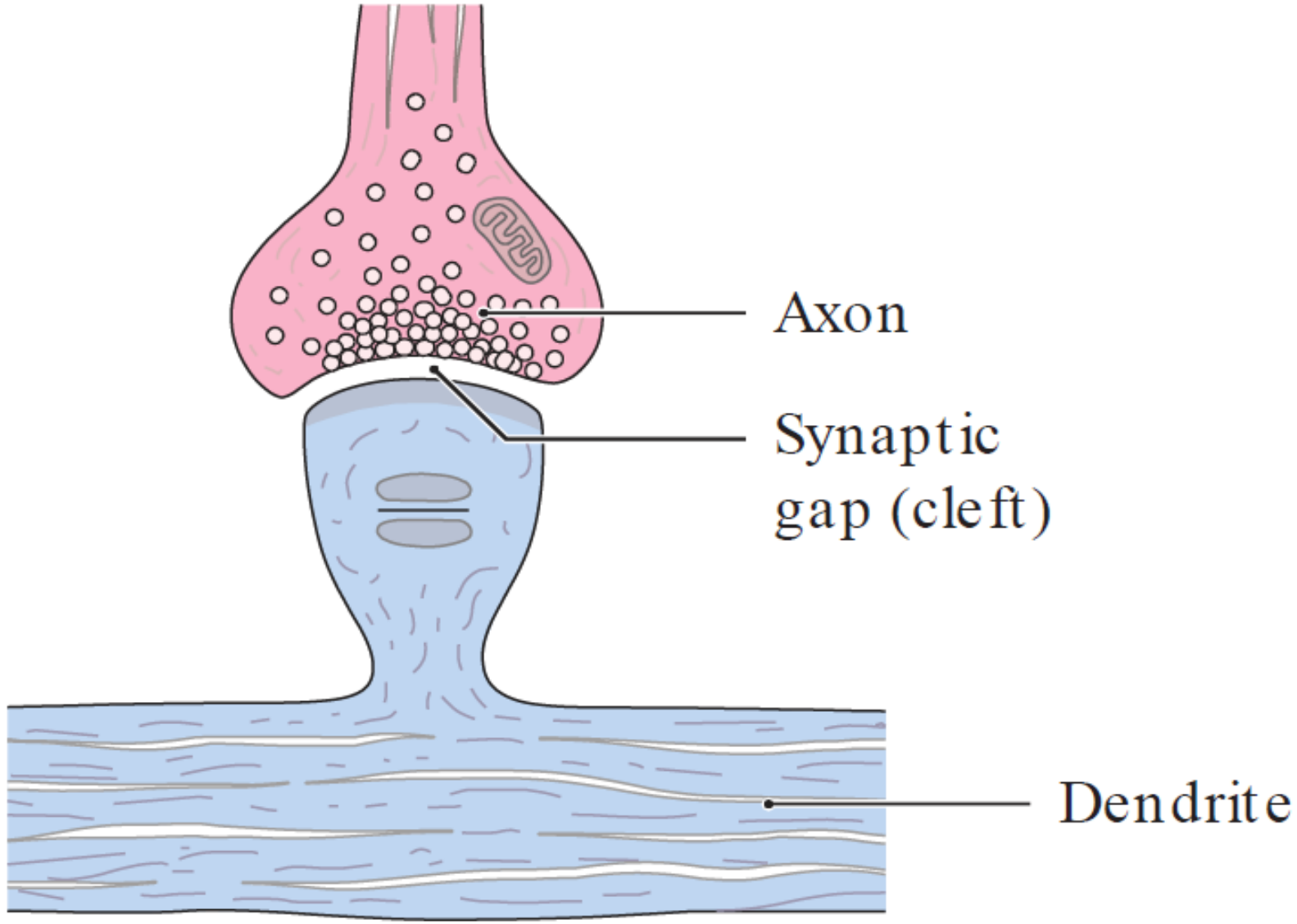
# Sinapsis - Neurotransmisores

*Nelson D. Villalba M.D. M.Sc.*

