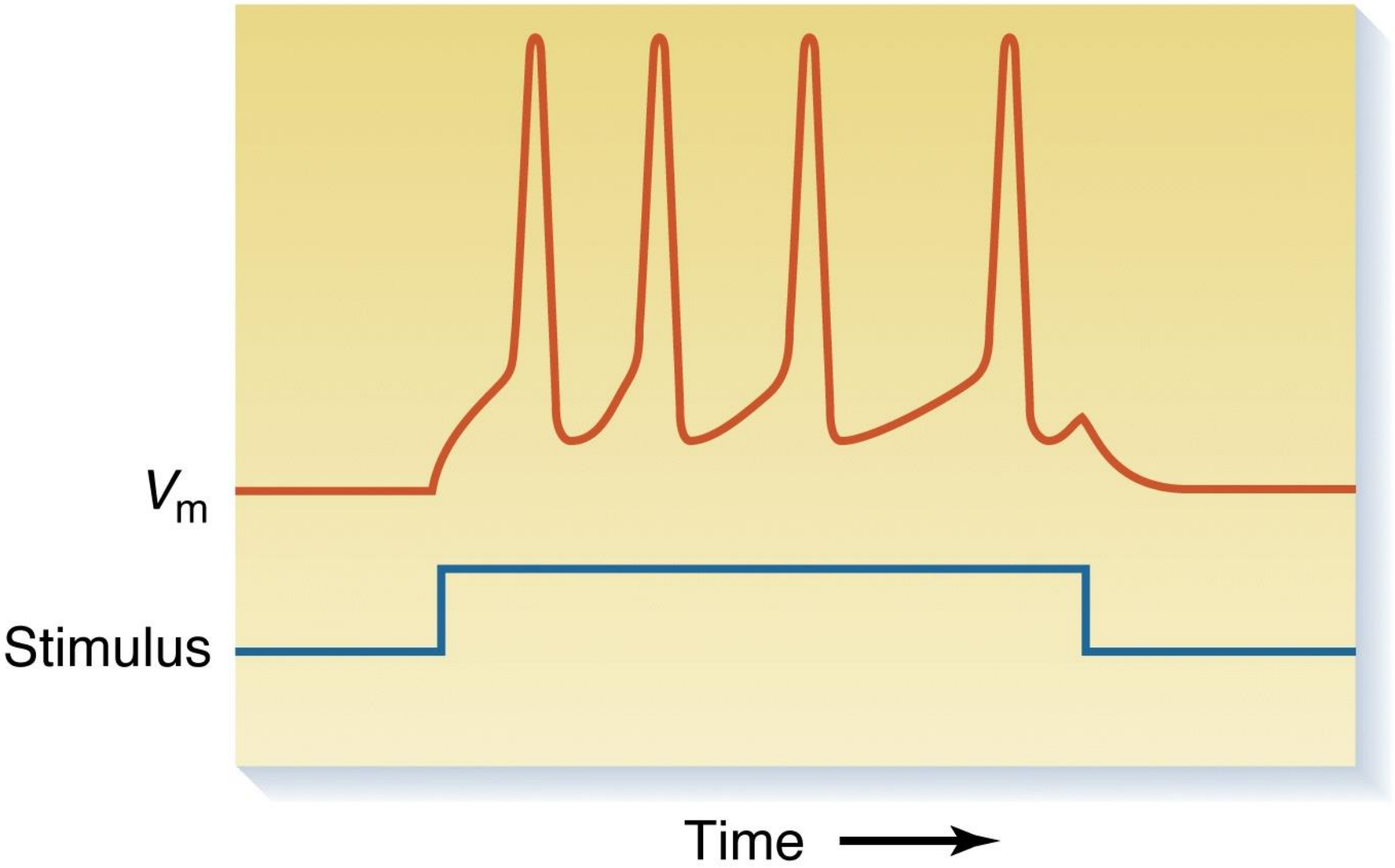

(c)
Current
Inward
Current carried
by $Na^+(I_{total} - I_k)$
0
2
4
Time (ms)

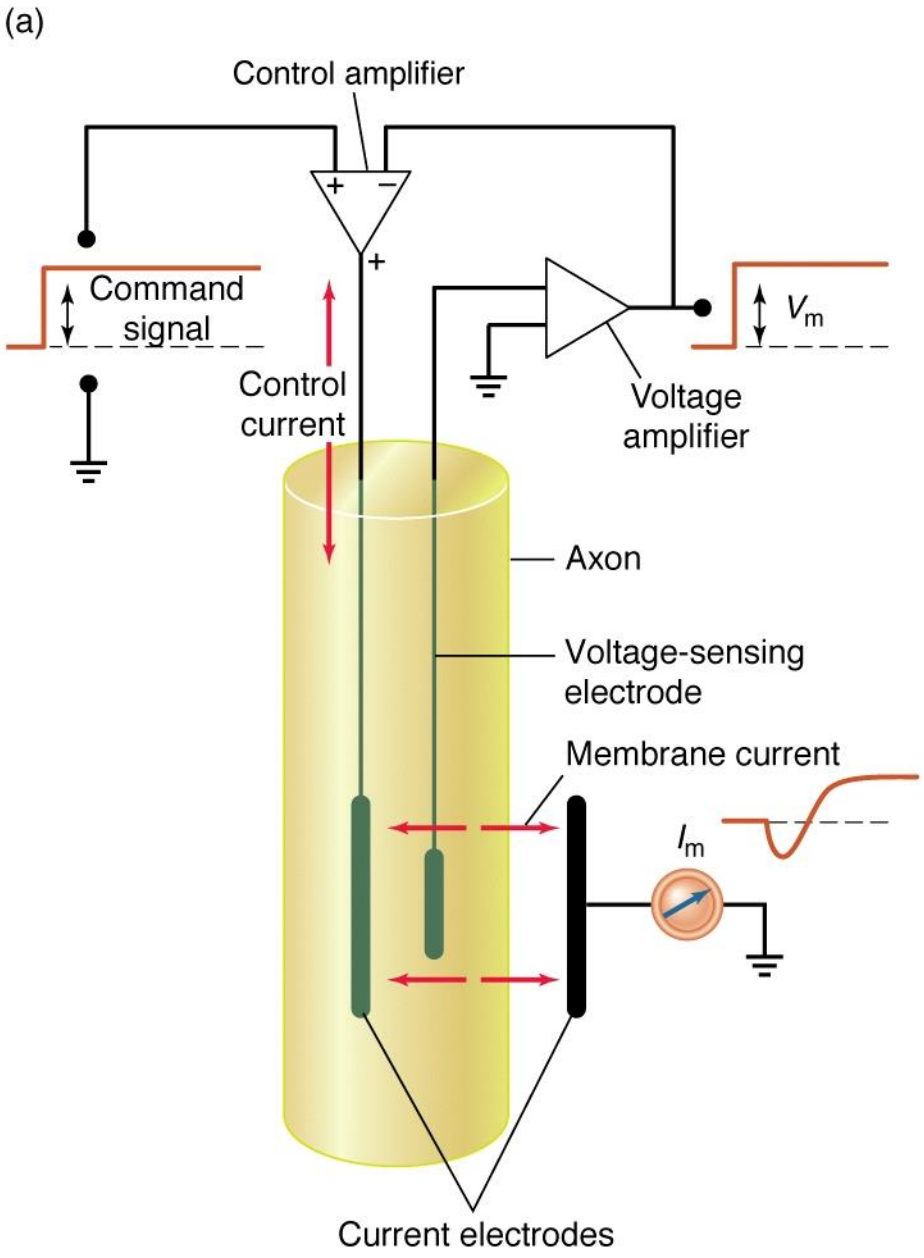

(a)
Absolute refractory period
Relative refractory period
1
Stimuli
2
3
V_m (mV)
(b)
Excitability
Time

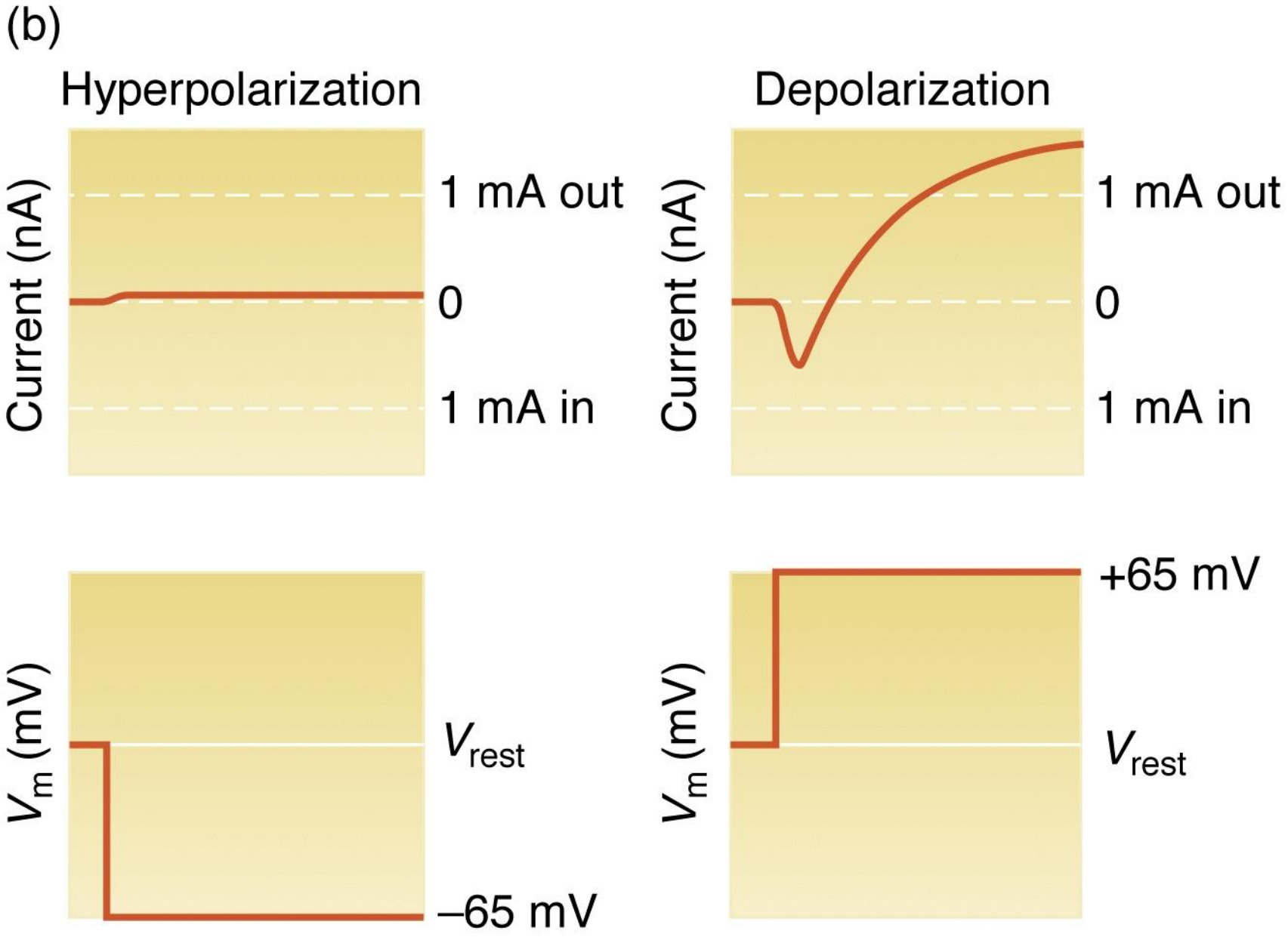
(a) Phasic response

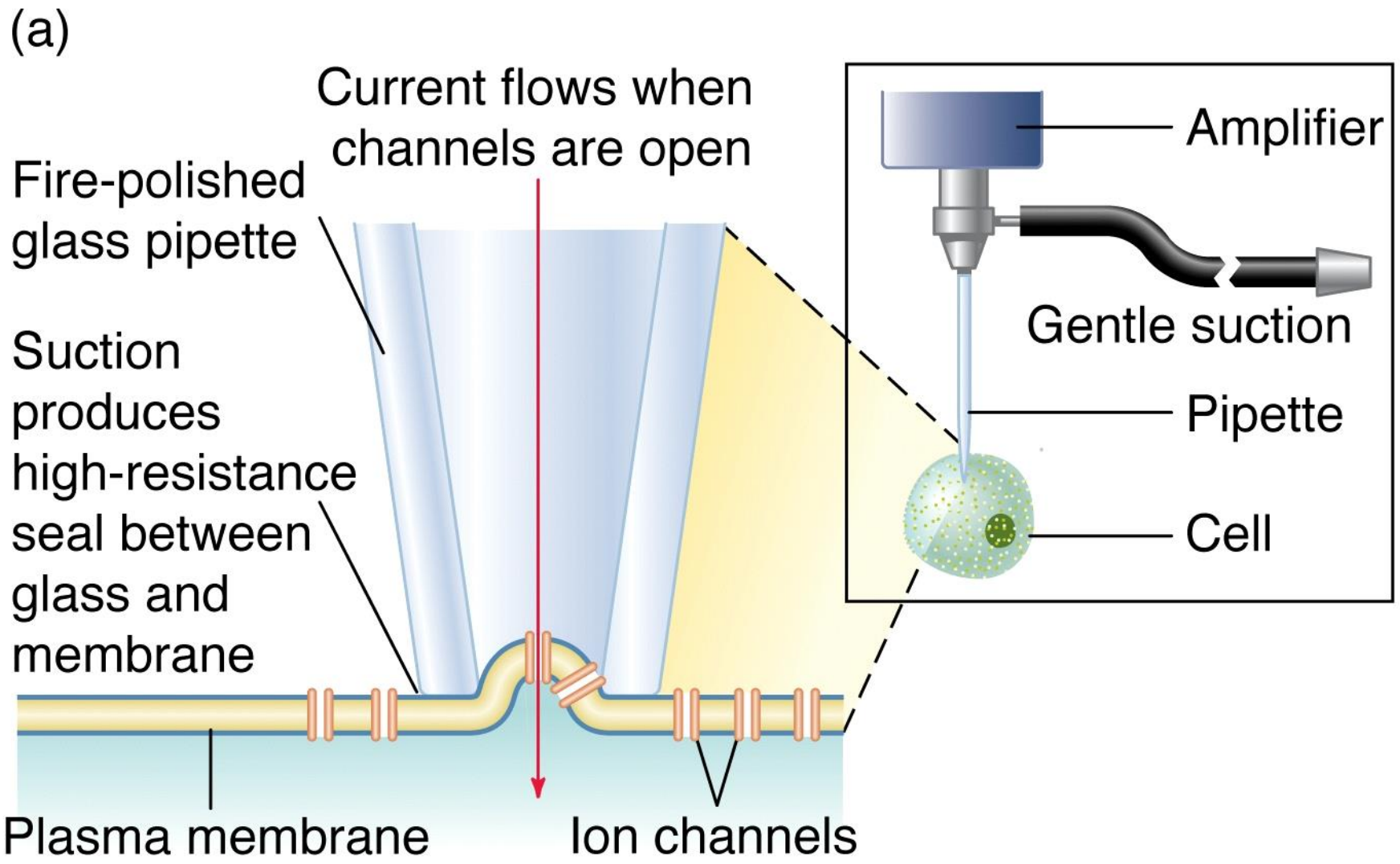


(b) Tonic response

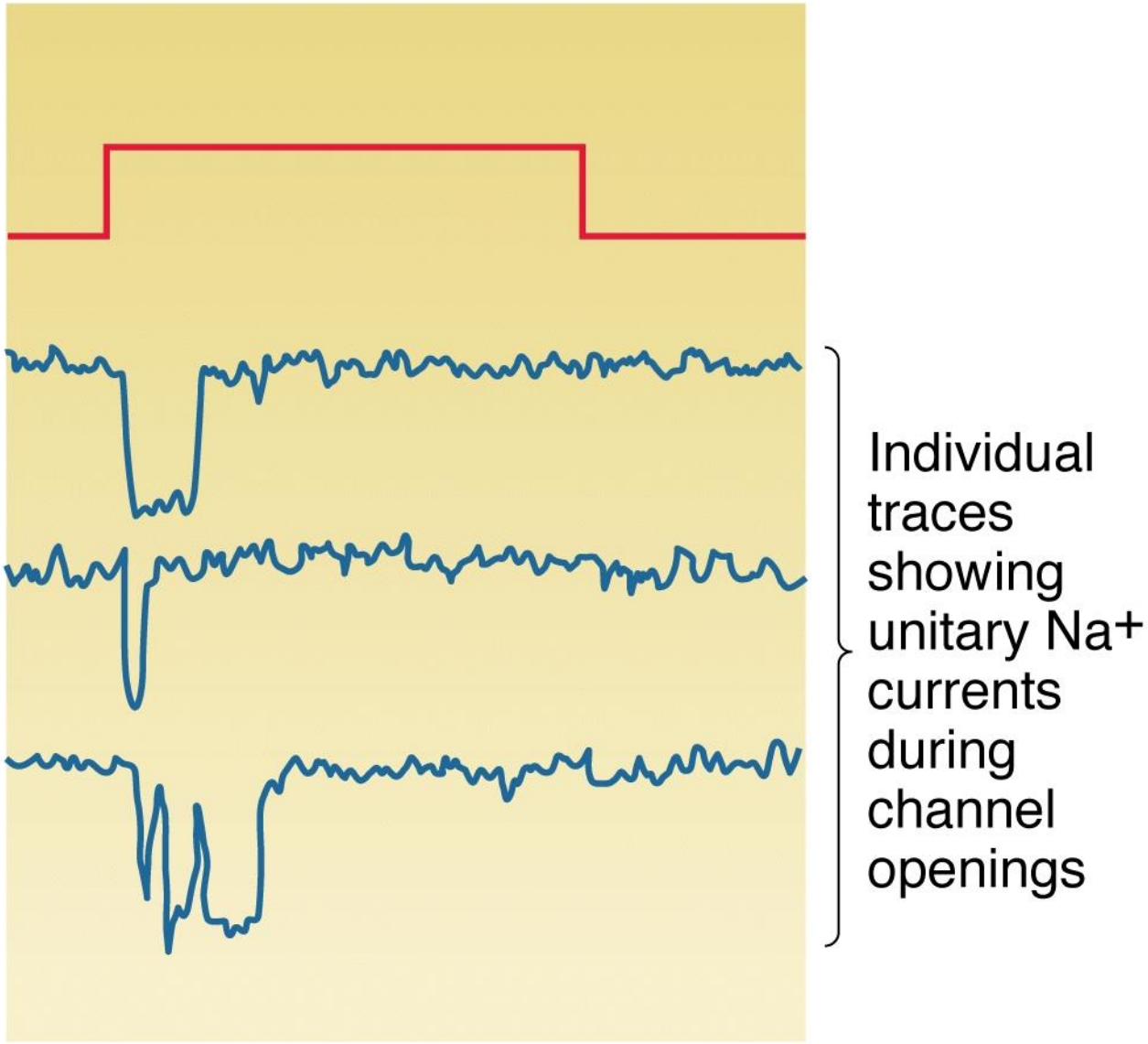



(a)
Control amplifier
+
−
+
Command
signal
Control
current
Voltage
amplifier
V_m
Axon
Voltage-sensing
electrode
Membrane current
I_m
Current electrodes

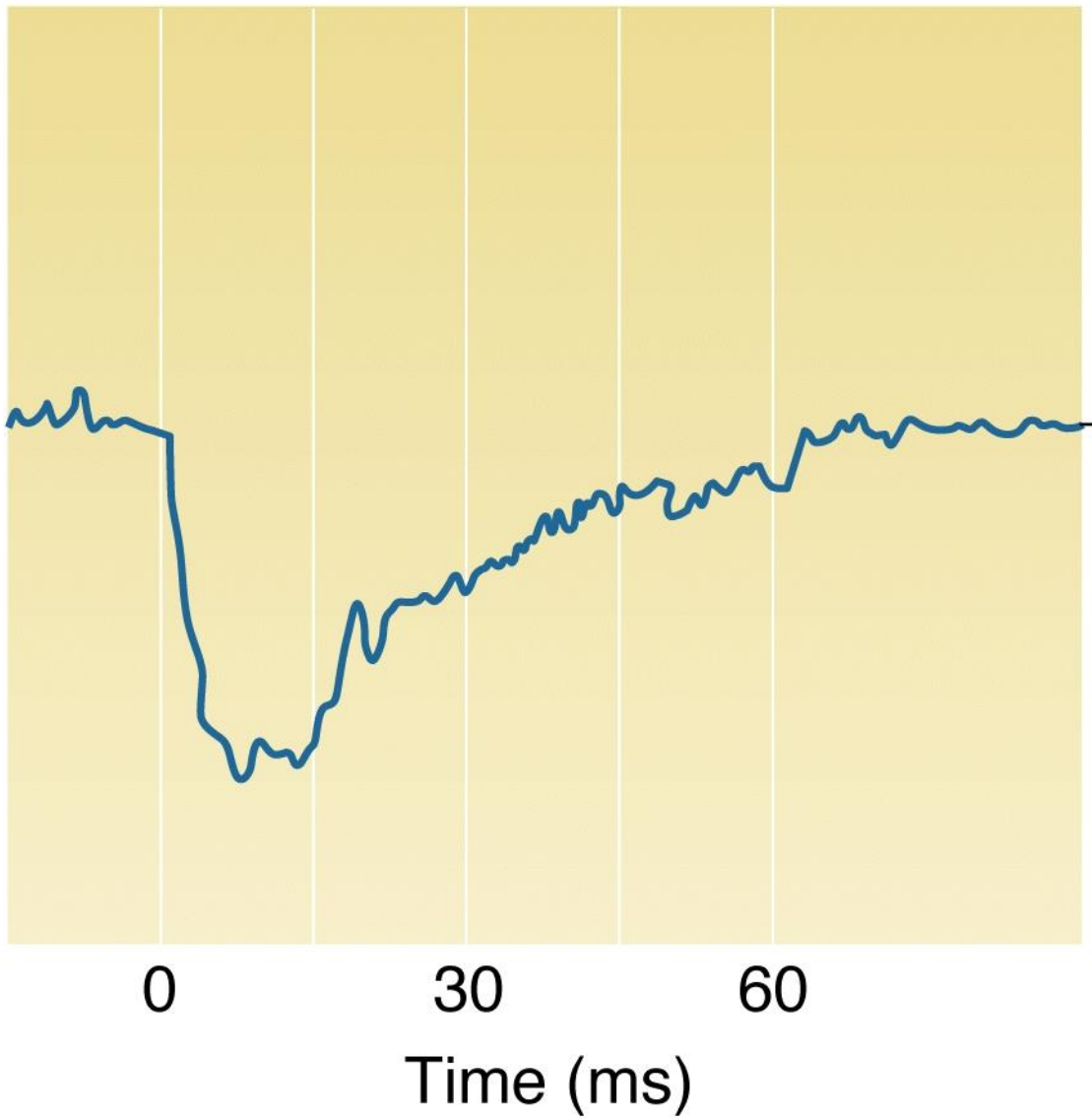

(b)
Hyperpolarization
Depolarization
Current (nA)
1 mA out
0
1 mA in
Current (nA)
1 mA out
0
1 mA in
V_m (mV)
V_{rest}
–65 mV
V_m (mV)
+65 mV
V_{rest}