# ¿Qué es la SINAPSIS?

# Sinapsis



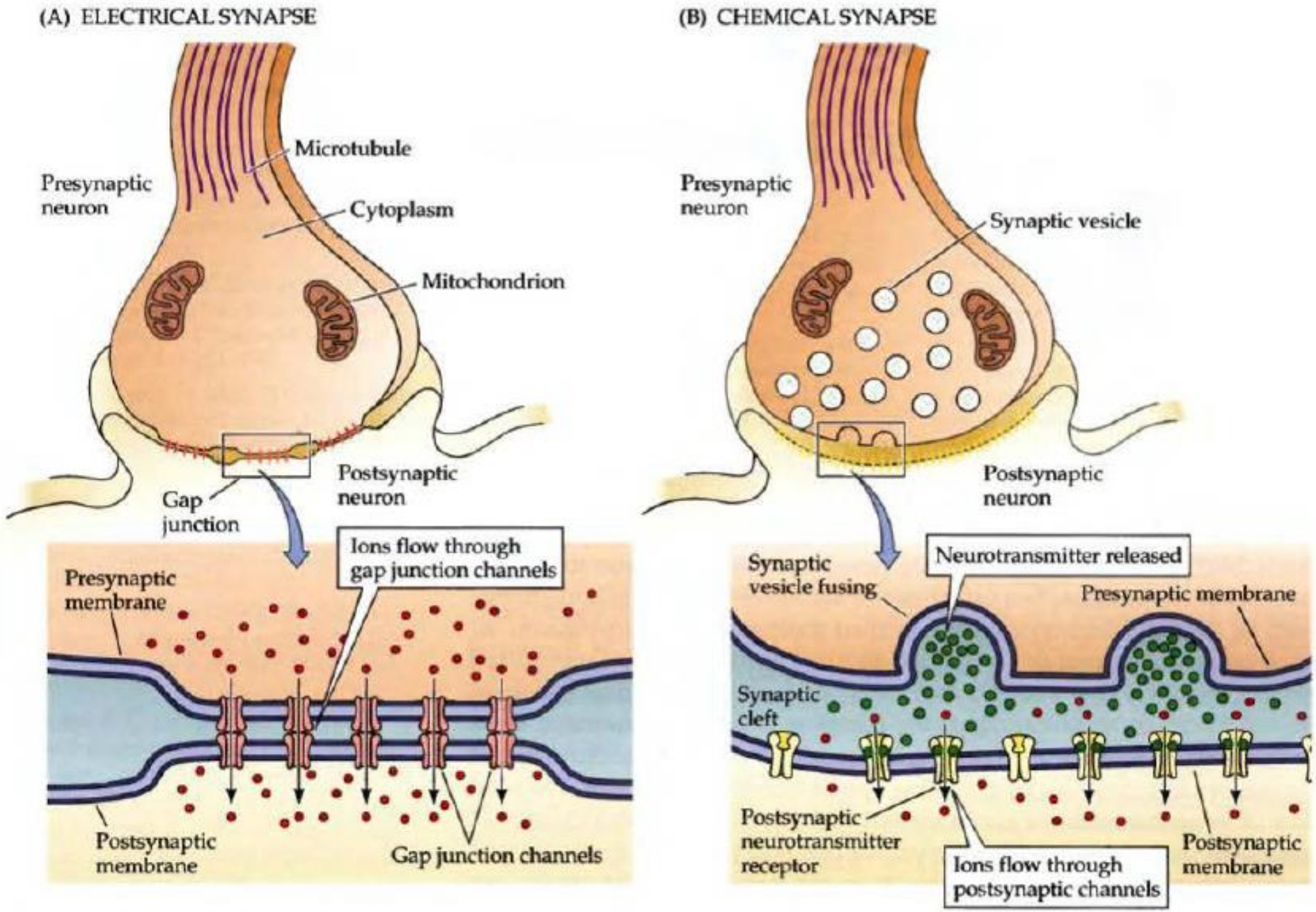
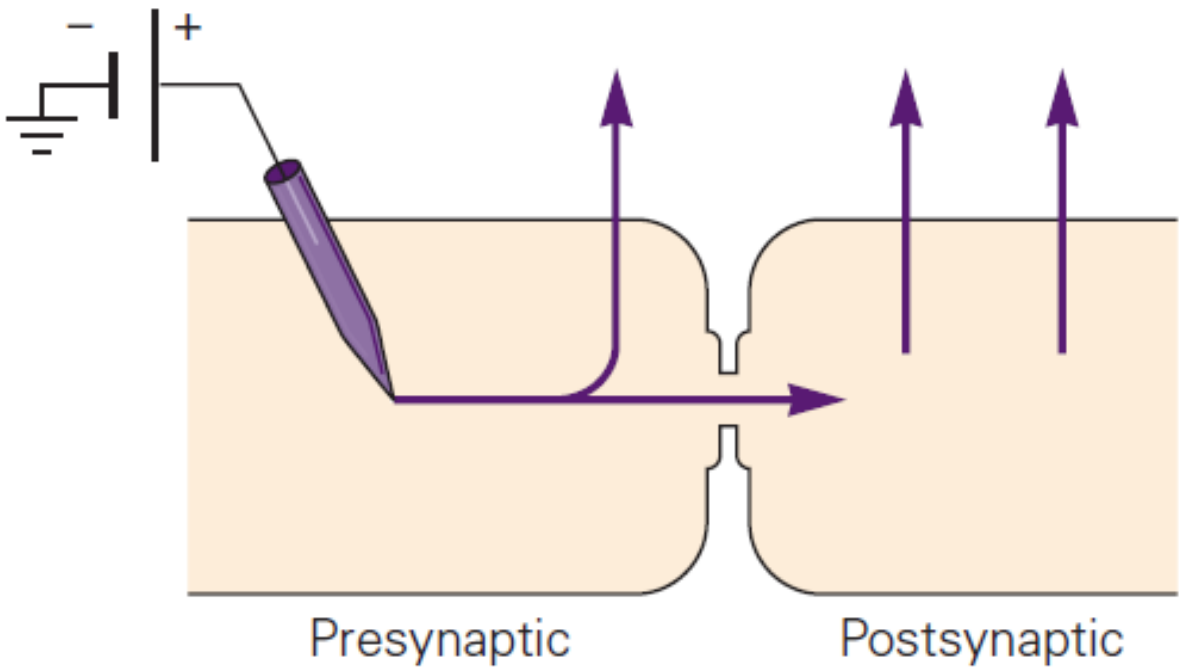

(A) ELECTRICAL SYNAPSE
Microtubule
Presynaptic neuron
Cytoplasm
Mitochondrion
Postsynaptic neuron
Gap junction
Ions flow through gap junction channels
Presynaptic membrane
Postsynaptic membrane
Gap junction channels
(B) CHEMICAL SYNAPSE
Presynaptic neuron
Synaptic vesicle
Postsynaptic neuron
Neurotransmitter released
Synaptic vesicle fusing
Presynaptic membrane
Synaptic cleft
Postsynaptic neurotransmitter receptor
Ions flow through postsynaptic channels
Postsynaptic membrane

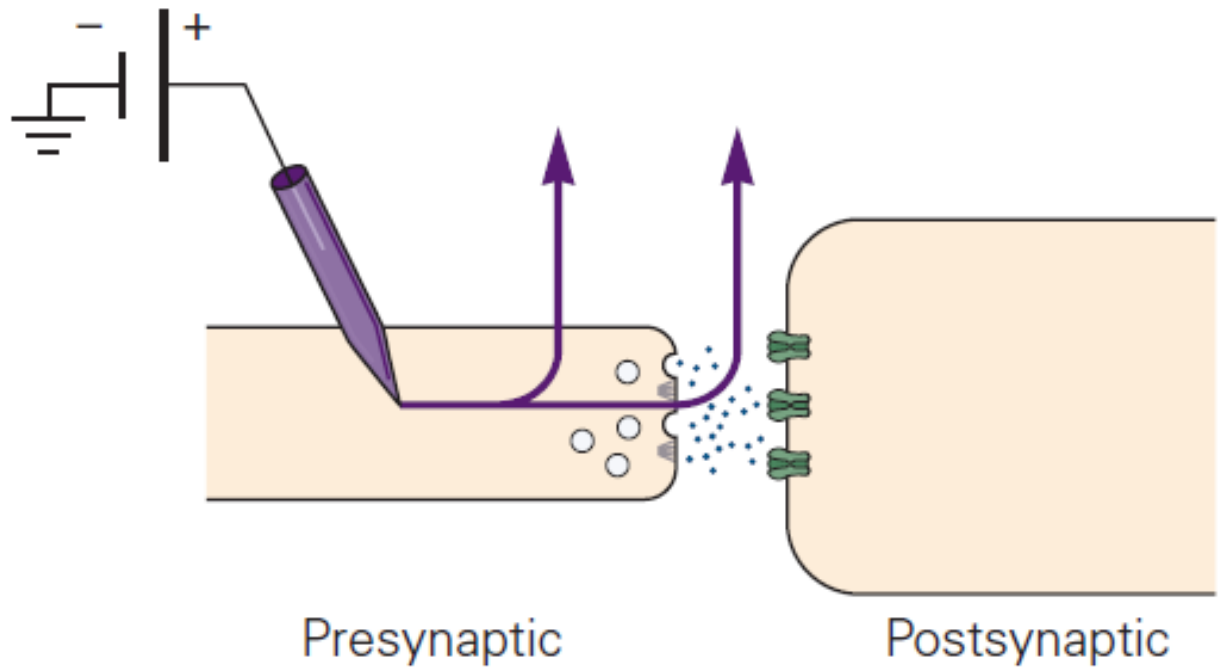
**Table 8–1** Distinguishing Properties of Electrical and Chemical Synapses