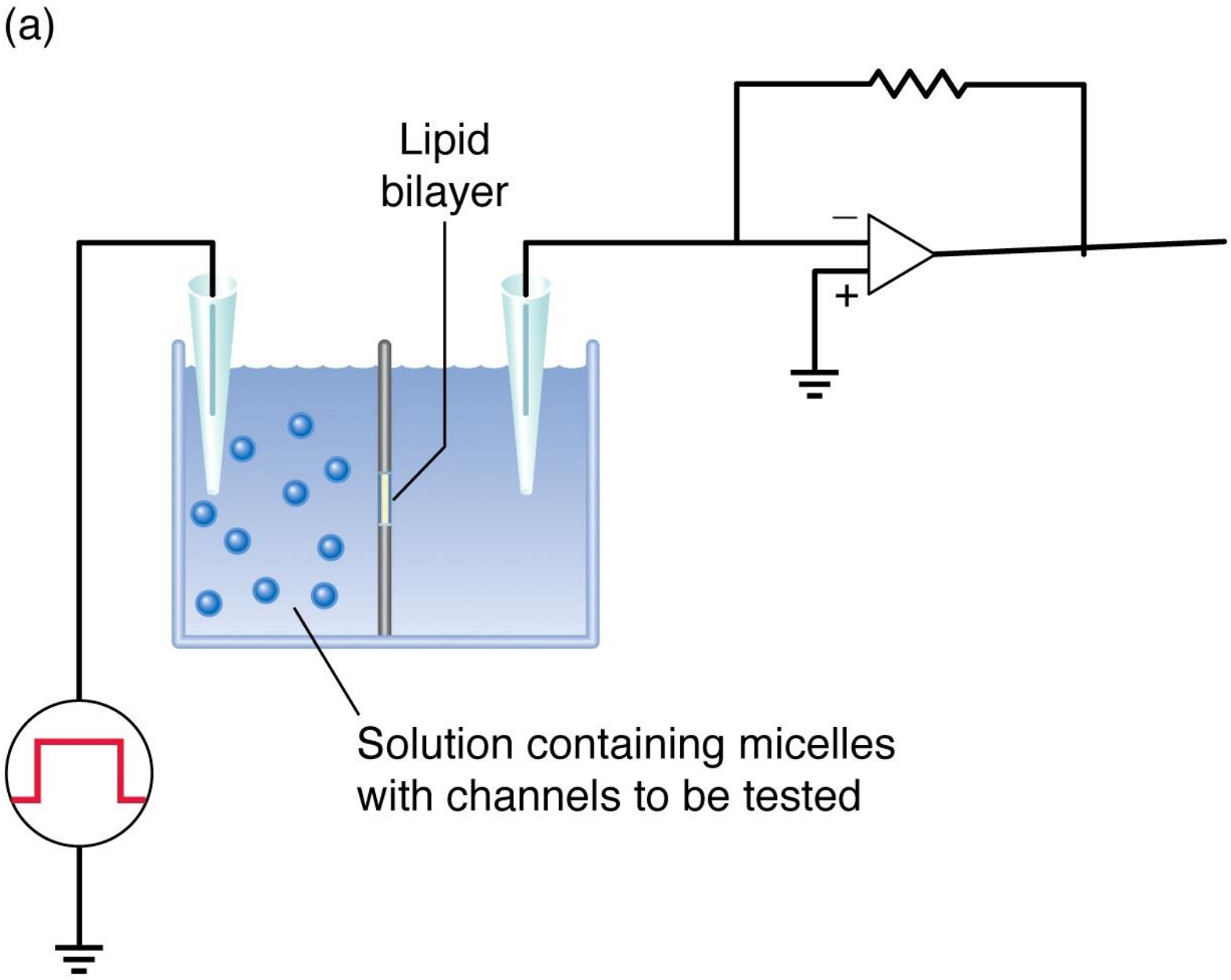

(a)
Current flows when channels are open
Fire-polished glass pipette
Suction produces high-resistance seal between glass and membrane
Amplifier
Gentle suction
Pipette
Cell
Plasma membrane
Ion channels

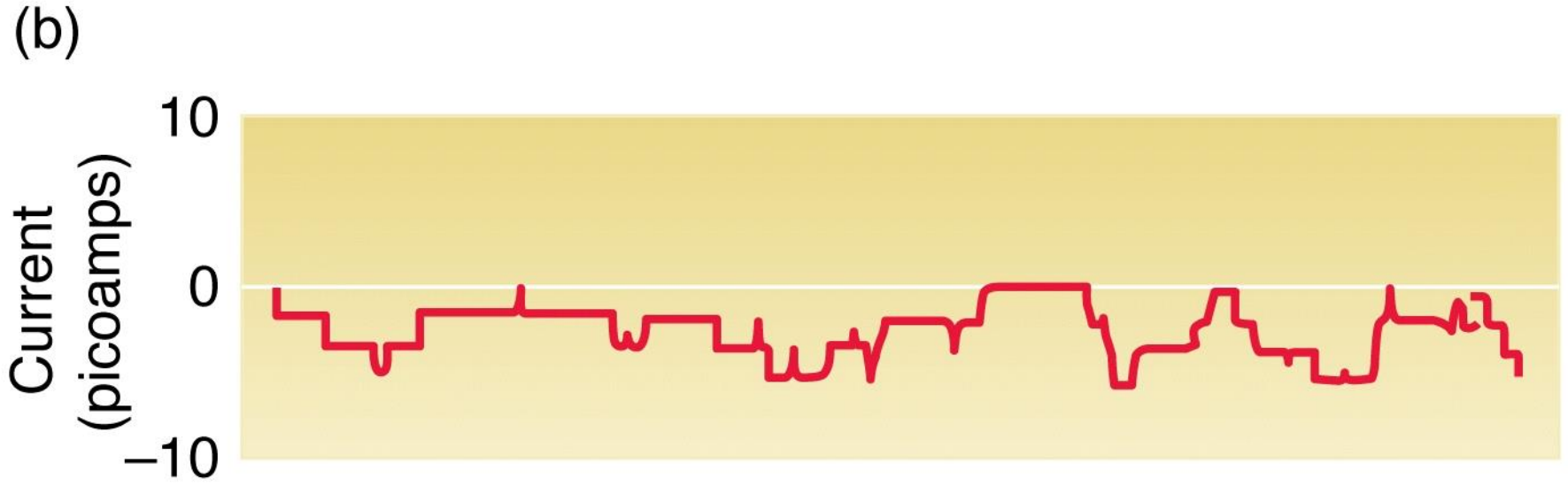
(b)

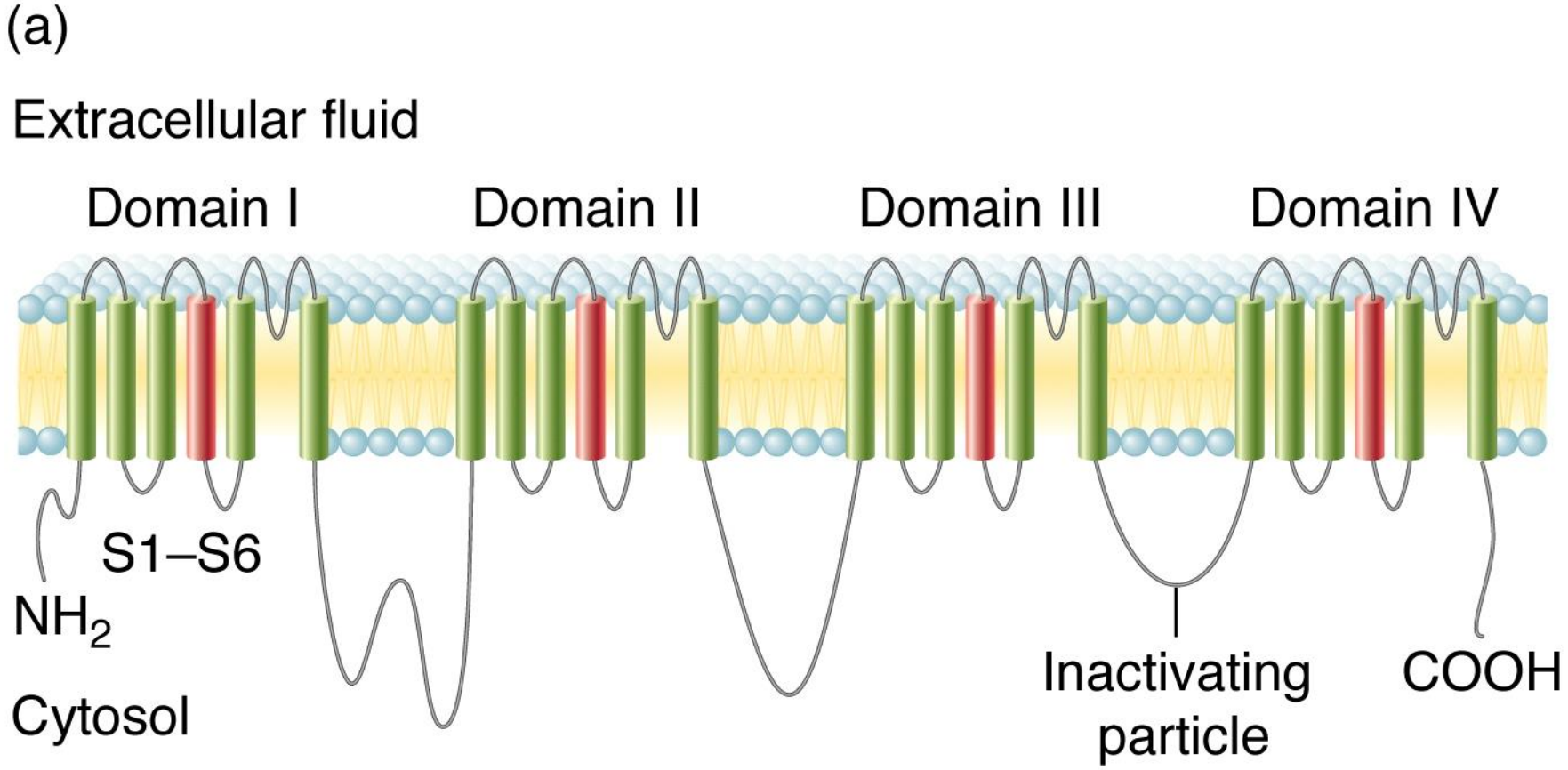

Individual traces showing unitary Na+ currents during channel openings

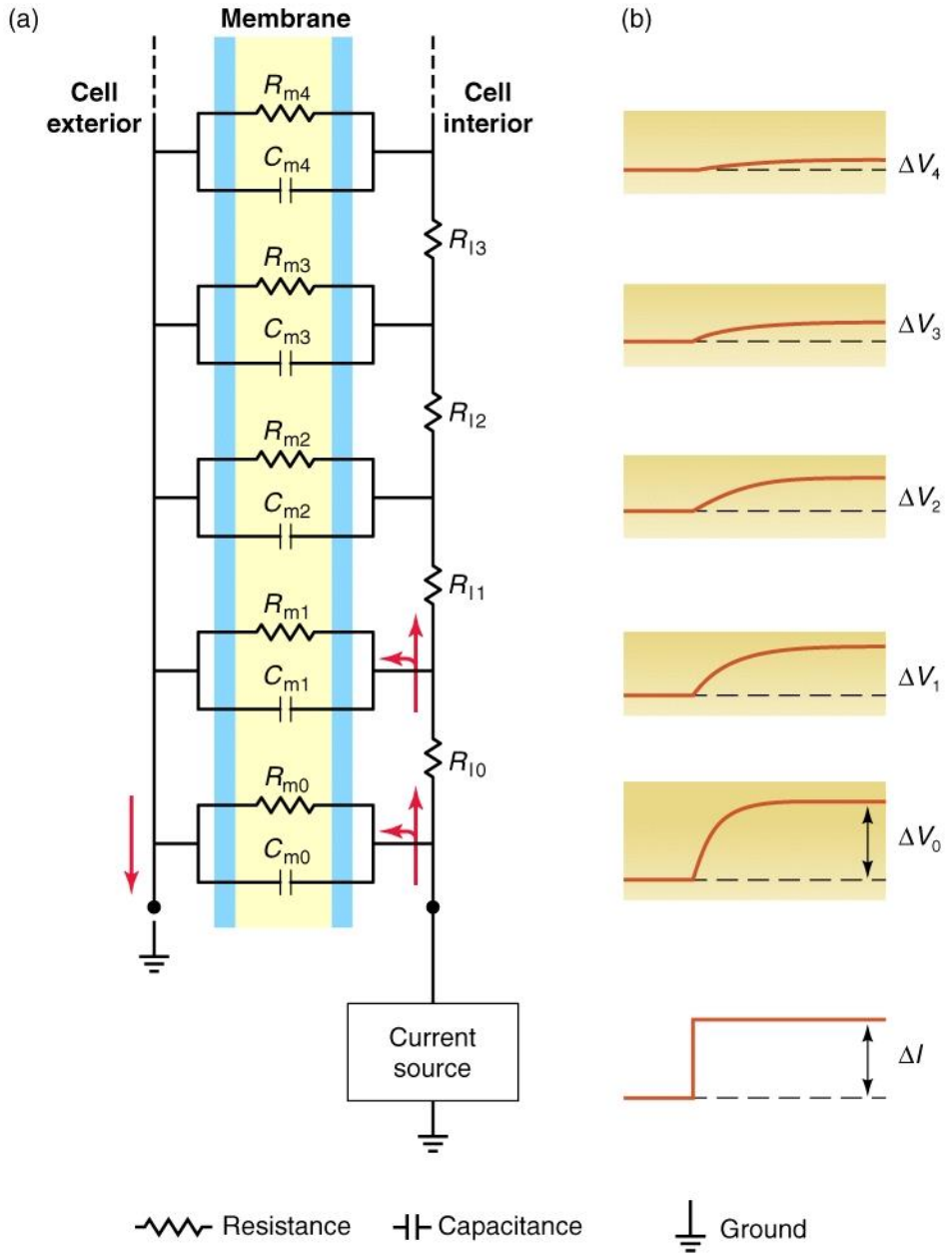
(c)

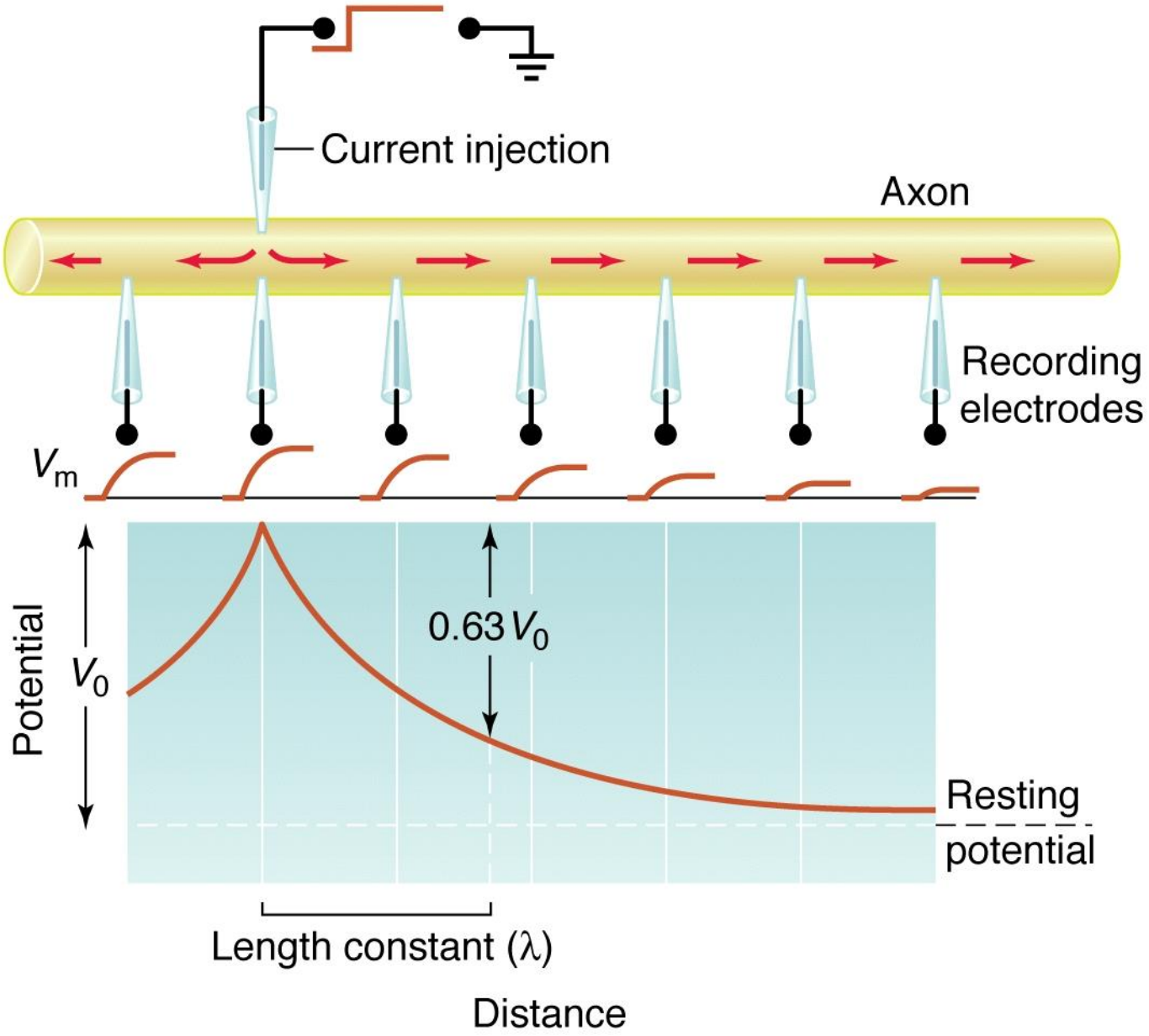

Ensemble current reconstructed by summing many traces like those in part b
0
30
60
Time (ms)

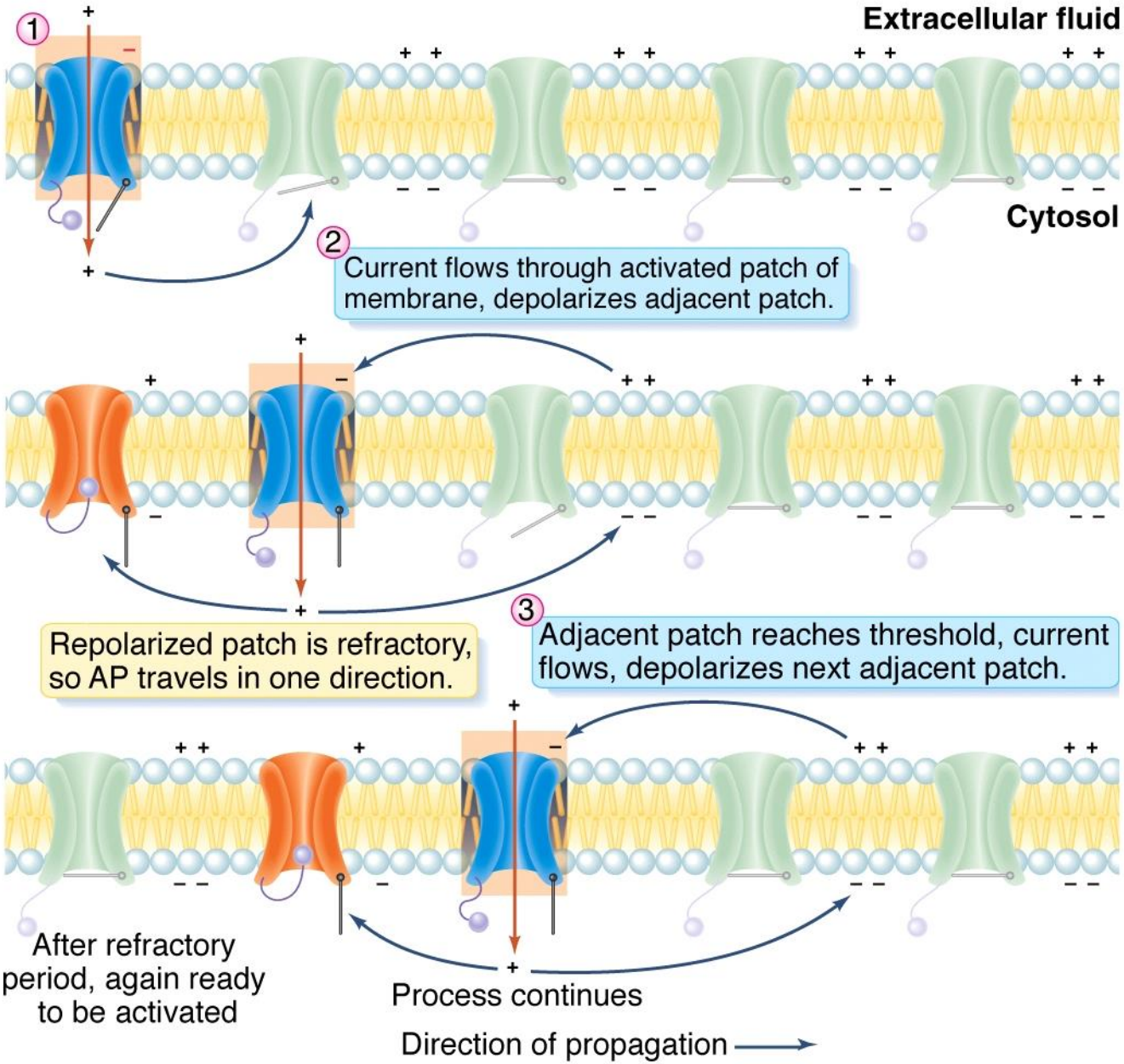

(a)
Lipid
bilayer
–
+
Solution containing micelles
with channels to be tested

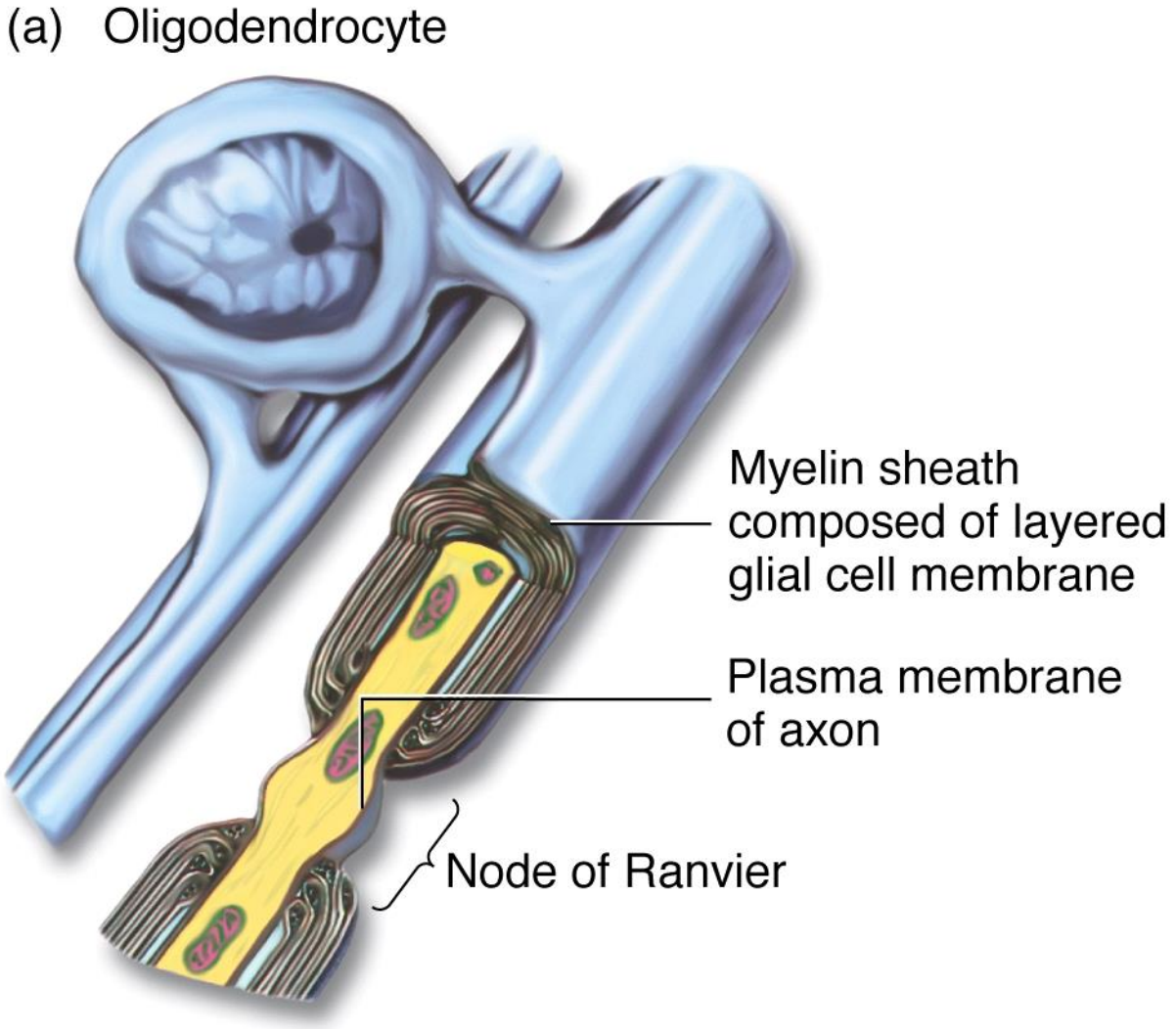

(b)
Current (picoamps)
10
0
–10

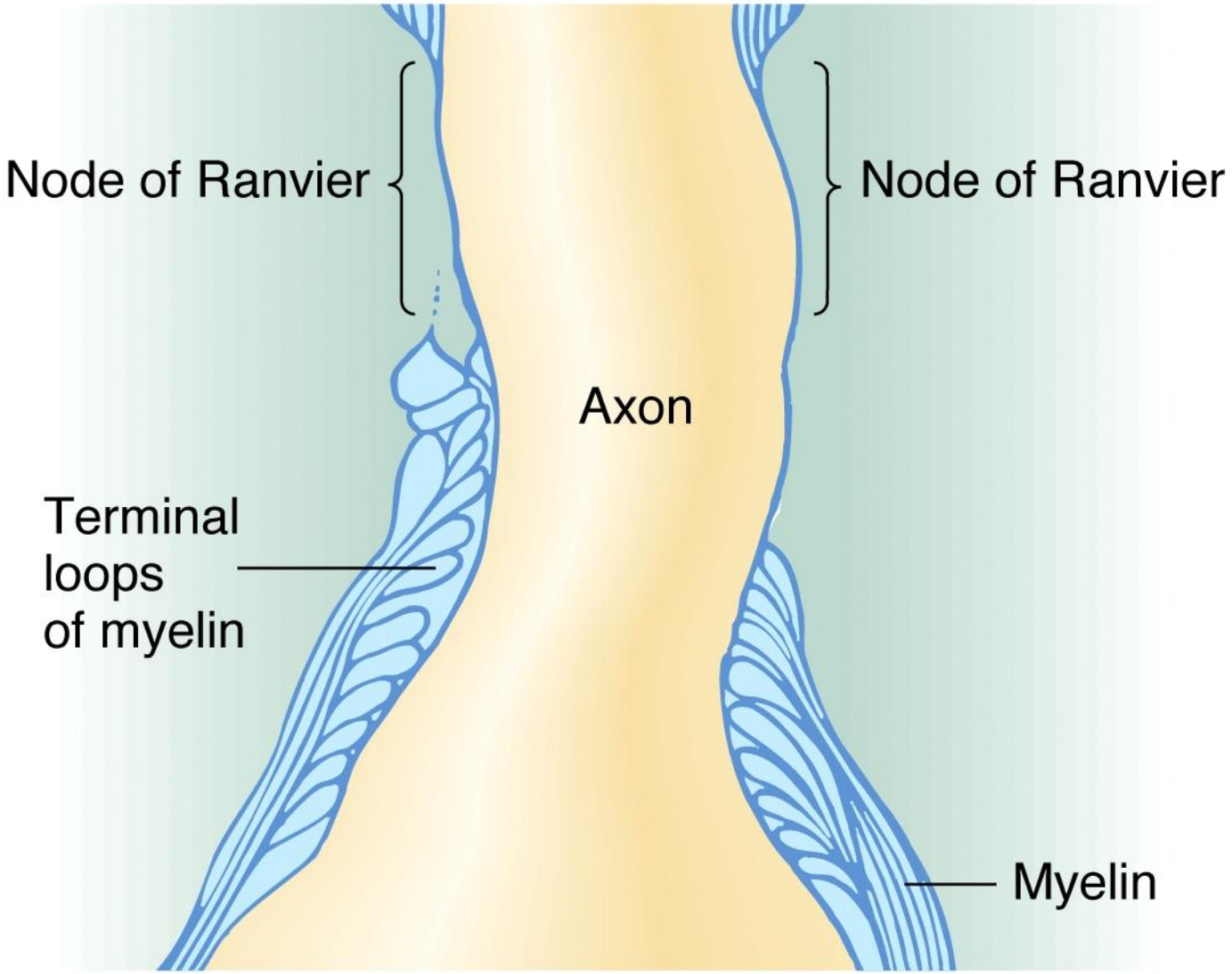

(a)
Extracellular fluid
Domain I
Domain II
Domain III
Domain IV
S1–S6
NH2
Cytosol
Inactivating particle
COOH


(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.
3
Adjacent patch reaches threshold, current flows, depolarizes next adjacent patch.
Repolarized patch is refractory, so AP travels in one direction.
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)

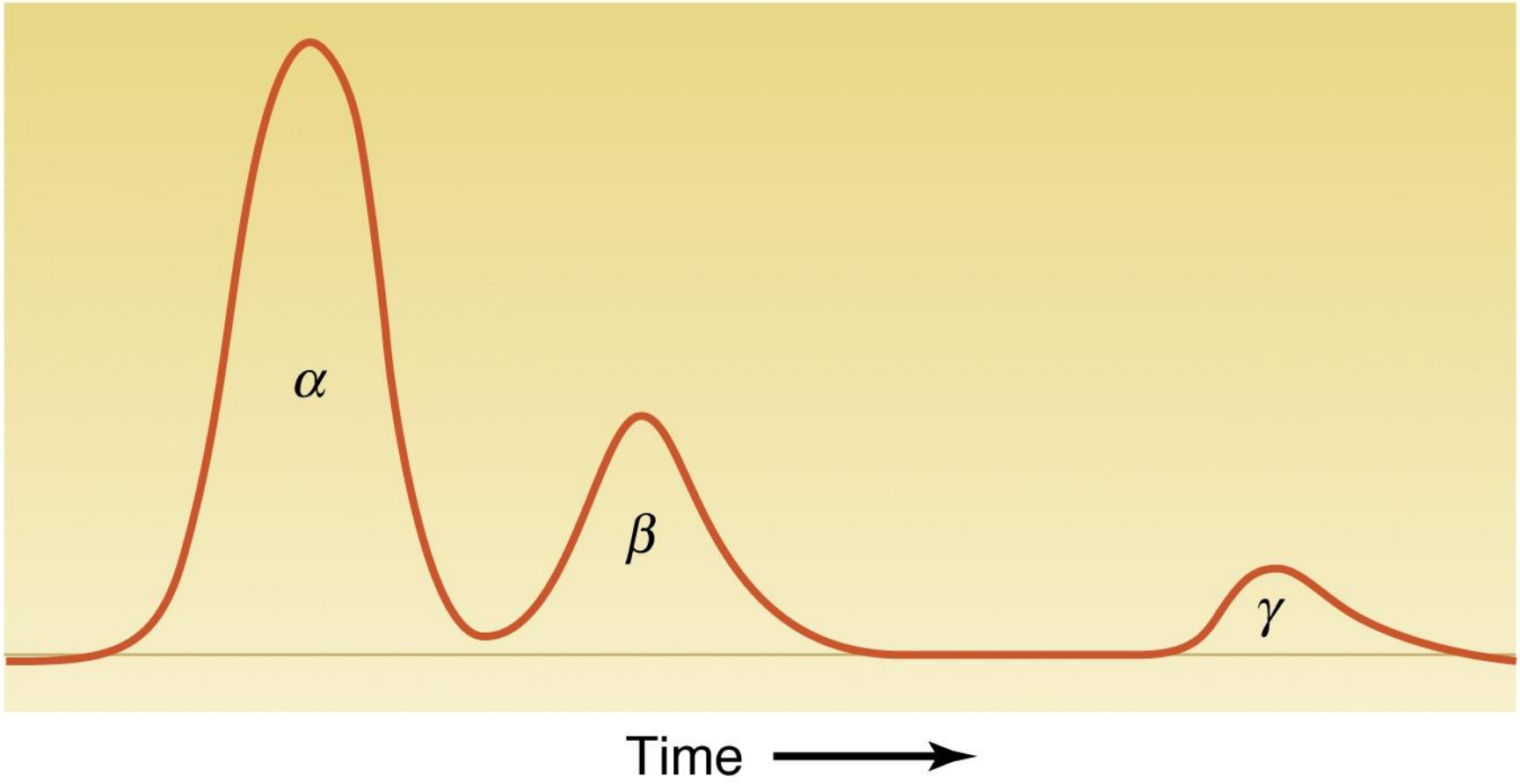
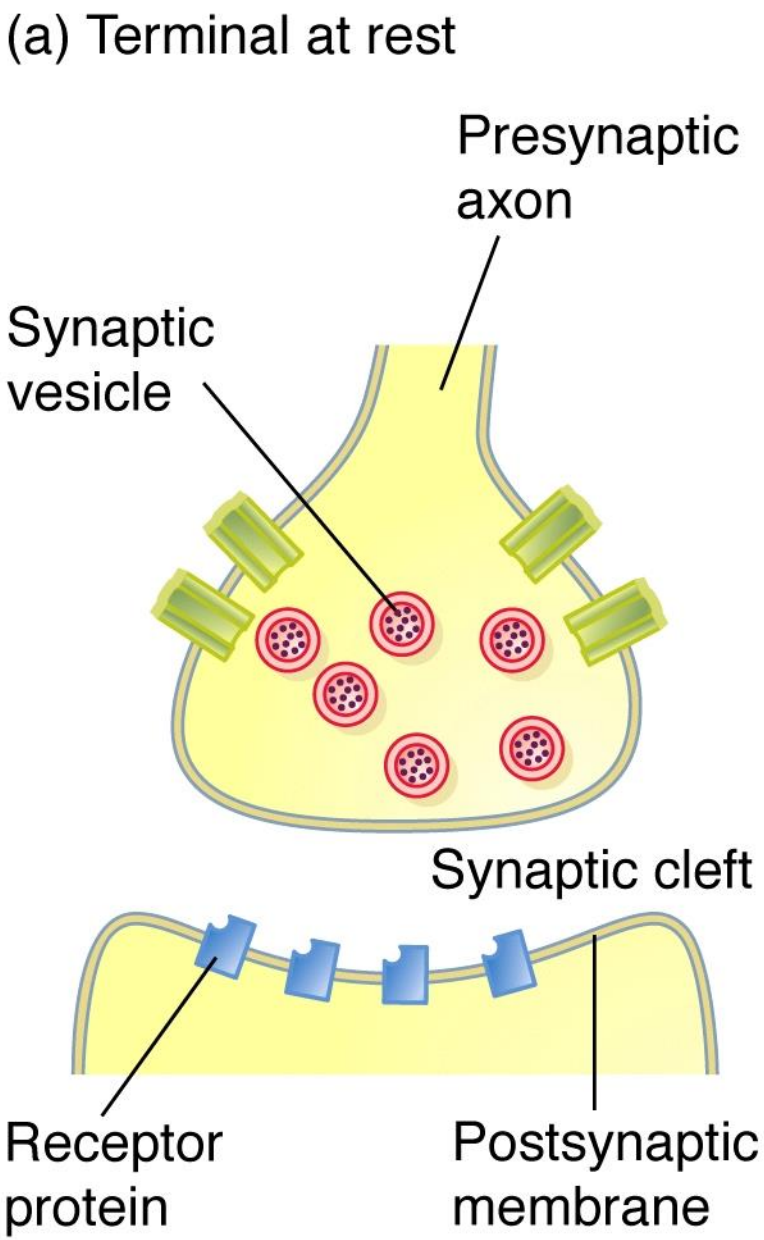


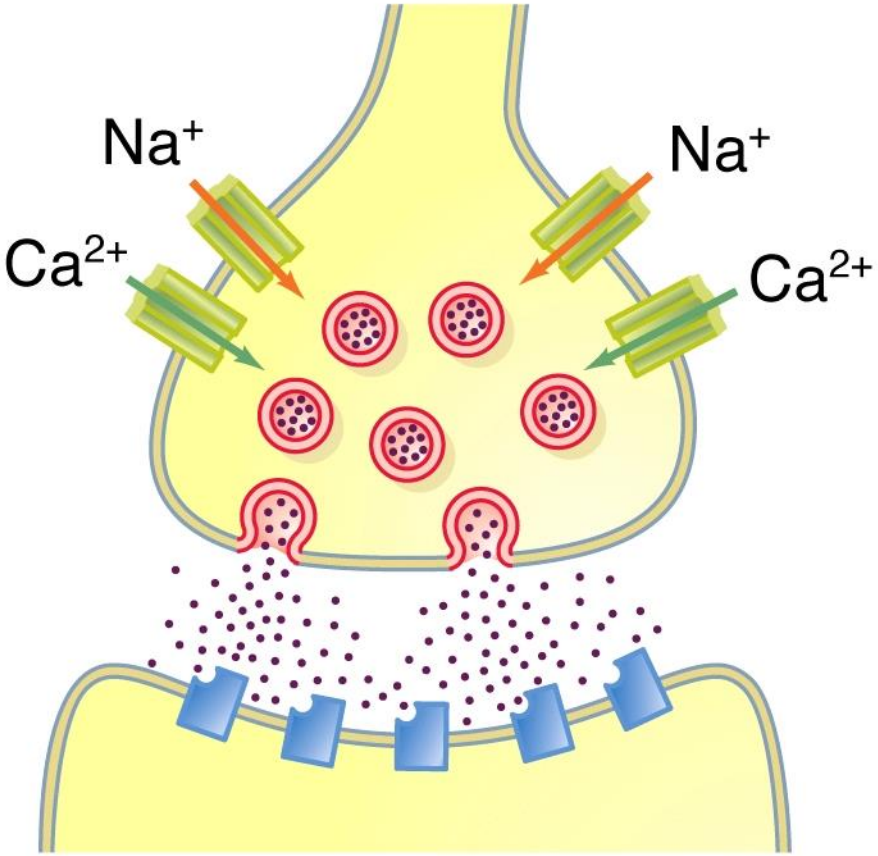
Table 6-1 **The diameter of frog axons and the presence or absence of myelination control the conduction velocity.**

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

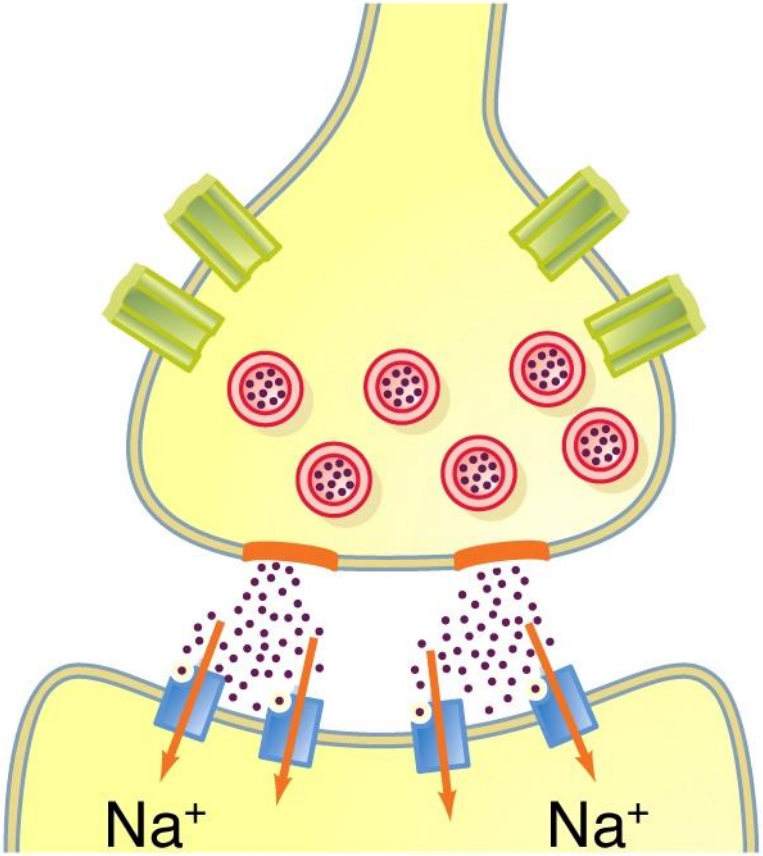
Source: Erlanger and Gasser, 1937.


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

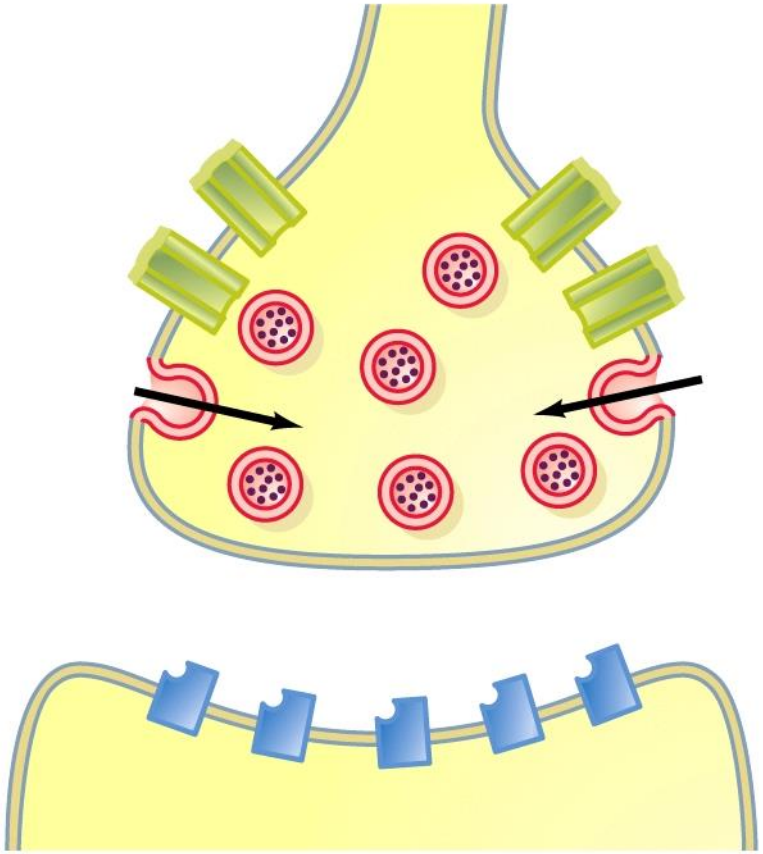
(b) AP arrives; vesicles fuse with terminal membrane, producing exocytosis of transmitter.