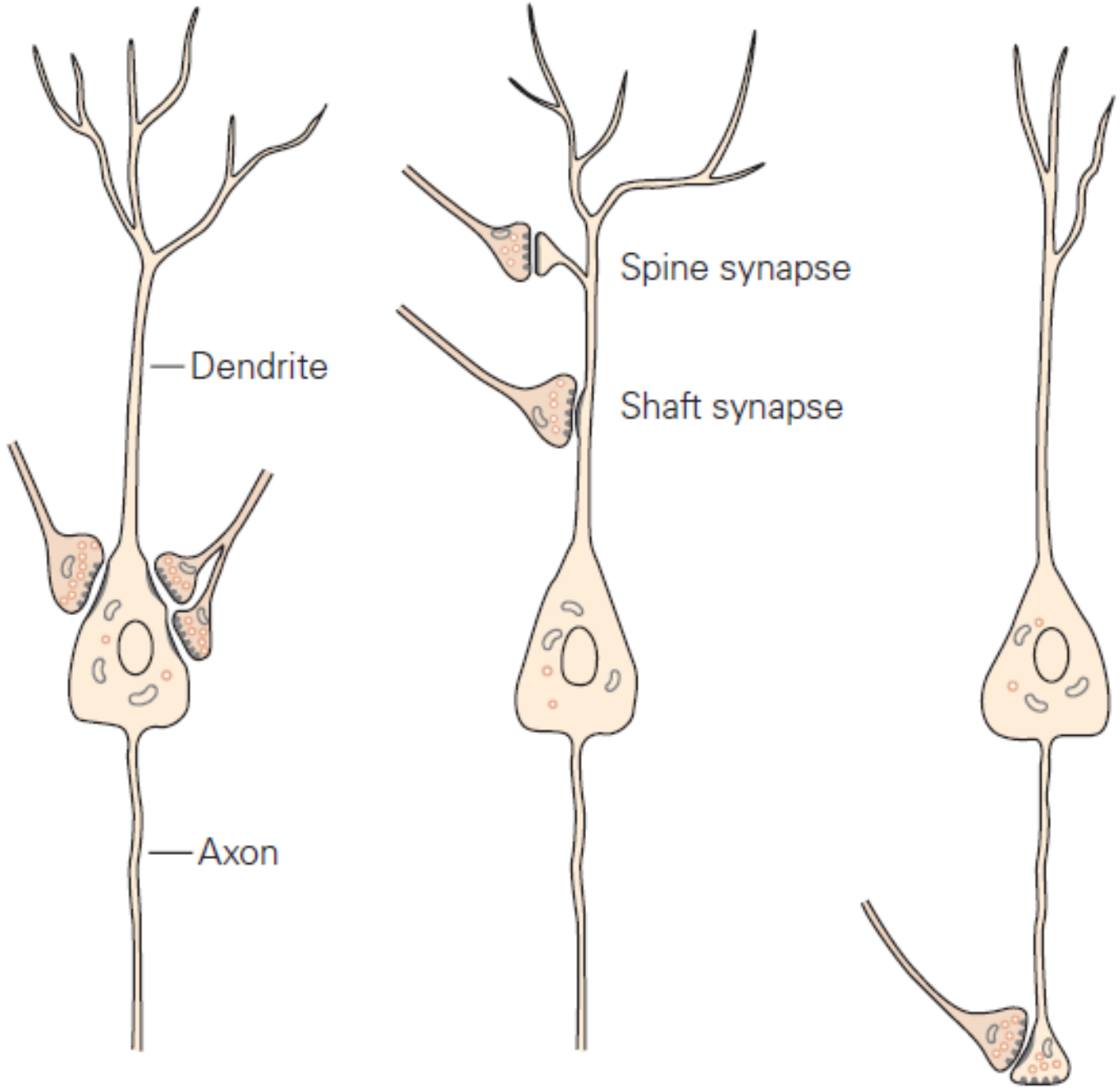
| Type of synapse | Distance between pre- and postsynaptic cell membranes | Cytoplasmic continuity between pre- and postsynaptic cells | Ultrastructural components | Agent of transmission | Synaptic delay | Direction of transmission |
|---|---|---|---|---|---|---|
| Electrical | 4 nm | Yes | Gap-junction channels | Ion current | Virtually absent | Usually bidirectional |
| Chemical | 20–40 nm | No | Presynaptic vesicles and active zones; postsynaptic receptors | Chemical transmitter | Significant: at least 0.3 ms, usually 1–5 ms or longer | Unidirectional |