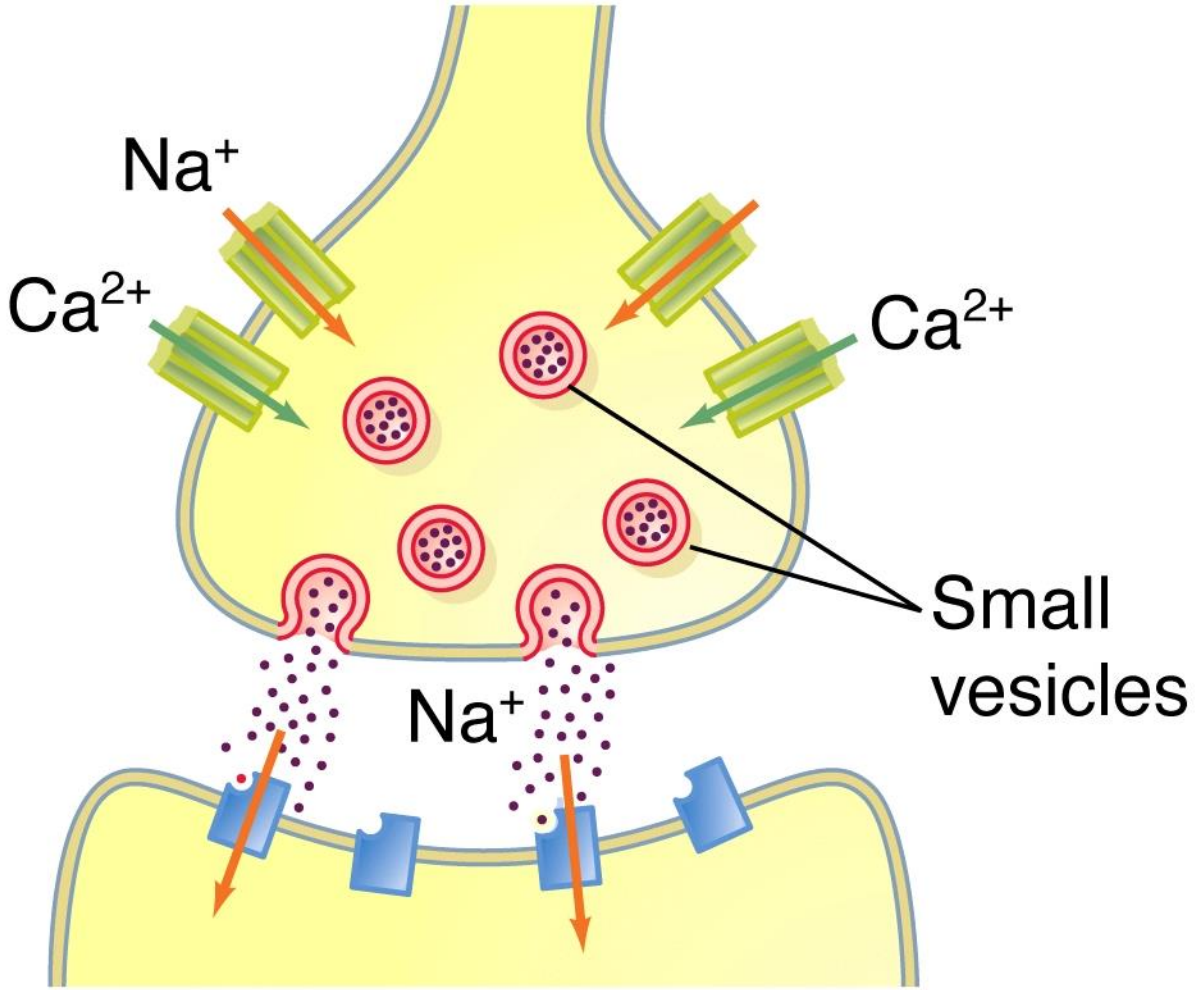
(c) Transmitter binds to postsynaptic receptor proteins; ion channels open.

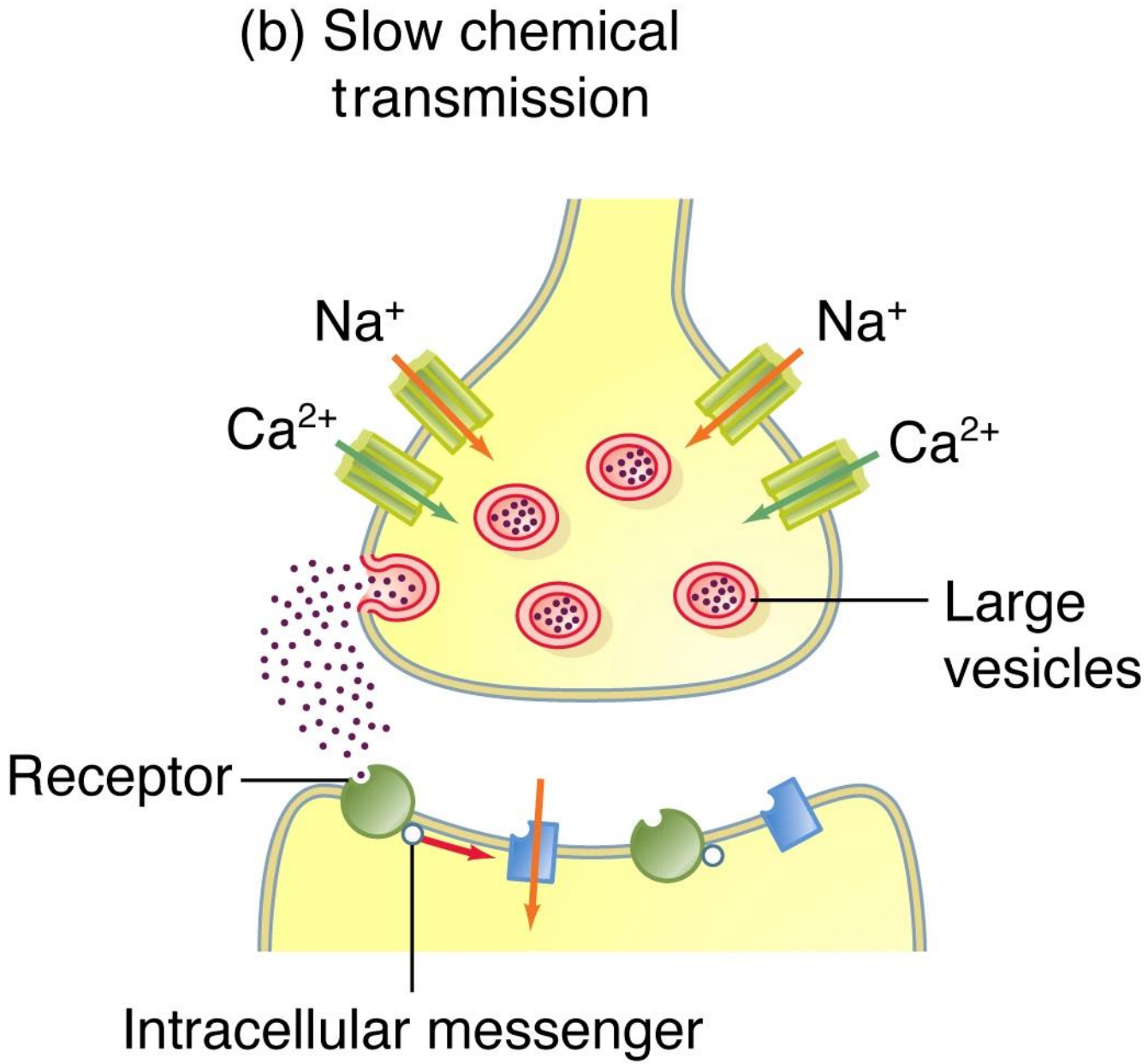


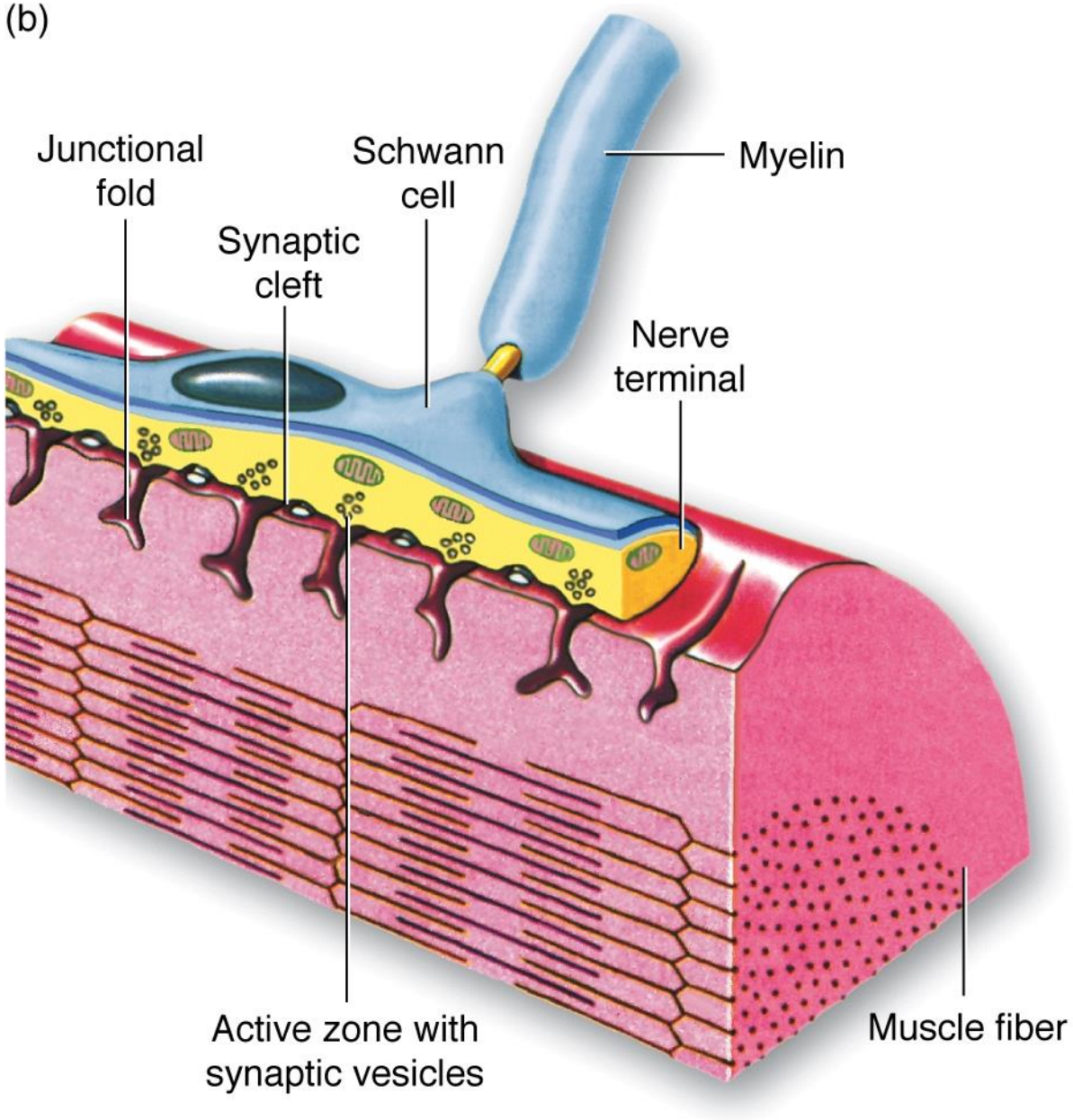
(d) Transmitter is removed from cleft; fused membrane is recycled.



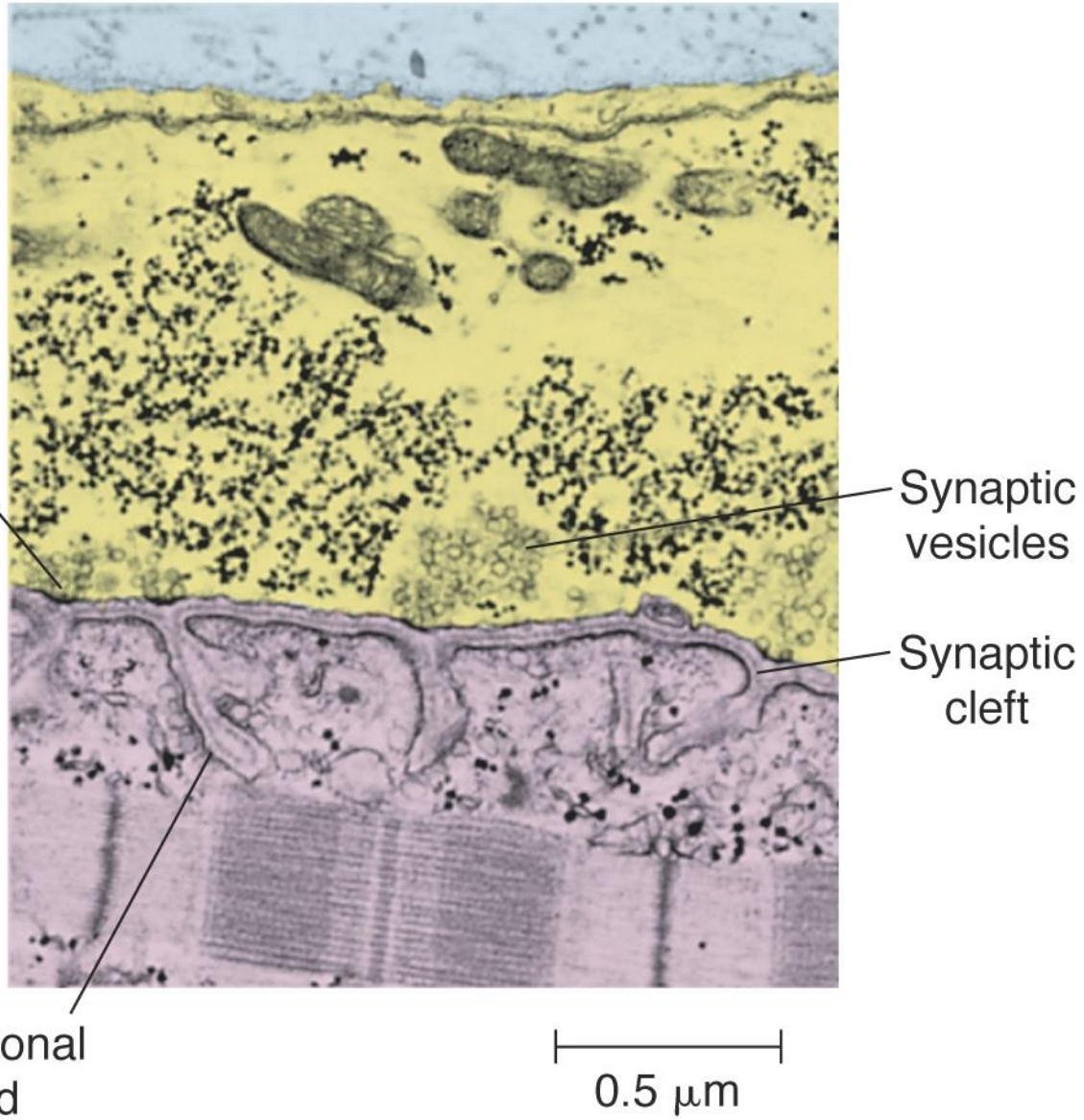
(a) Fast chemical transmission

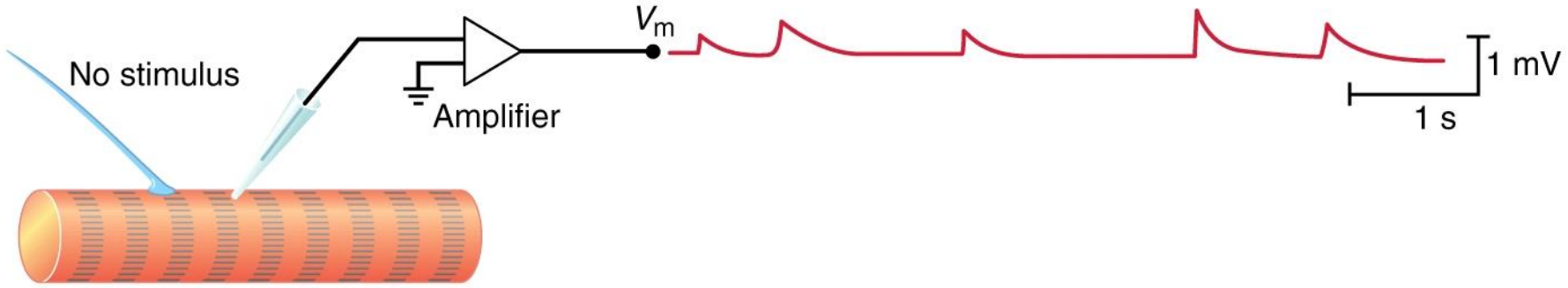


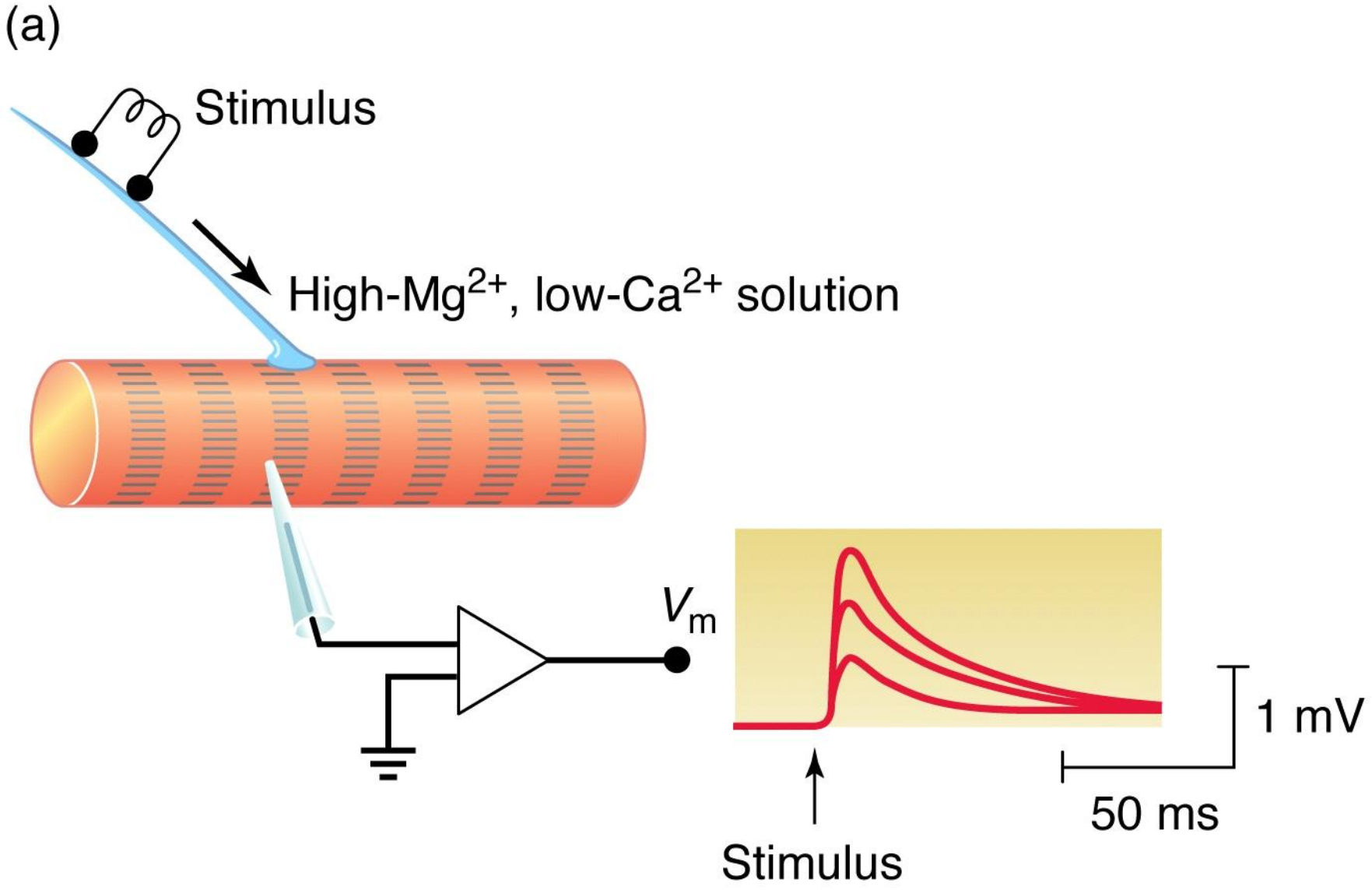

(b) Slow chemical transmission
Na+
Na+
Ca2+
Ca2+
Large vesicles
Receptor
Intracellular messenger

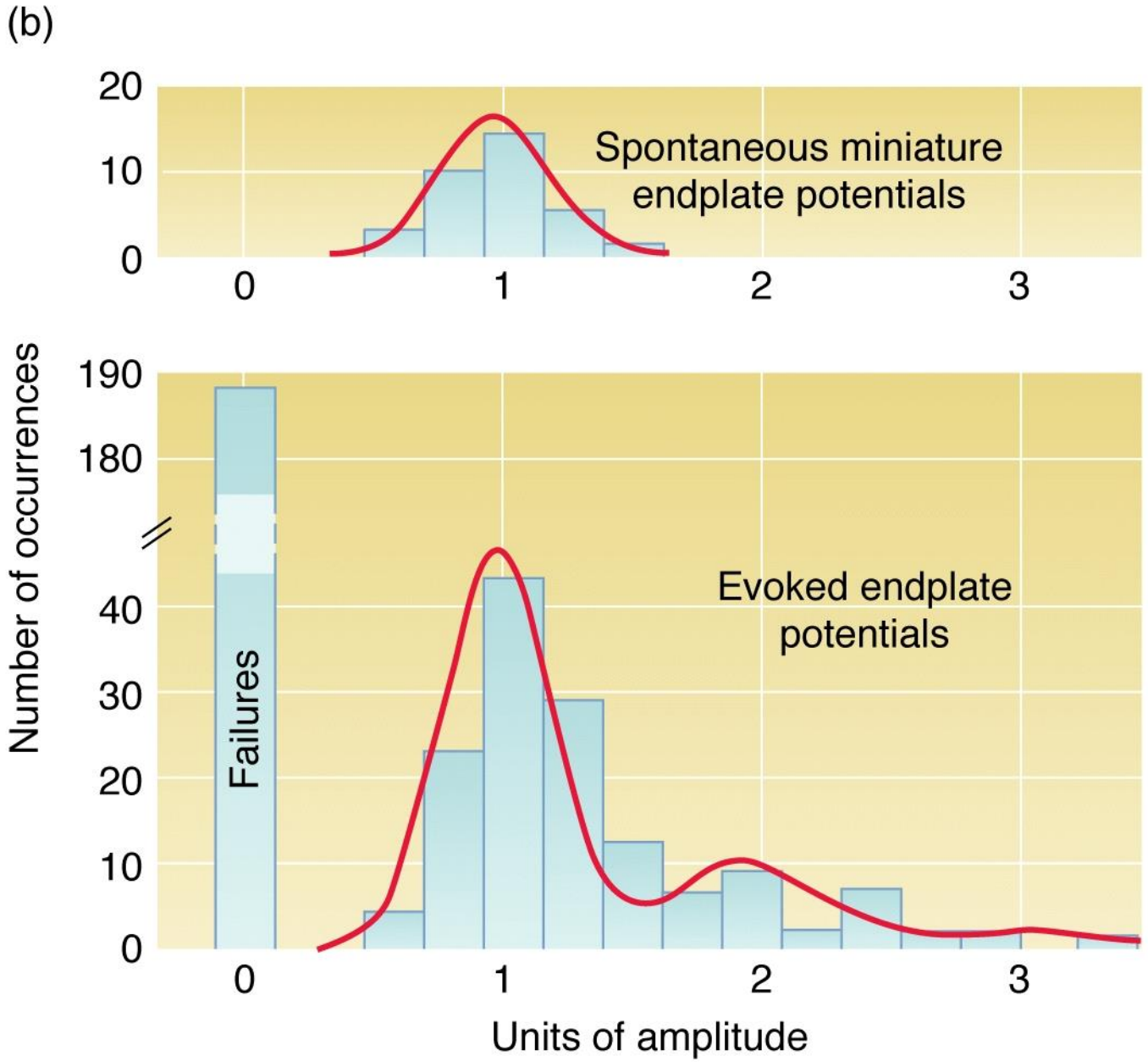

(b)
Junctional fold
Schwann cell
Myelin
Synaptic cleft
Nerve terminal
Active zone with synaptic vesicles
Muscle fiber

(c)


Thickened membrane
Synaptic vesicles
Synaptic cleft
Junctional fold
0.5 μm


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

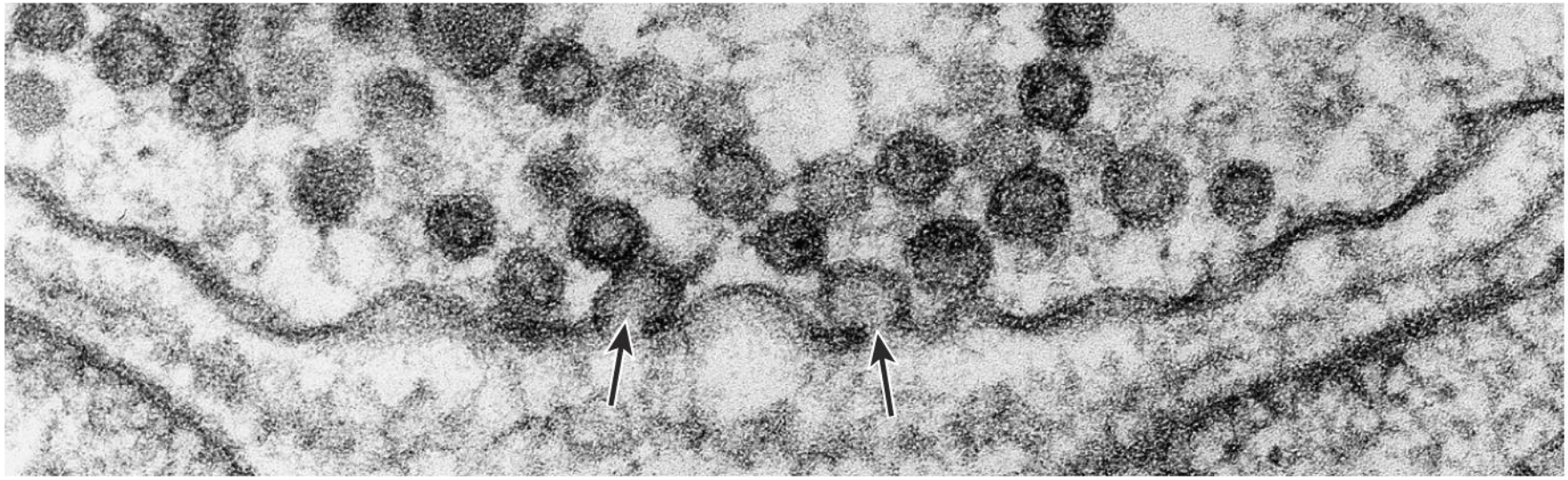
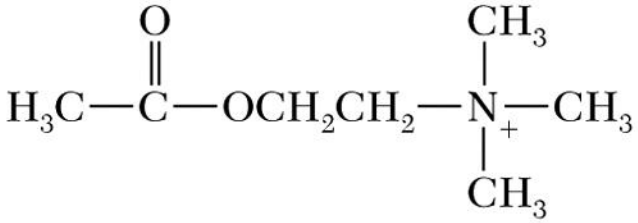
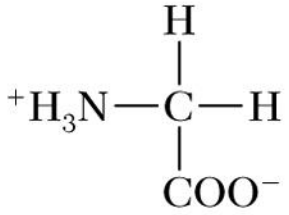
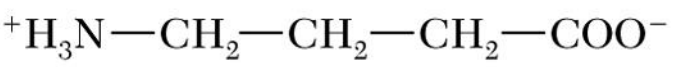
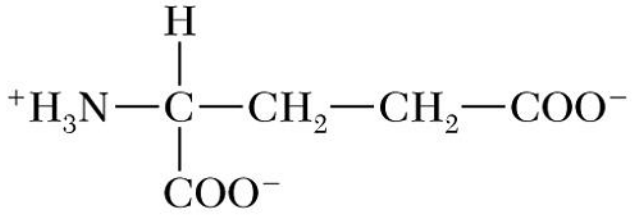
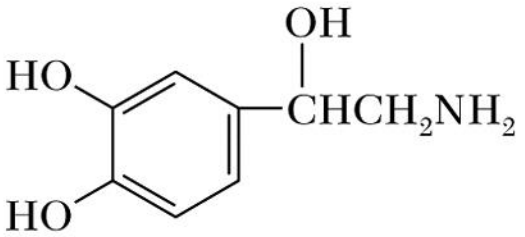
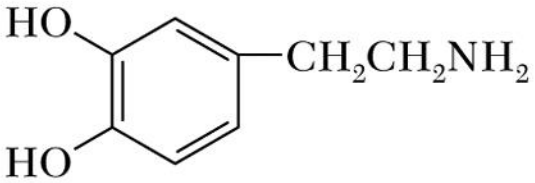
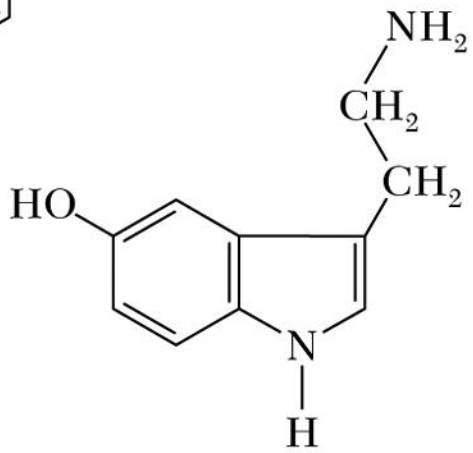


Table 6-2 Typical small neurotransmitters, their structures, and functions

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	

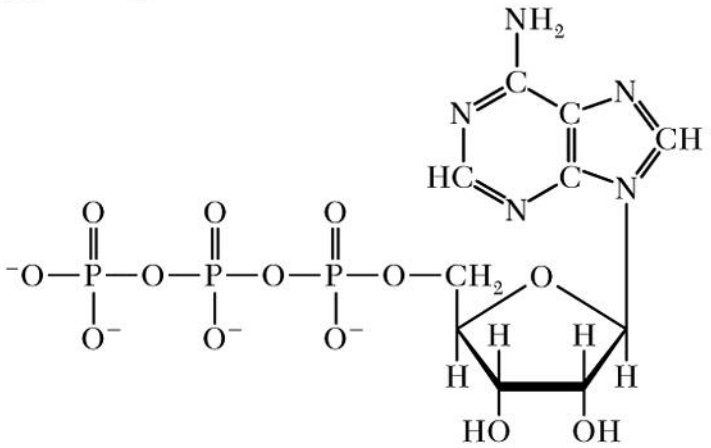
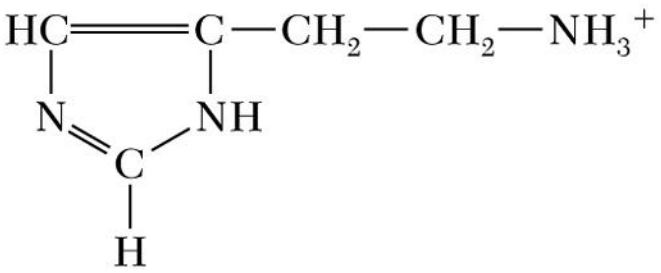
*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

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.

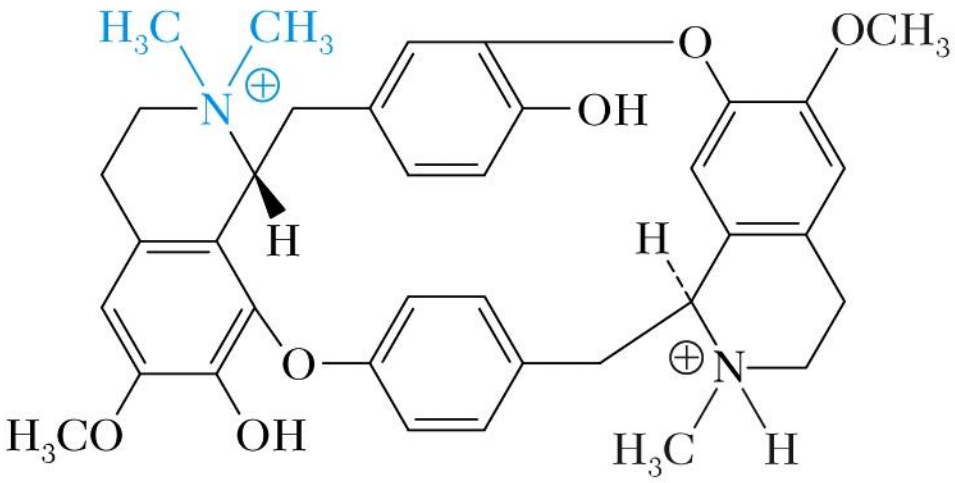
Table 6-2 Typical small neurotransmitters, their structures, and functions

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

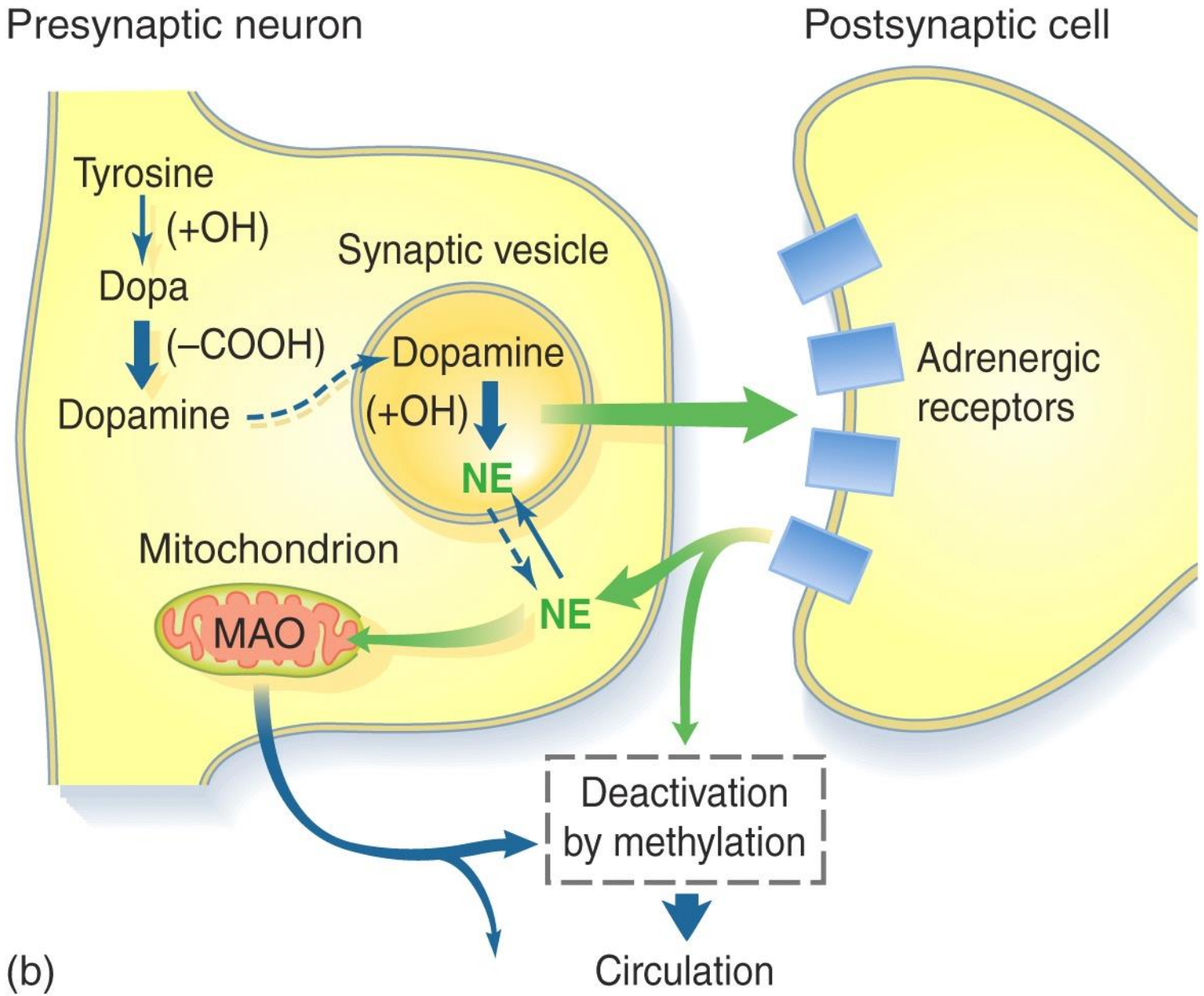
*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

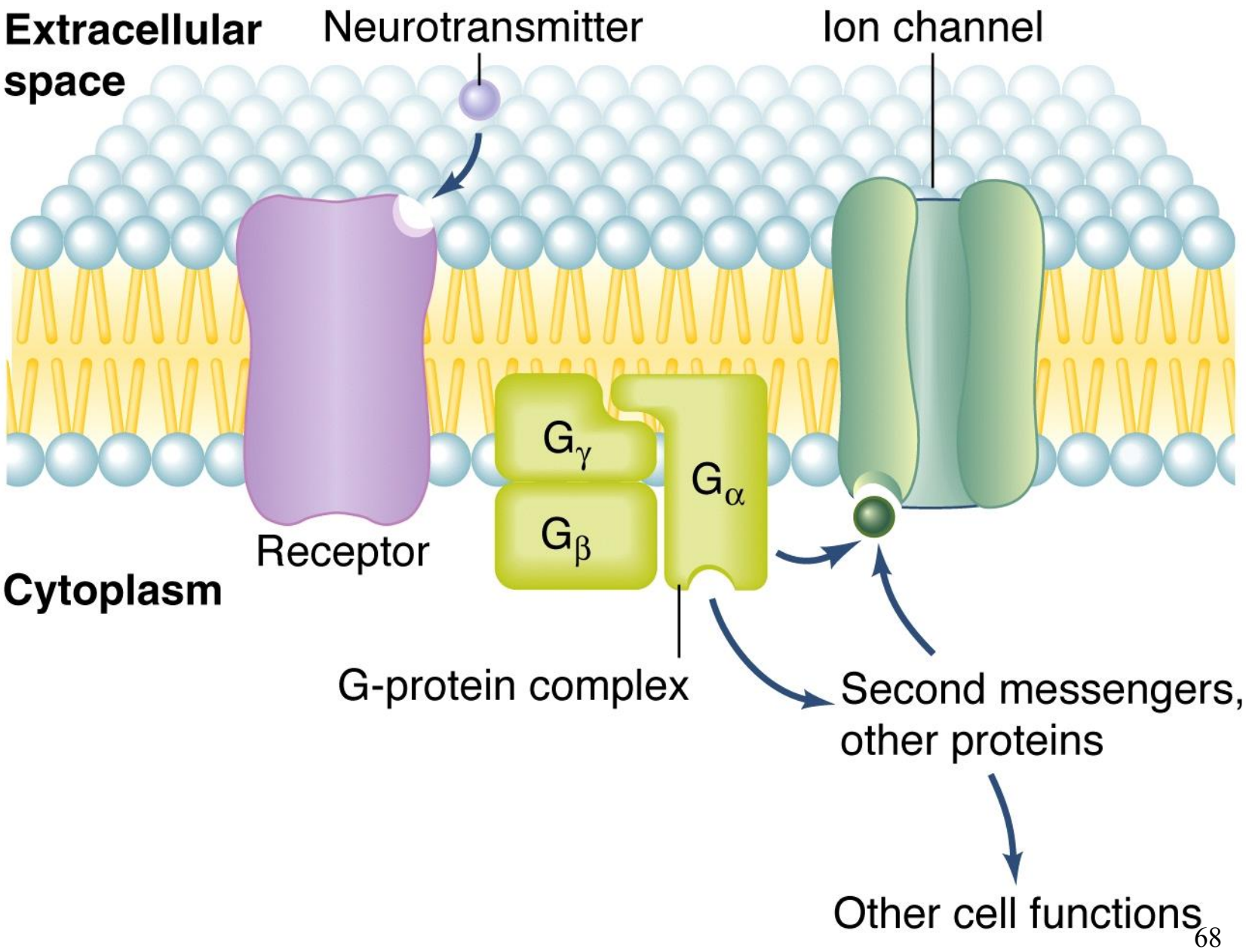
Acetylcholine (ACh)