A Current pathways at electrical synapses




B Current pathways at chemical synapses



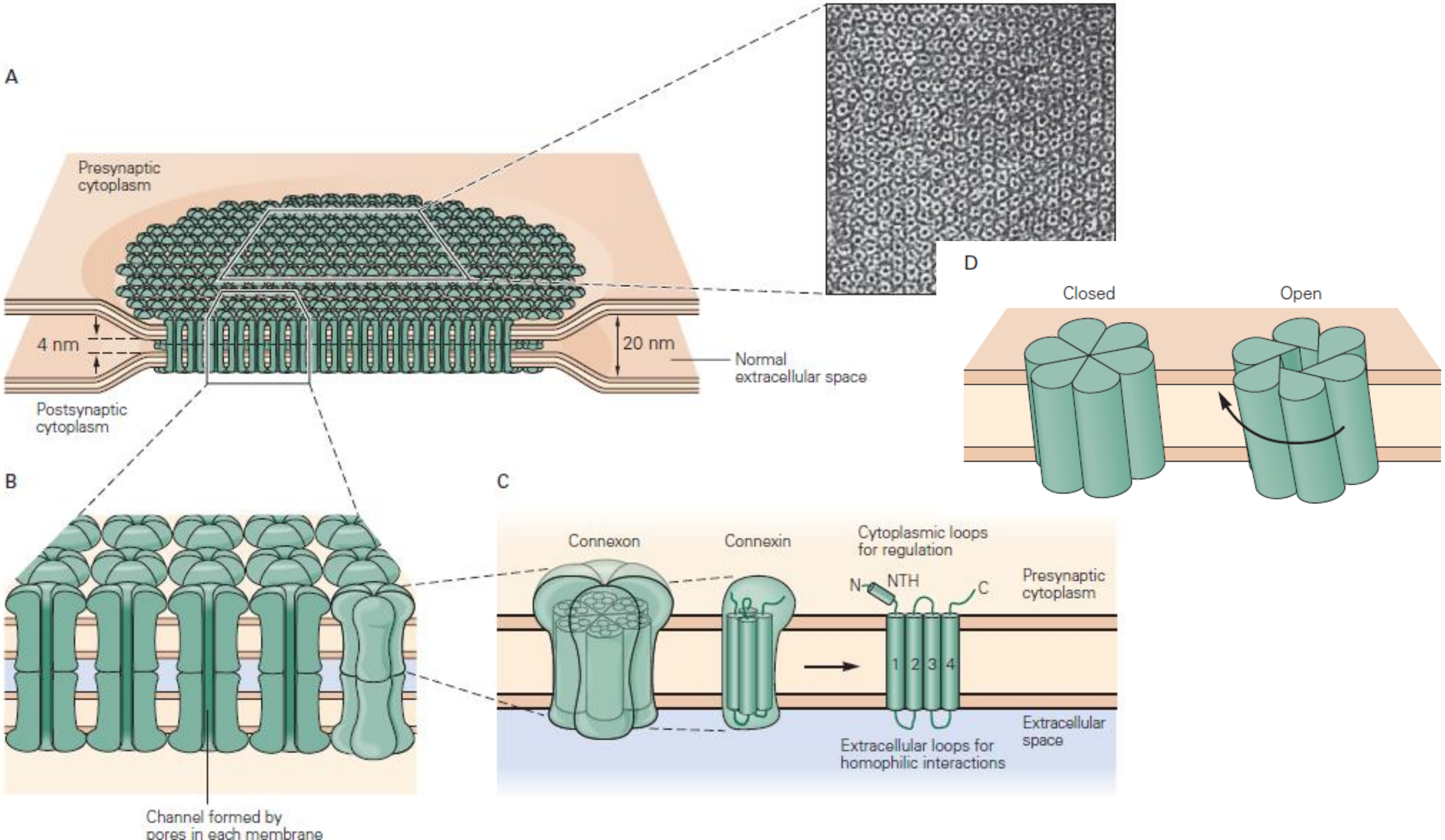


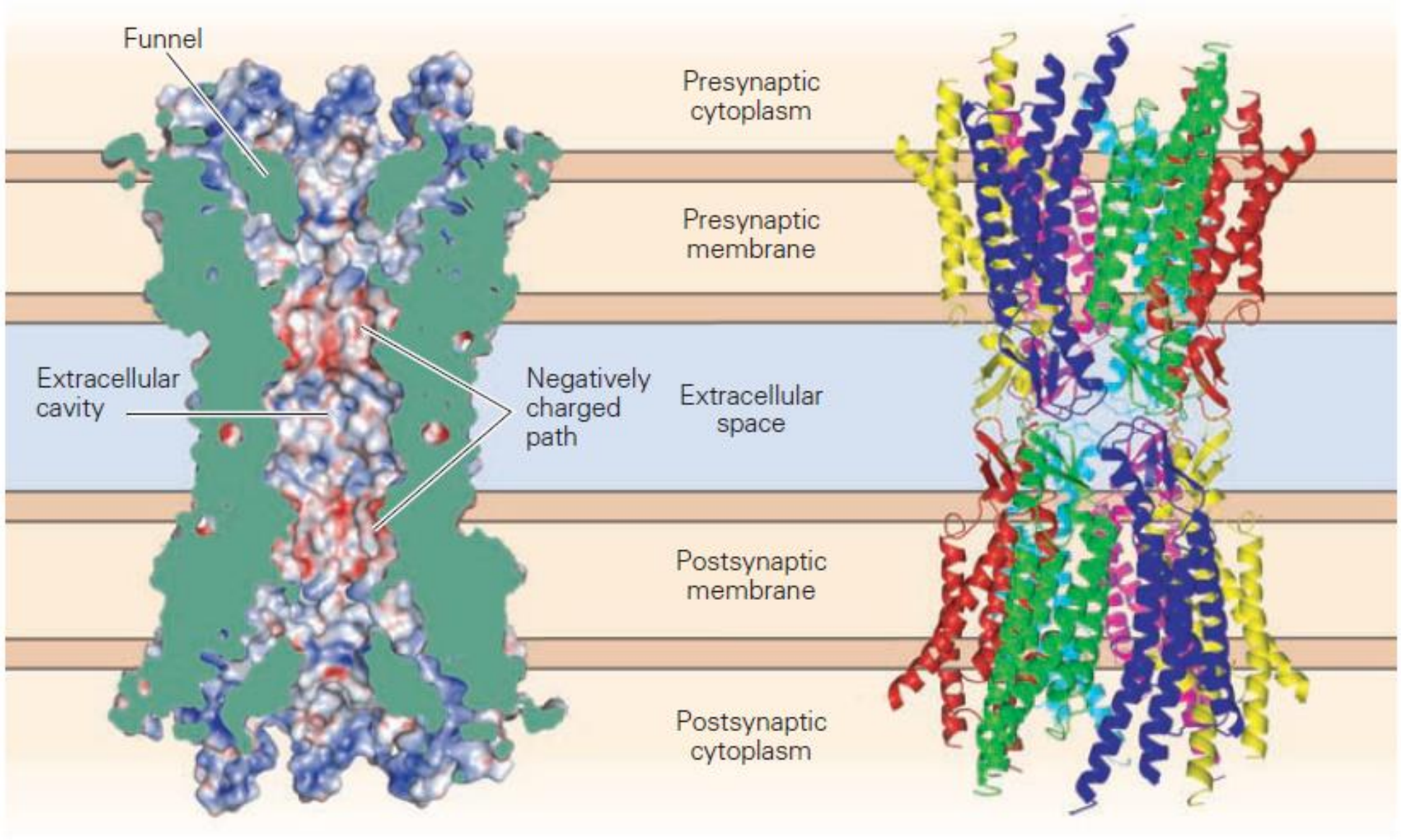

Axosomatic synapses

Axodendritic synapses