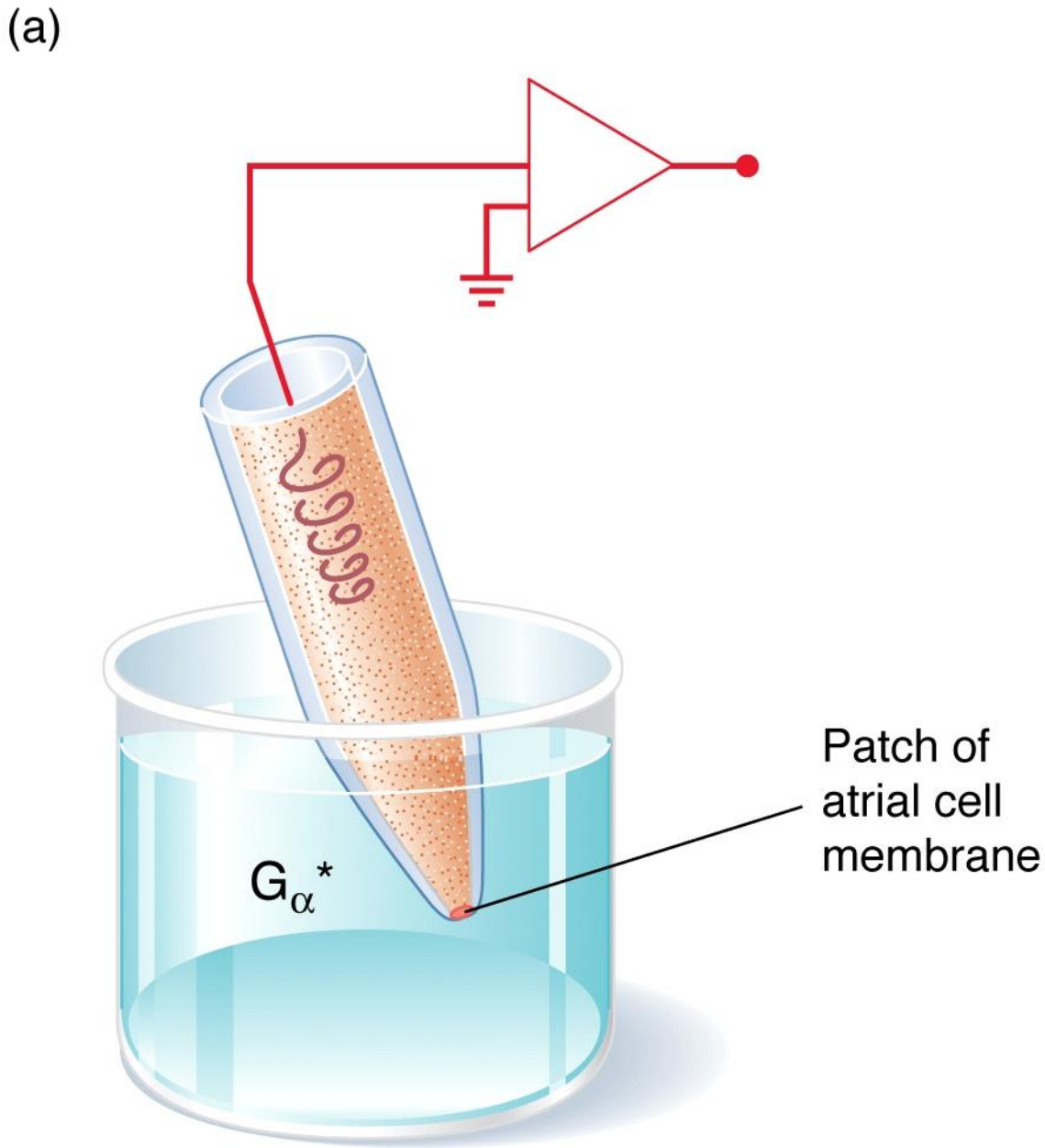
Carbachol, an ACh agonist



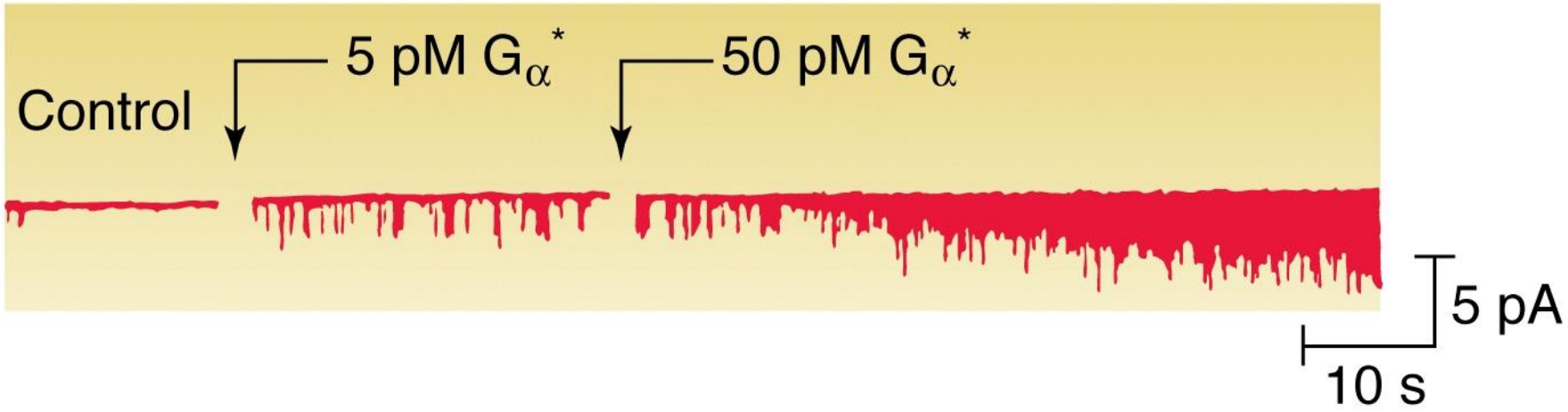
D-Tubocurarine, an ACh antagonist

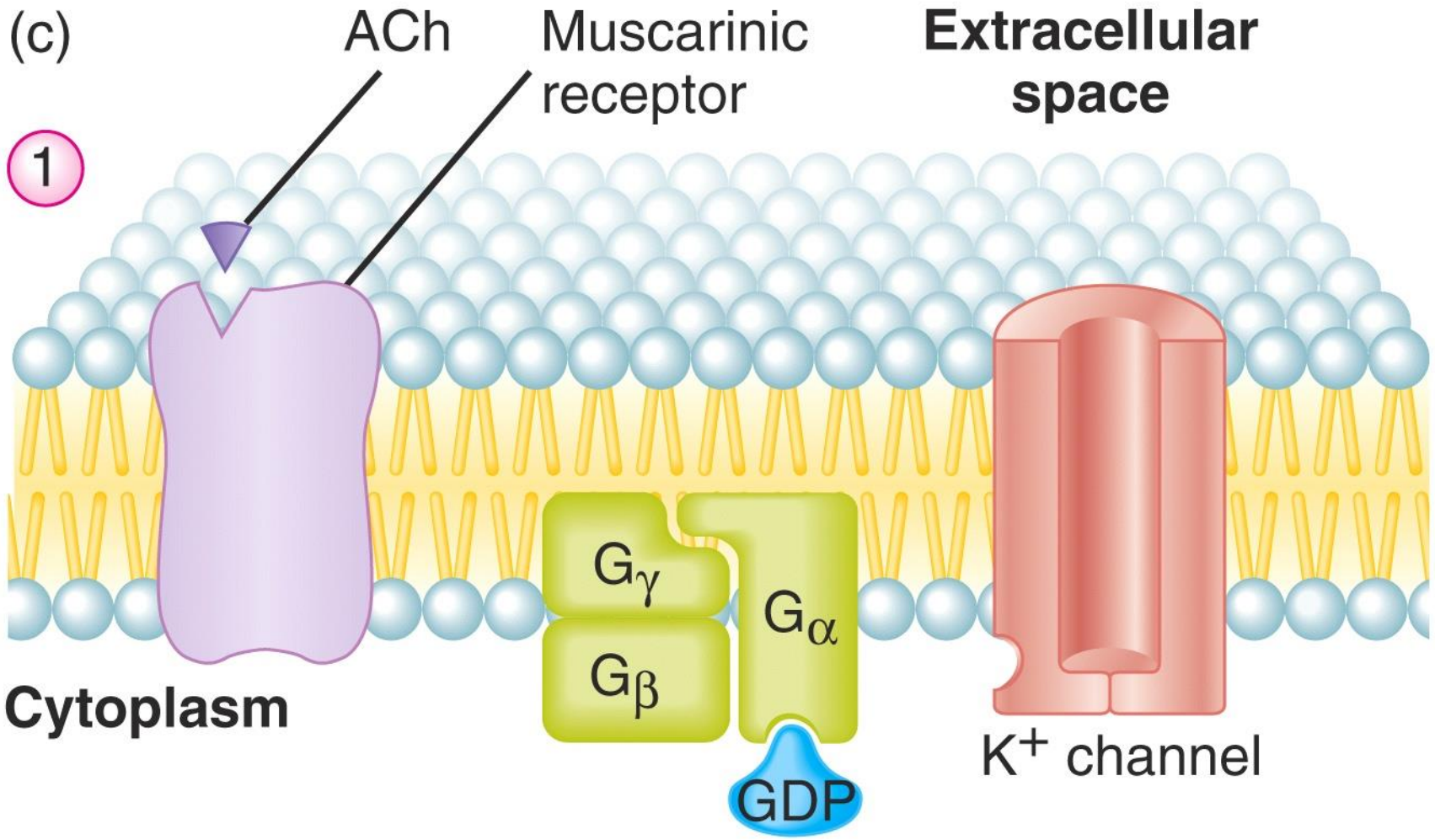

Presynaptic neuron
Postsynaptic cell
Tyrosine
(+OH)
Dopa
(–COOH)
Dopamine
Synaptic vesicle
Dopamine
(+OH)
NE
Mitochondrion
MAO
NE
Adrenergic receptors
Deactivation by methylation
Circulation
(b)

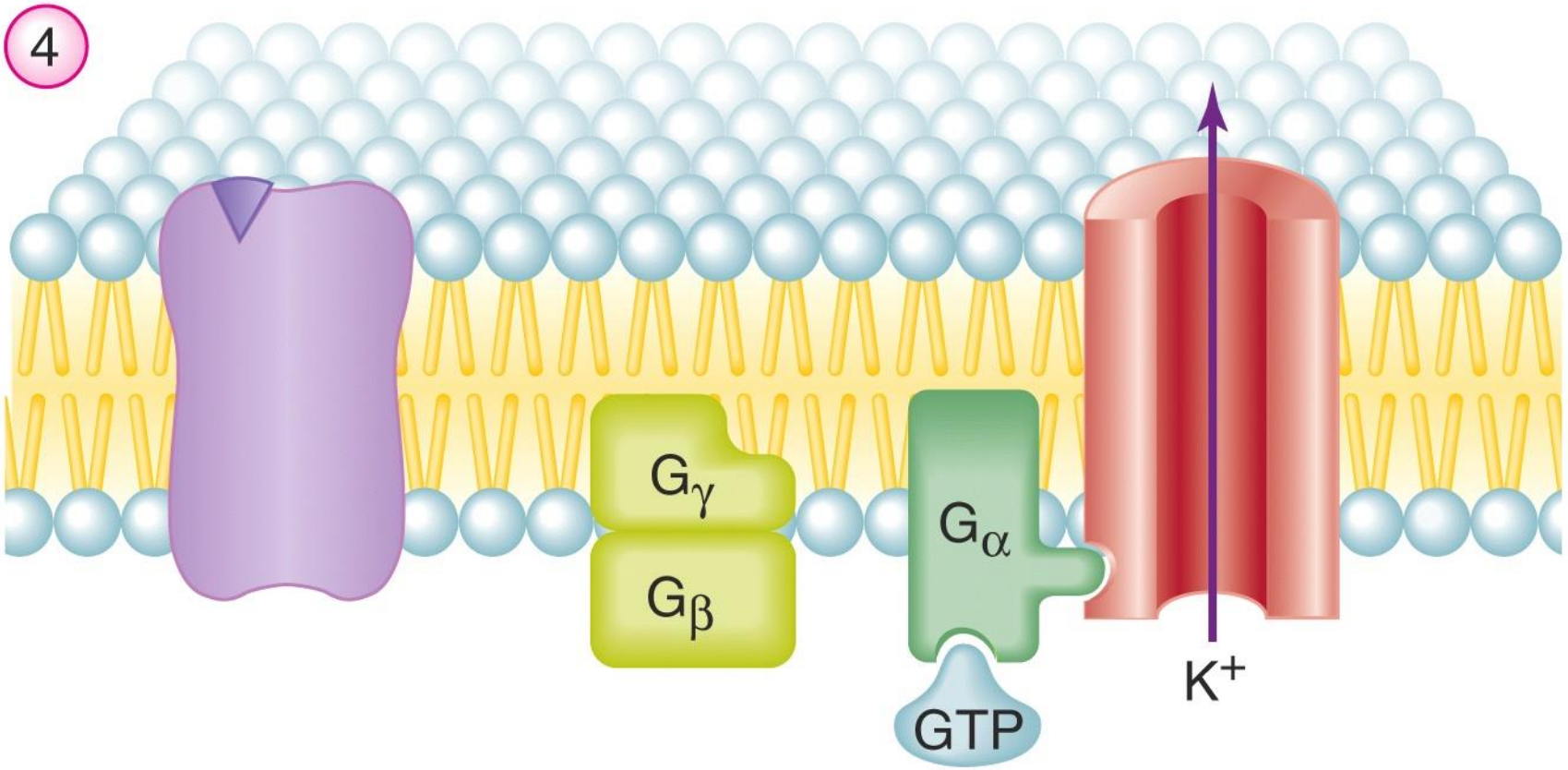

Extracellular space
Neurotransmitter
Ion channel
Receptor
G_γ
G_β
G_α
Cytoplasm
G-protein complex
Second messengers, other proteins
Other cell functions

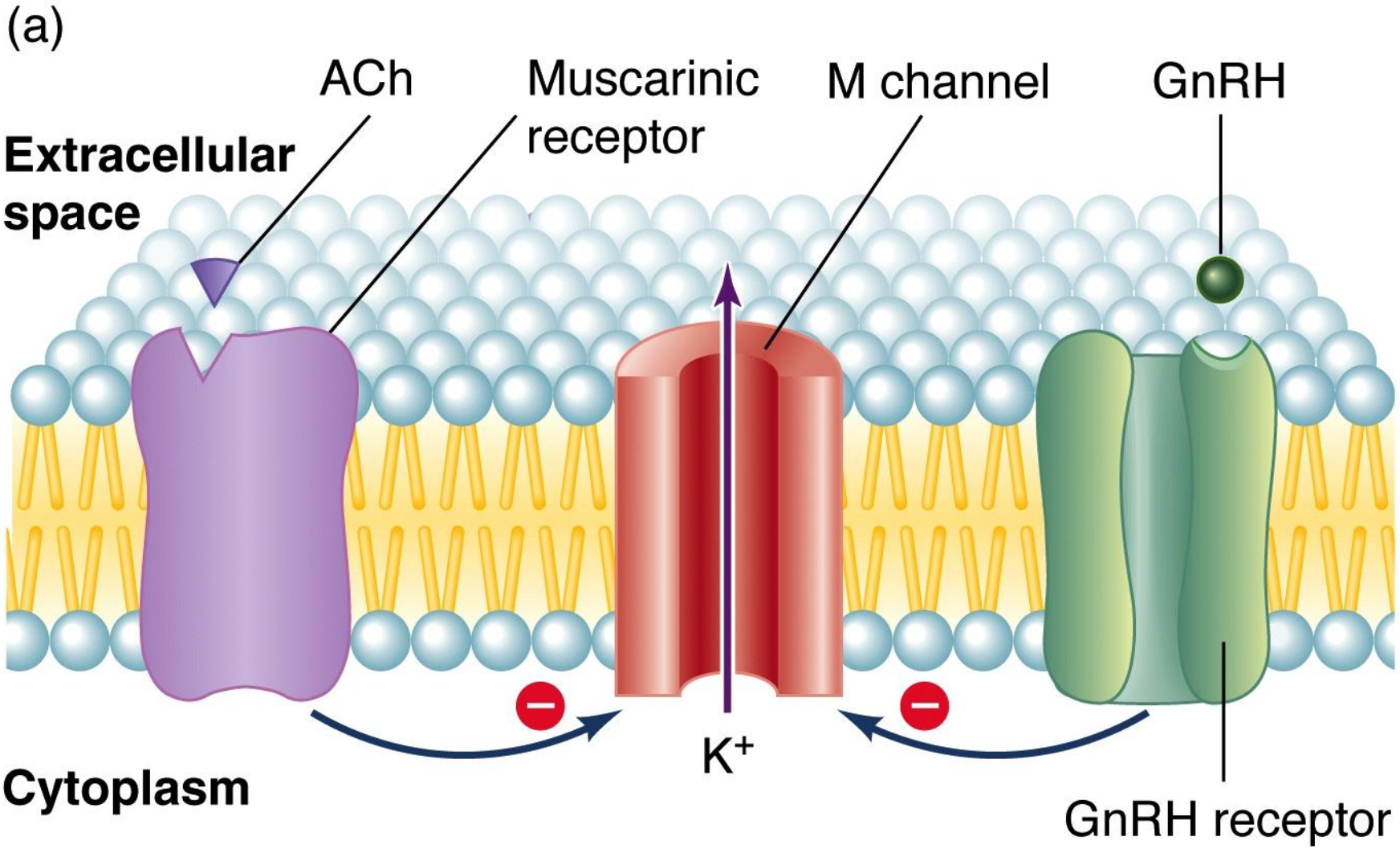

(a)
G_α*
Patch of
atrial cell
membrane

(b)

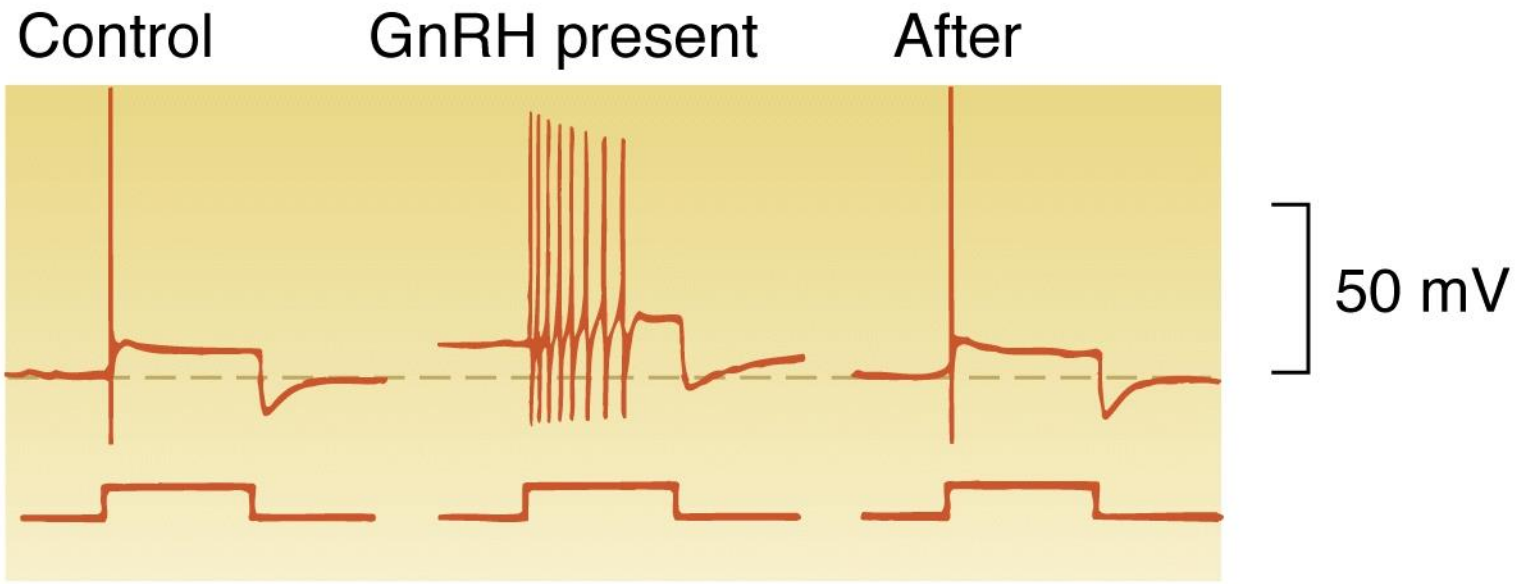


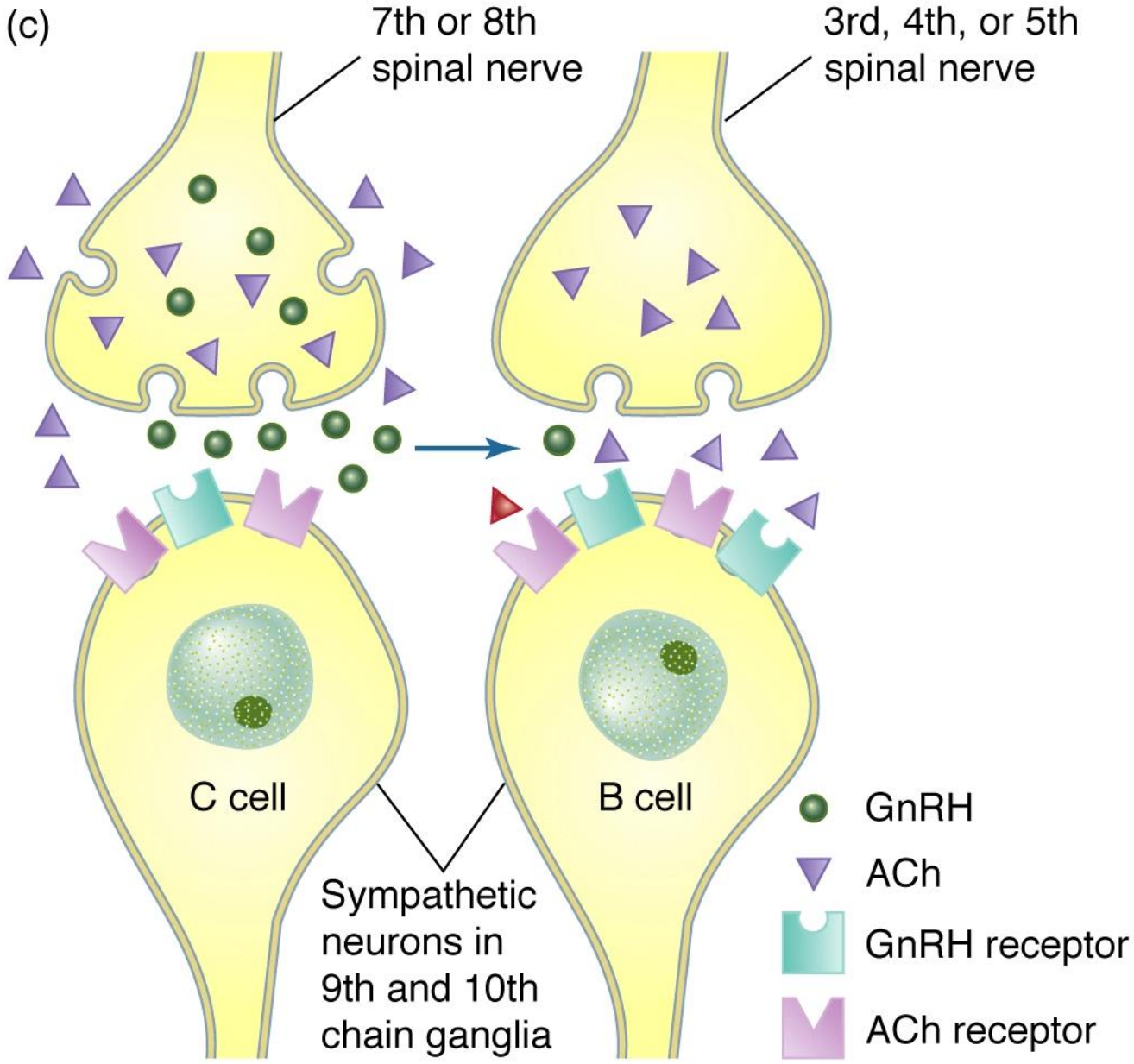

(c)
ACh
Muscarinic receptor
Extracellular space
1
Cytoplasm
Gγ
Gβ
Gα
GDP
K+ channel