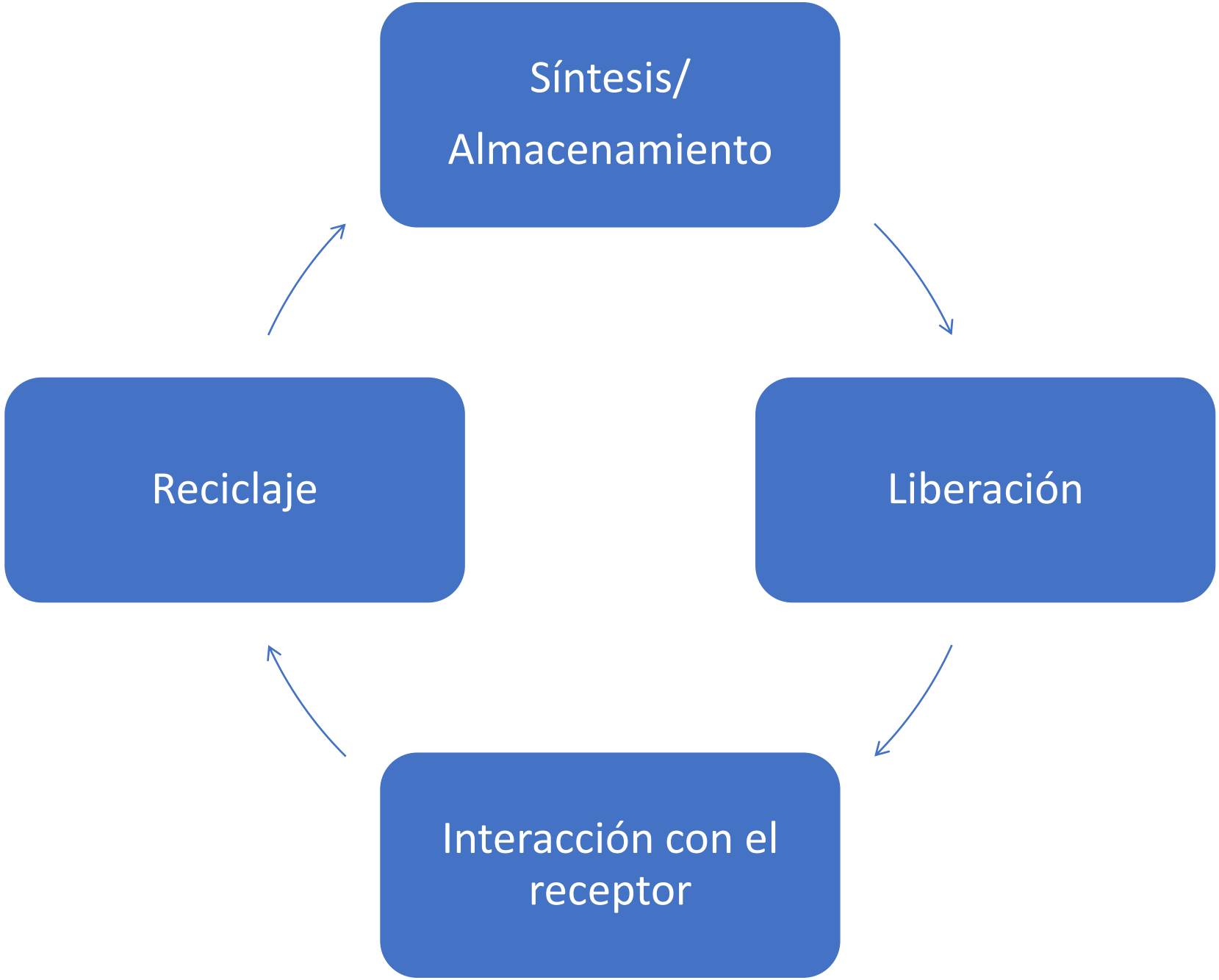
Axo-axonic synapse

# Sinapsis Eléctrica

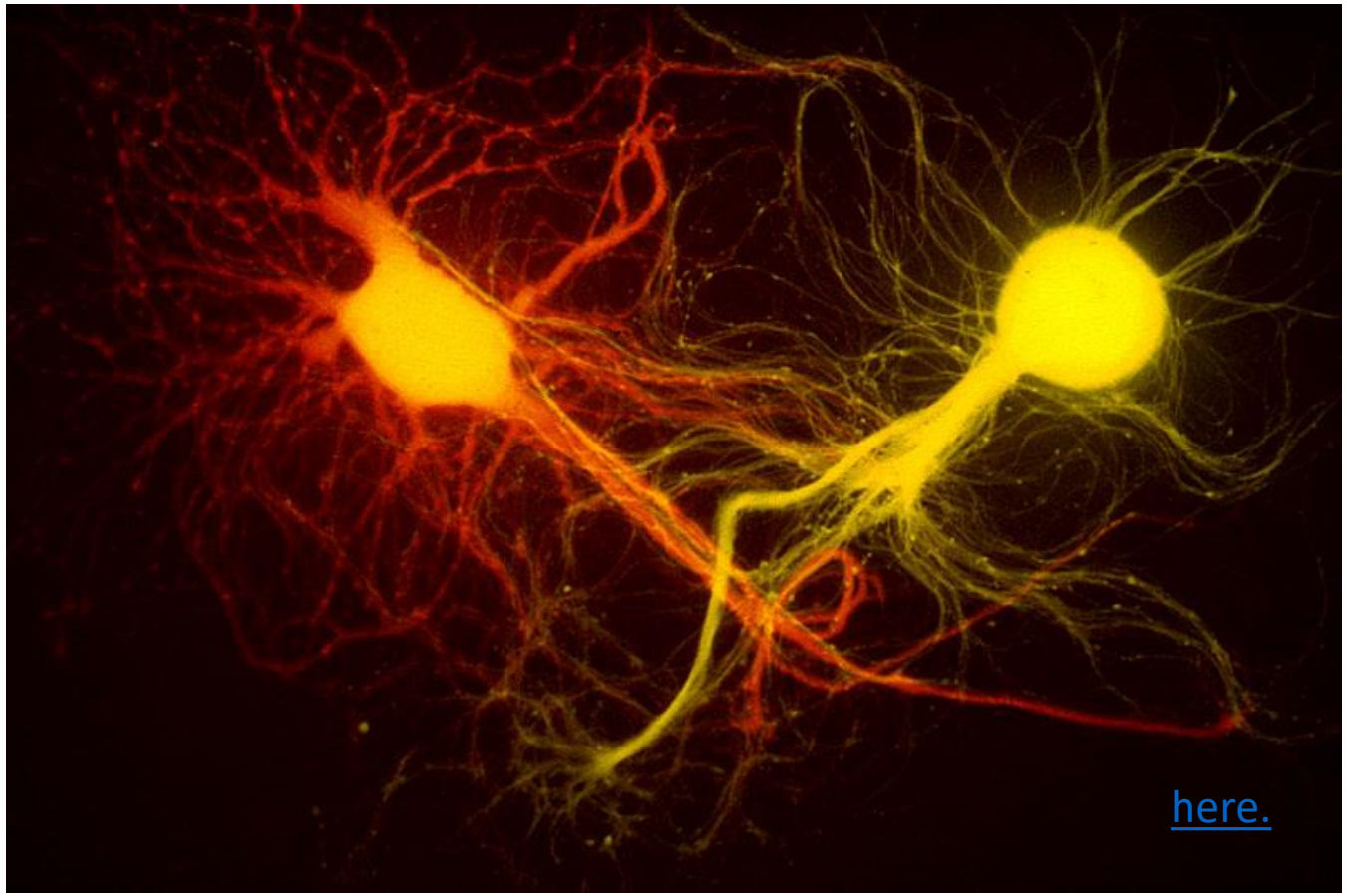

A
Presynaptic cytoplasm
4 nm
20 nm
Normal extracellular space
Postsynaptic cytoplasm