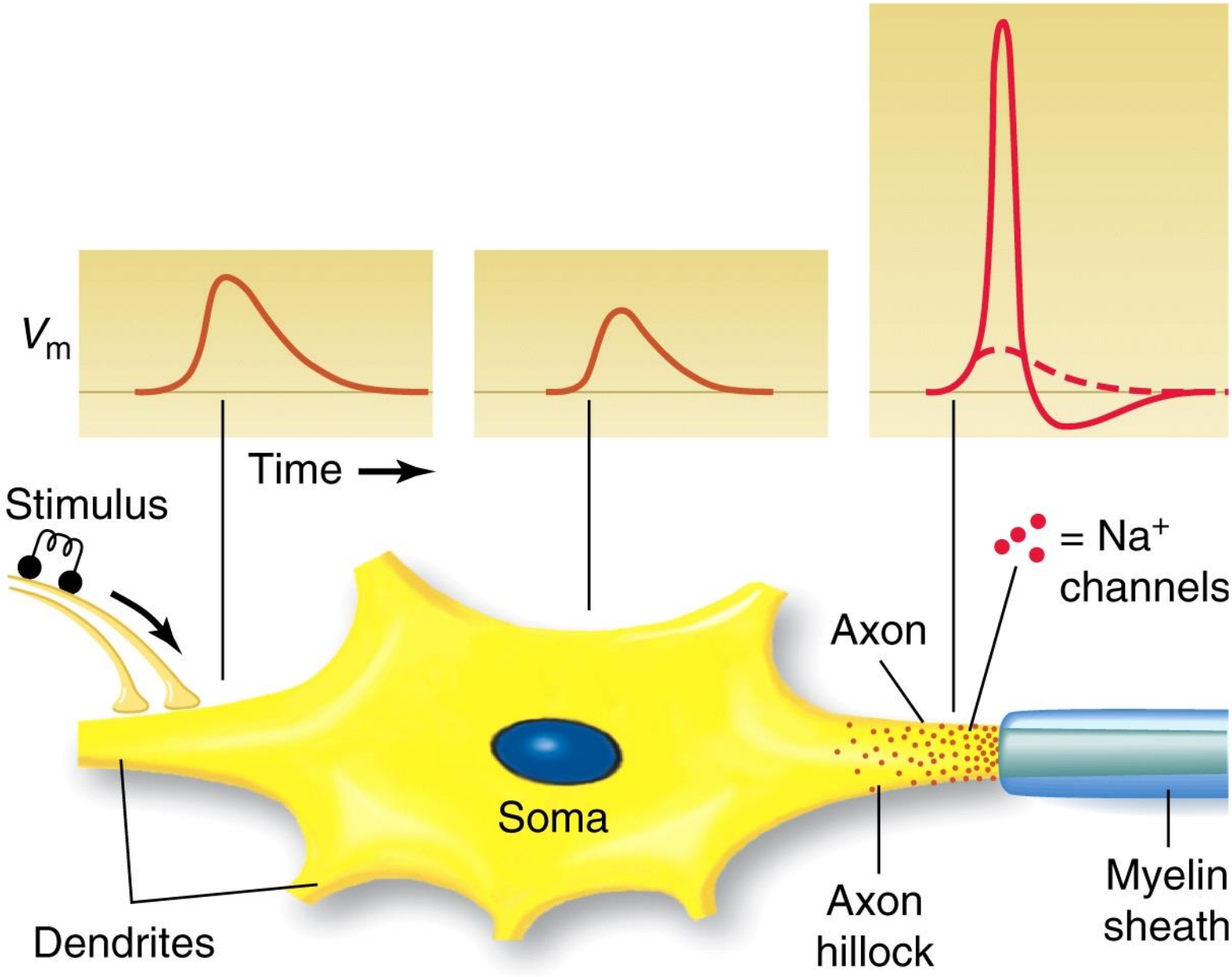

4
Gγ
Gβ
Gα
GTP
K+

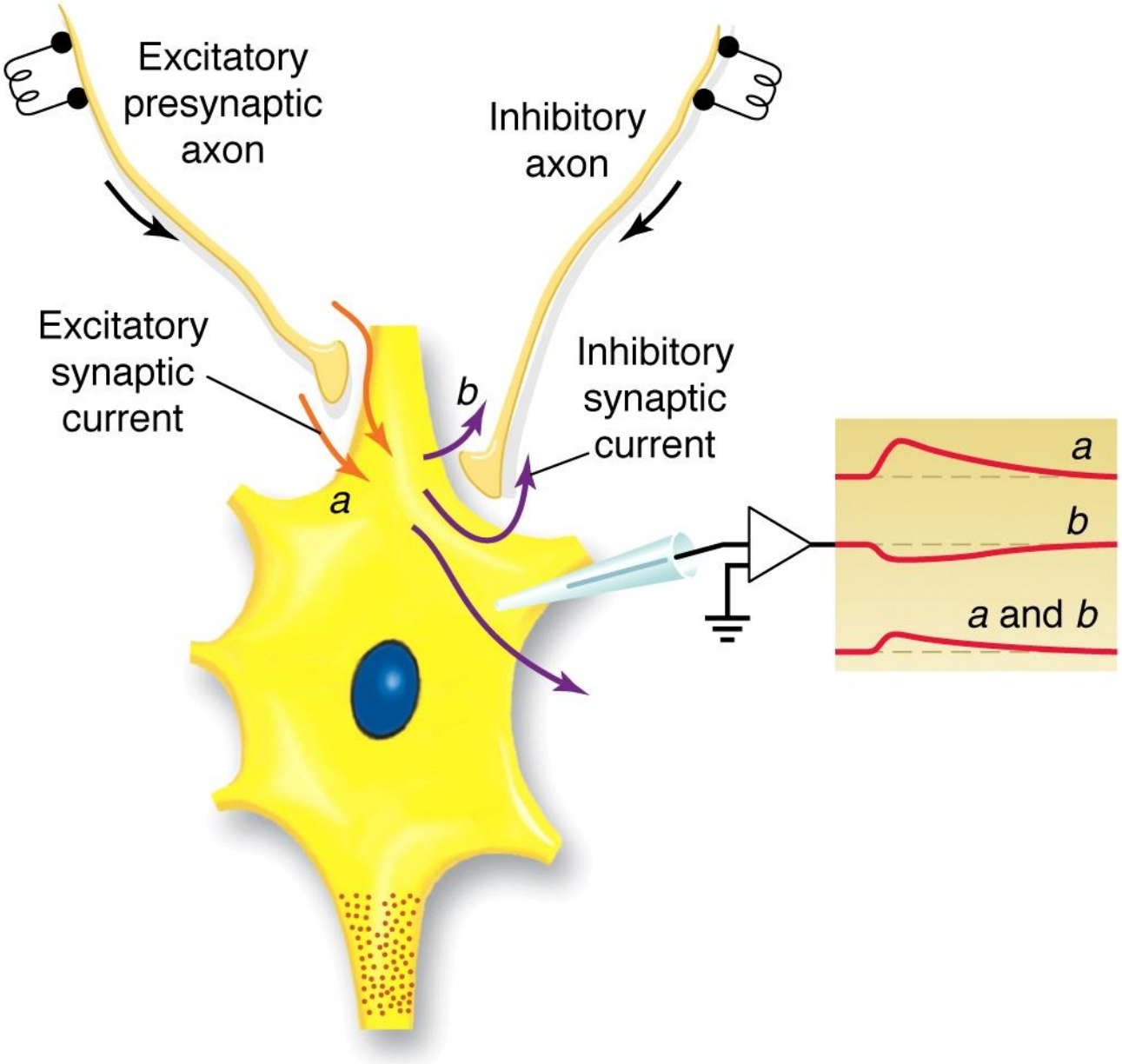

(a)
ACh
Muscarinic receptor
M channel
GnRH
Extracellular space
Cytoplasm
K+
GnRH receptor

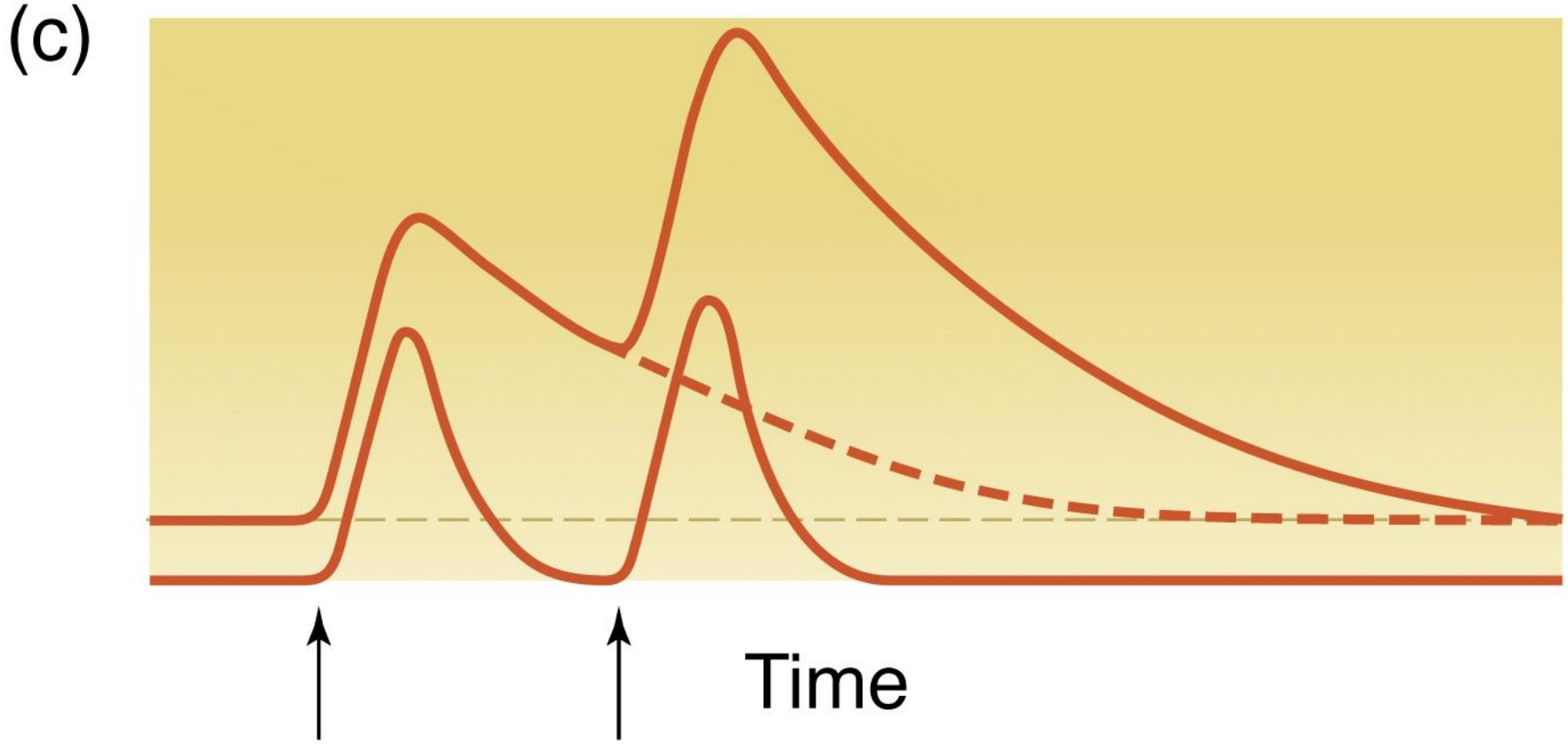
(b)

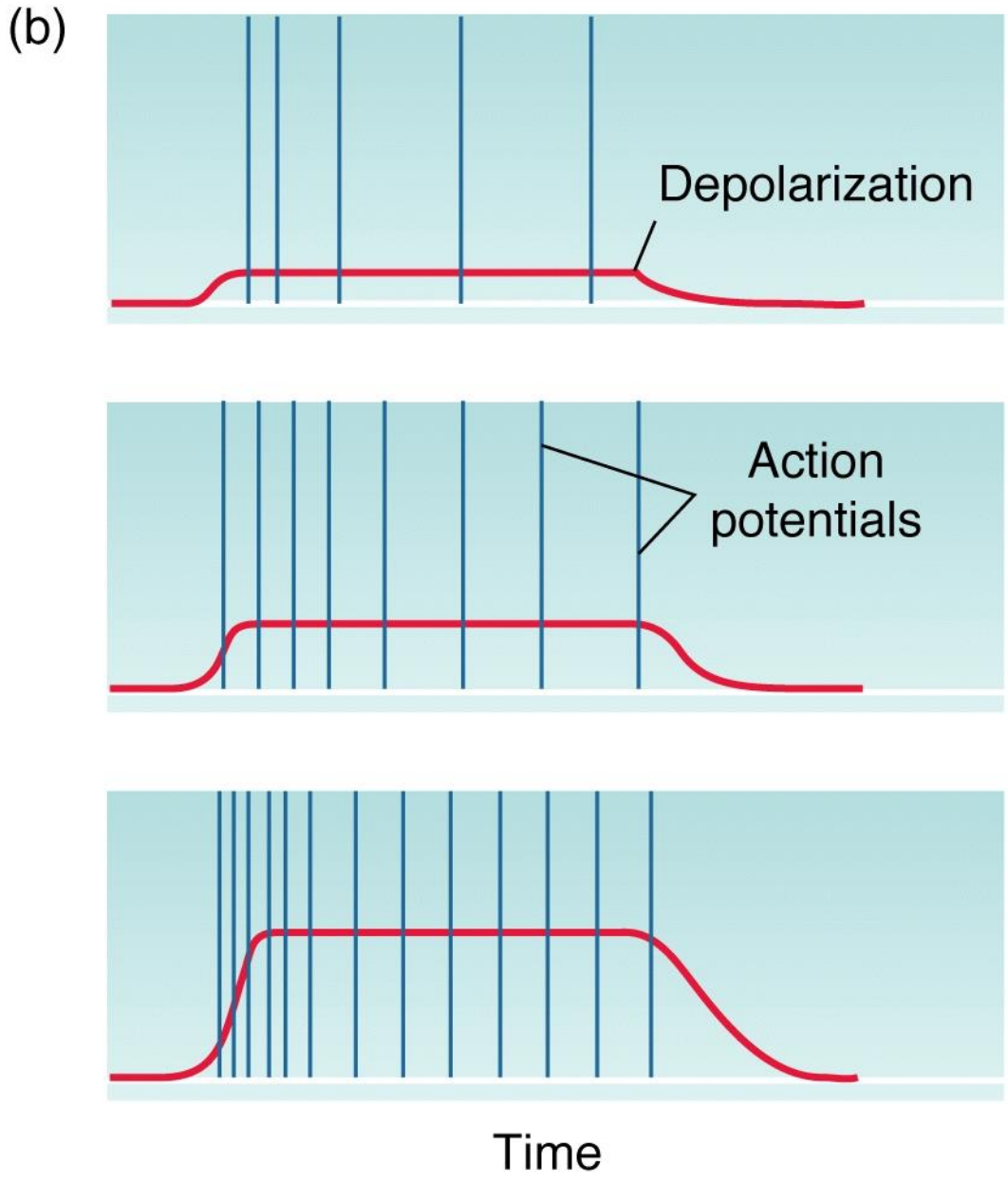


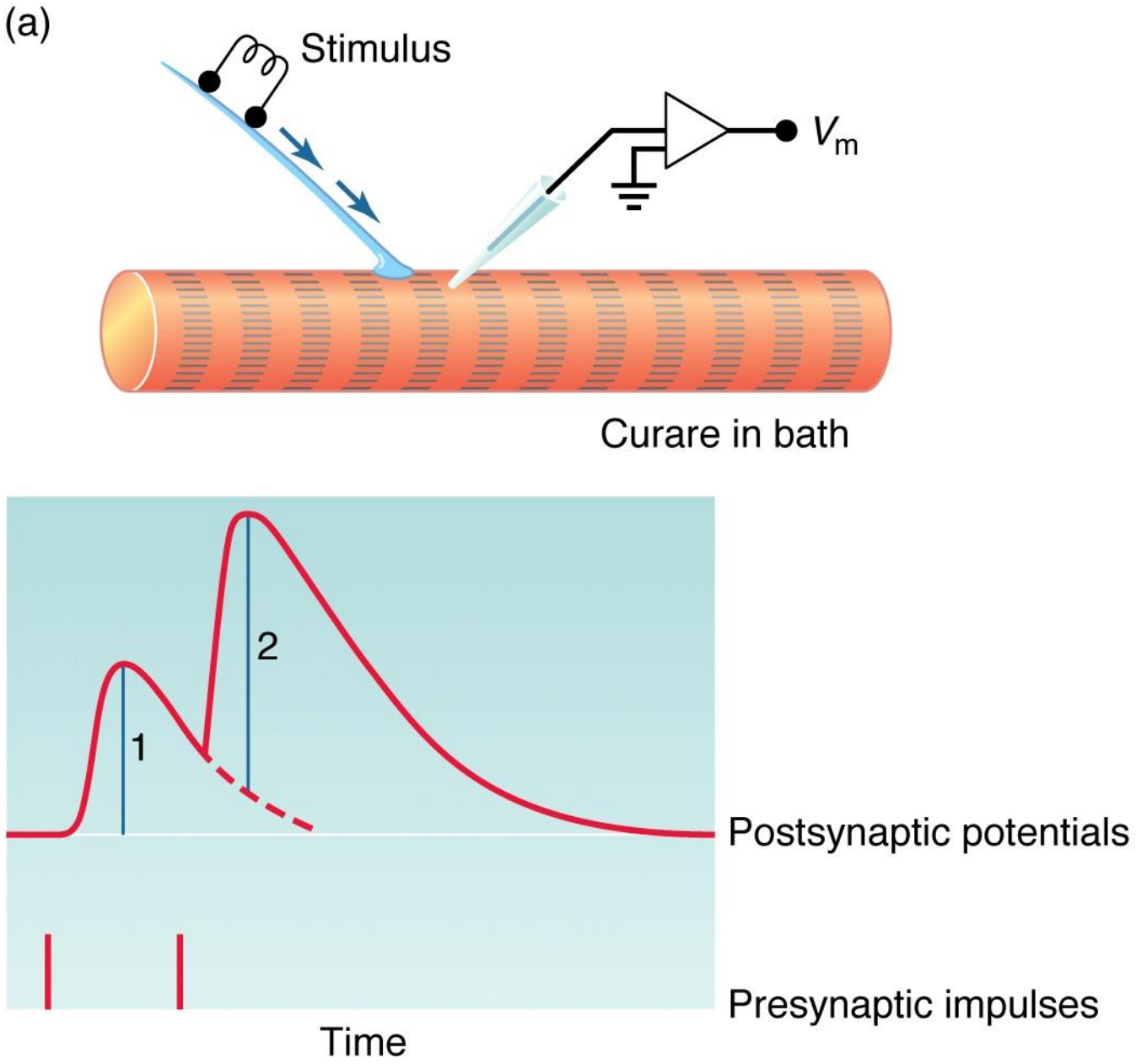

(c)
7th or 8th spinal nerve
3rd, 4th, or 5th spinal nerve
C cell
B cell
Sympathetic neurons in 9th and 10th chain ganglia
GnRH
ACh
GnRH receptor
ACh receptor

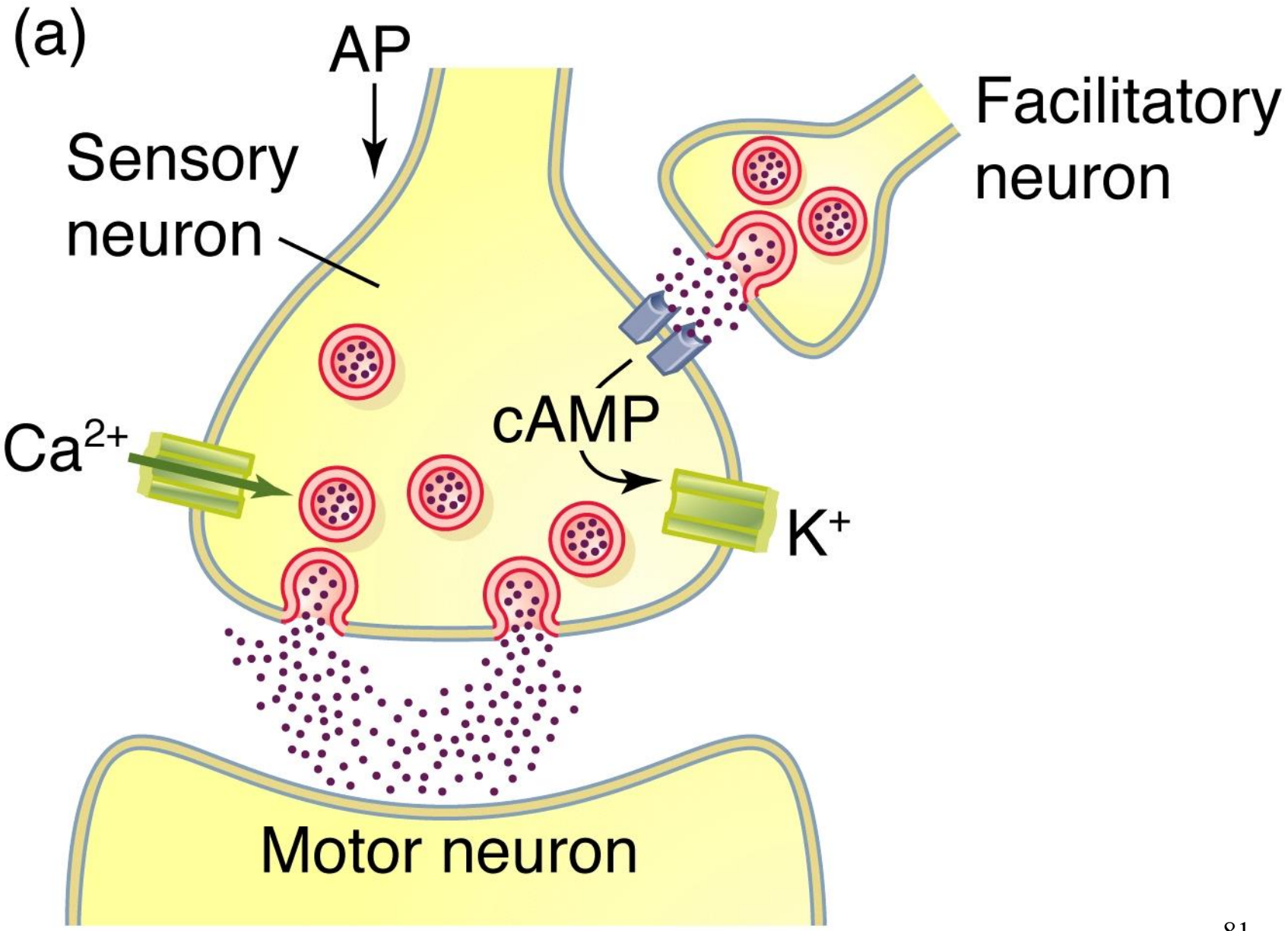

V_m
Time
Stimulus
= Na^+ channels
Axon
Soma
Dendrites
Axon hillock
Myelin sheath

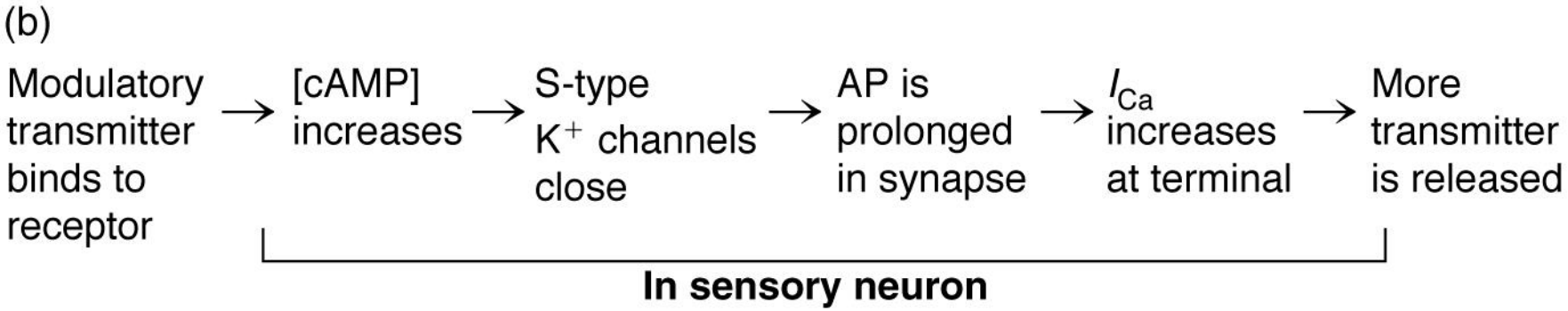

Excitatory presynaptic axon
Inhibitory axon
Excitatory synaptic current
Inhibitory synaptic current
a
b
a
b
a and b

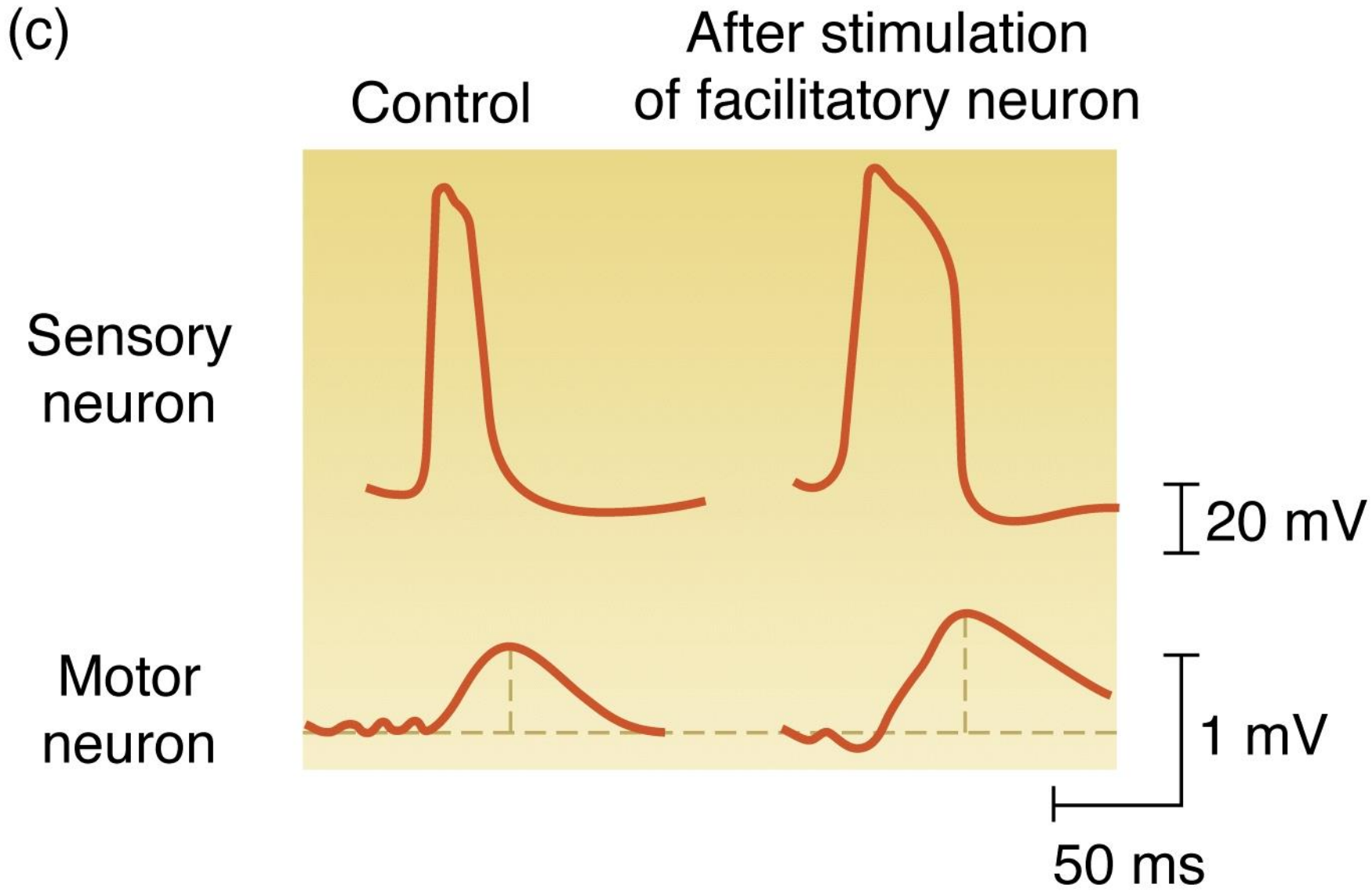

(c)
Time

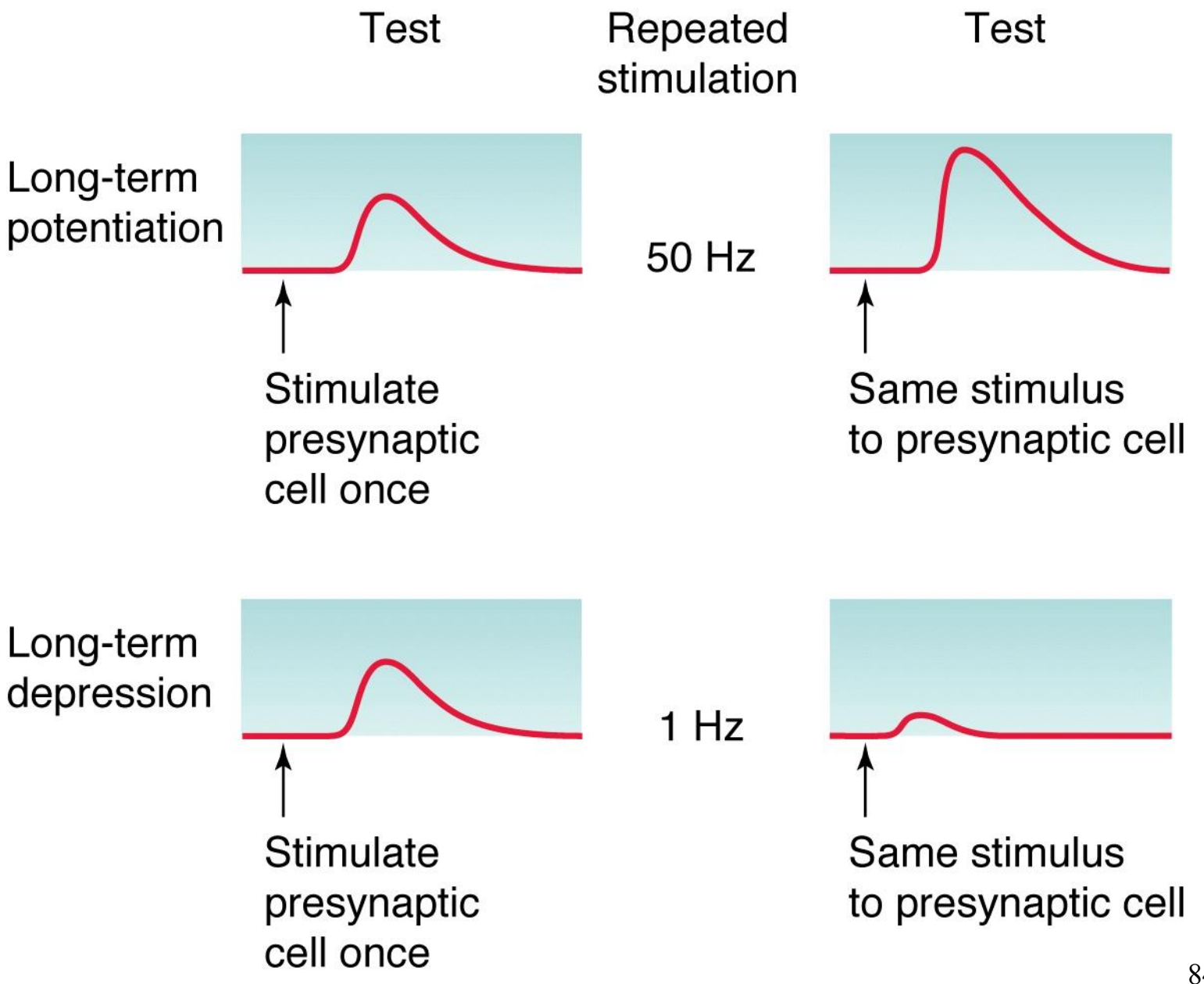

(b)
Depolarization
Action potentials
Time

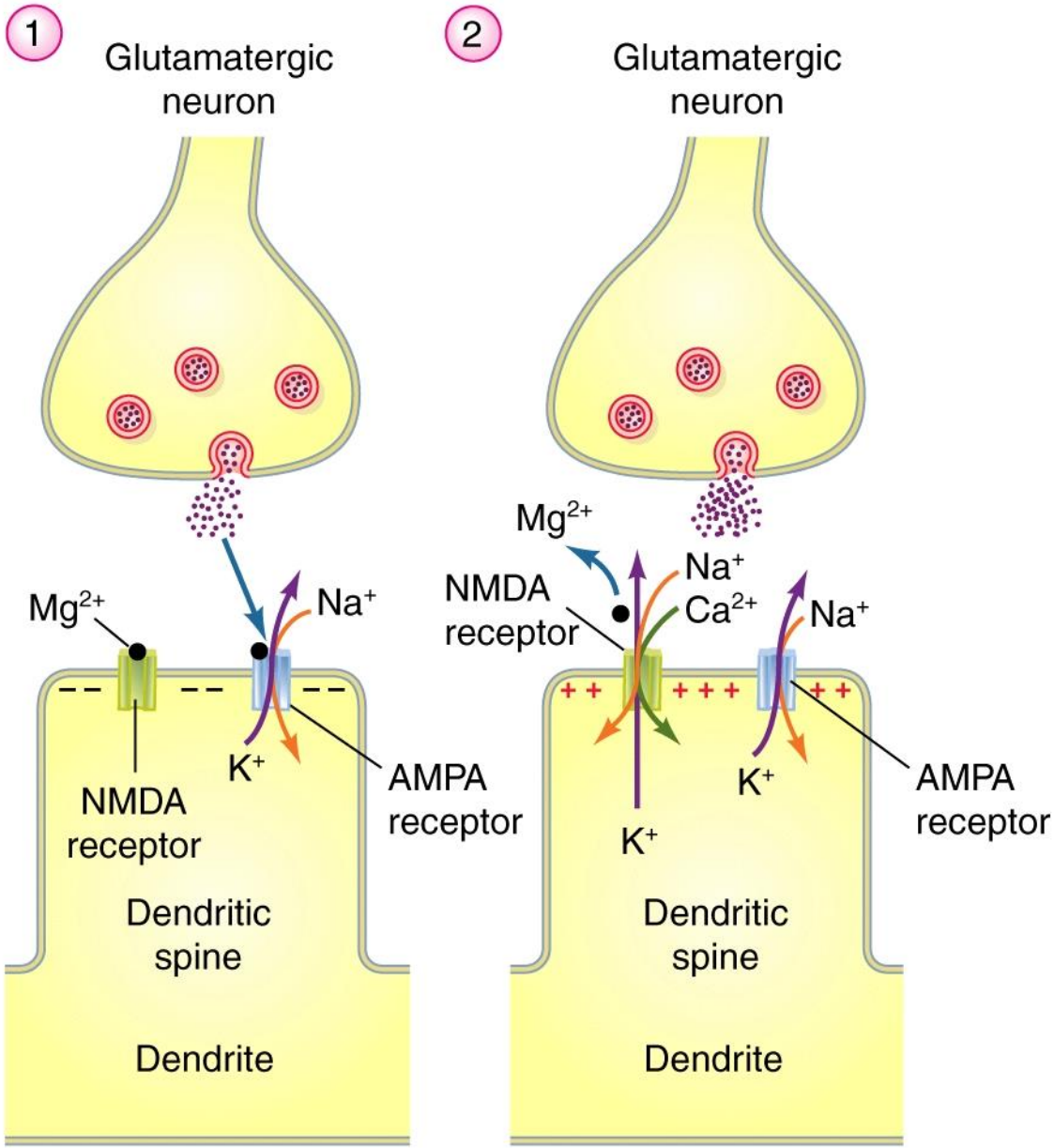

(a)
Stimulus
V_m
Curare in bath
2
1
Postsynaptic potentials
Presynaptic impulses
Time

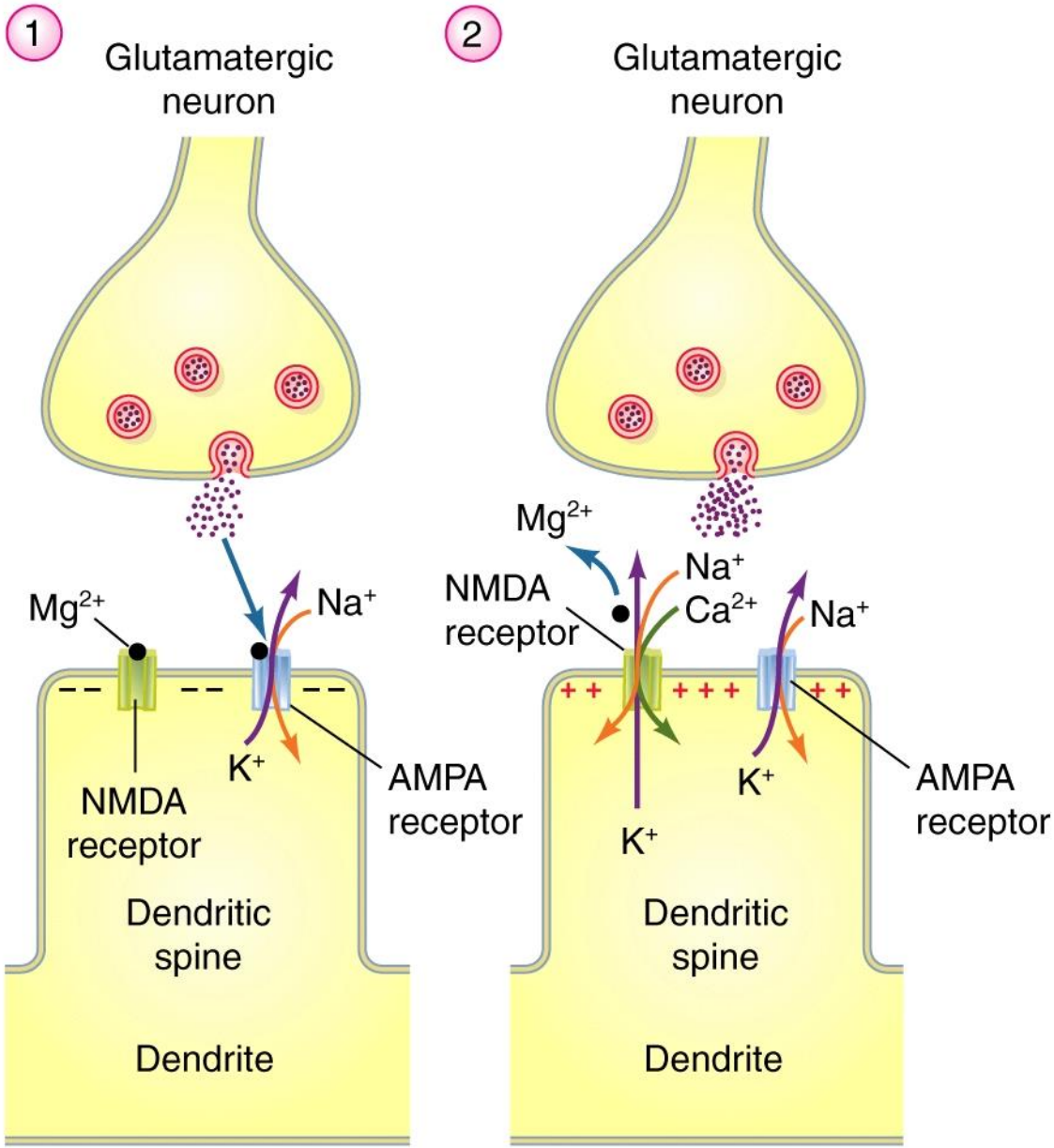

(a)
AP
Sensory neuron
Facilitatory neuron
cAMP
Ca^{2+}
K^+
Motor neuron

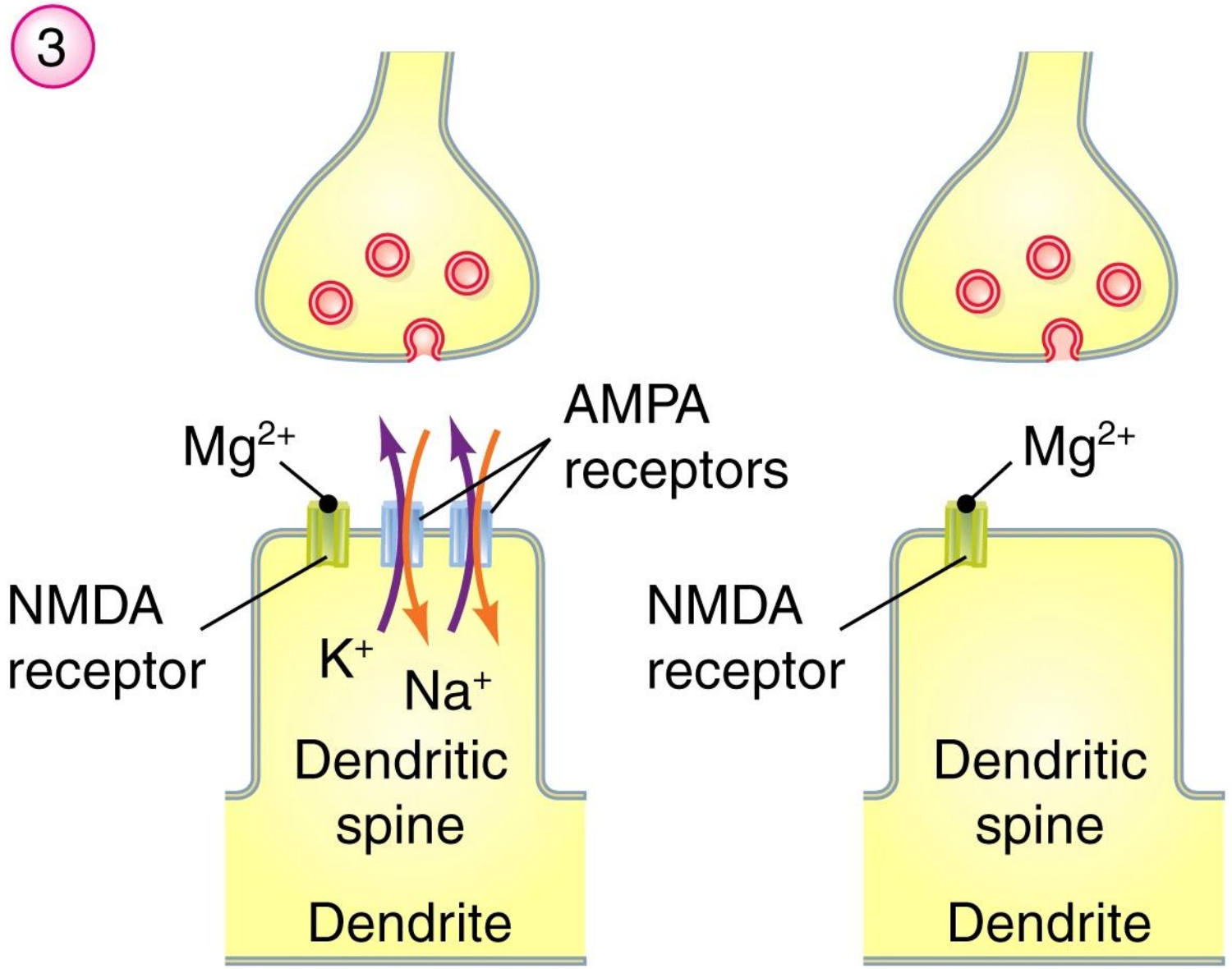

(b)
Modulatory transmitter binds to receptor
[cAMP] increases
S-type K^+ channels close
AP is prolonged in synapse
I_{Ca} increases at terminal
More transmitter is released
In sensory neuron

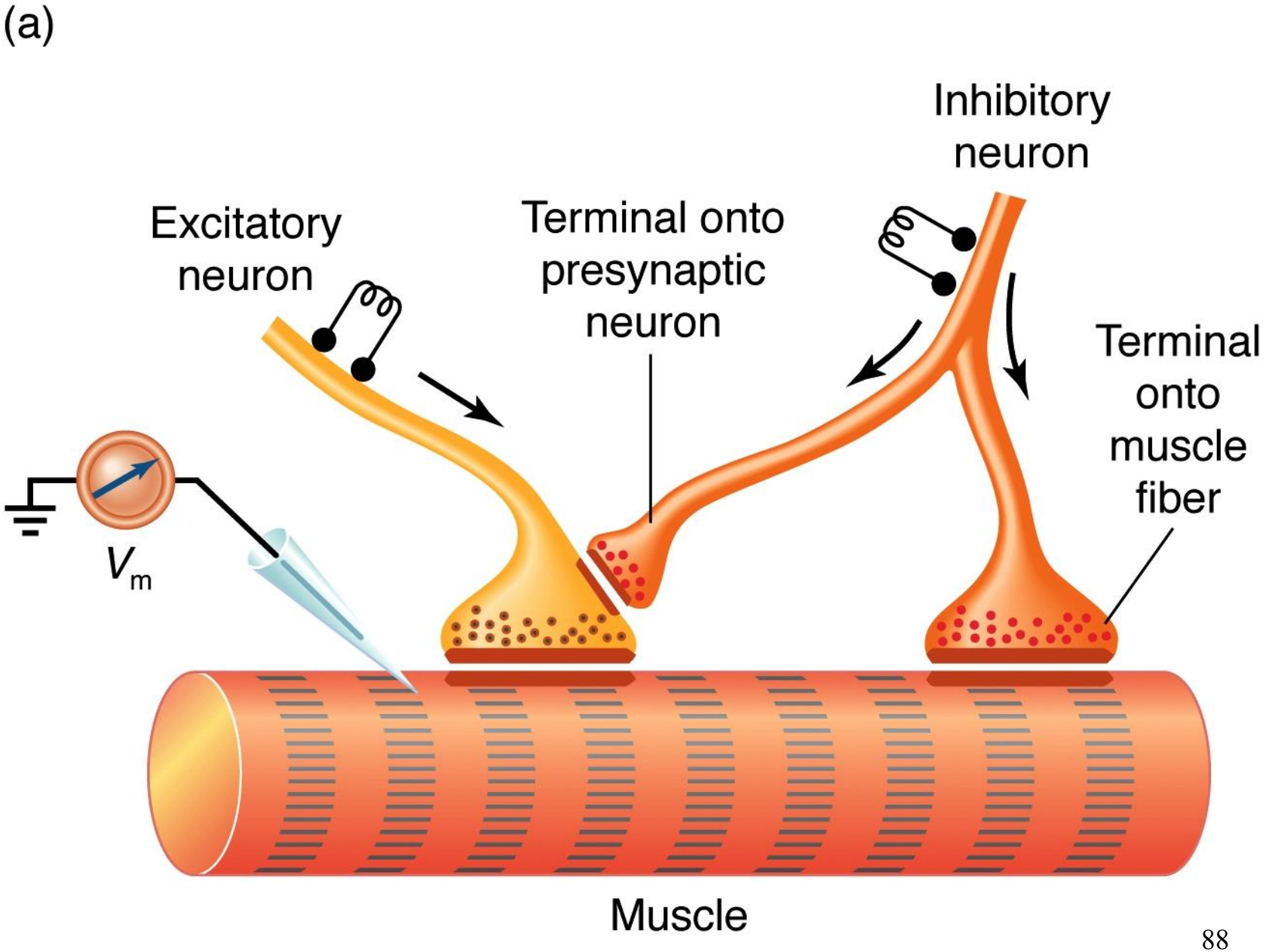

(c)
Control
After stimulation of facilitatory neuron
Sensory neuron
Motor neuron
20 mV
1 mV
50 ms


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


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


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

Neat extra fun facts about neurophysiology: Current literature