B
Channel formed by pores in each membrane
C
Connexon
Connexin
Cytoplasmic loops for regulation
N
NTH
C
Presynaptic cytoplasm
1 2 3 4
Extracellular space
Extracellular loops for homophilic interactions
D
Closed
Open

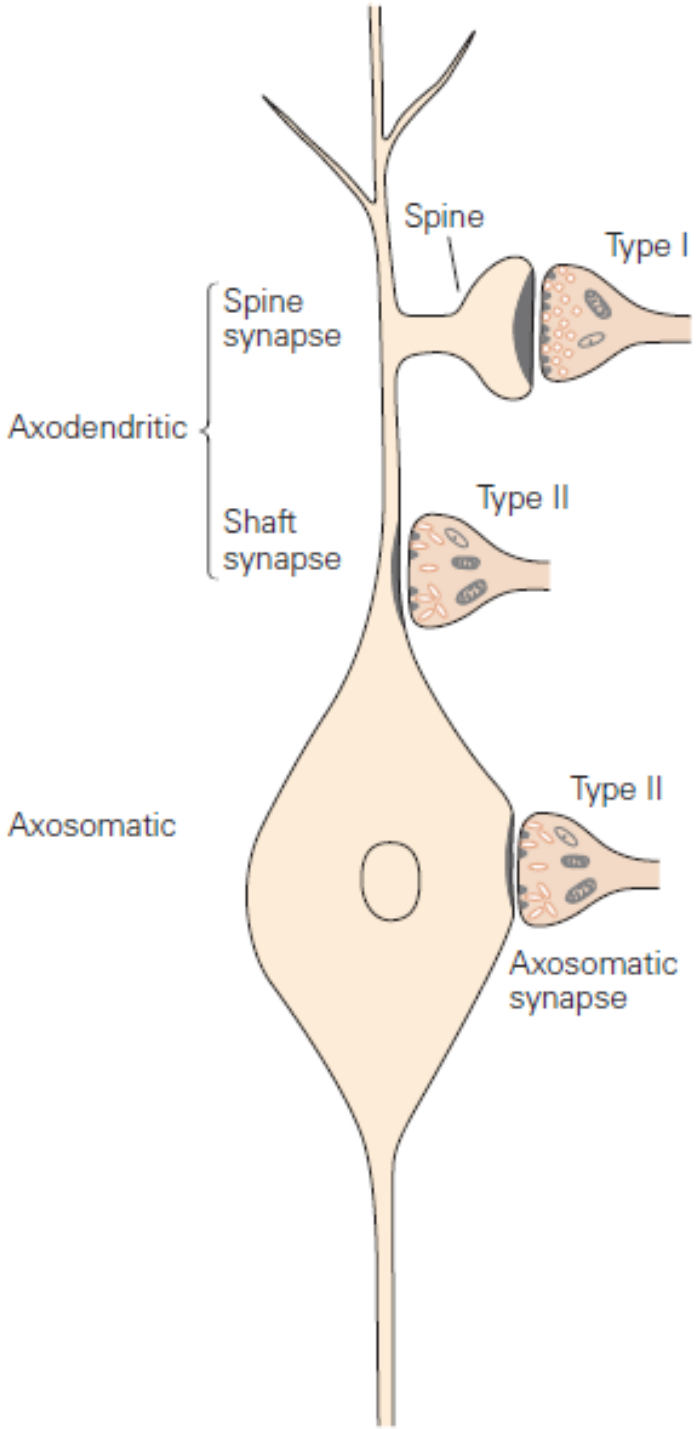

Funnel
Extracellular cavity
Negatively charged path
Presynaptic cytoplasm
Presynaptic membrane
Extracellular space
Postsynaptic membrane
Postsynaptic cytoplasm

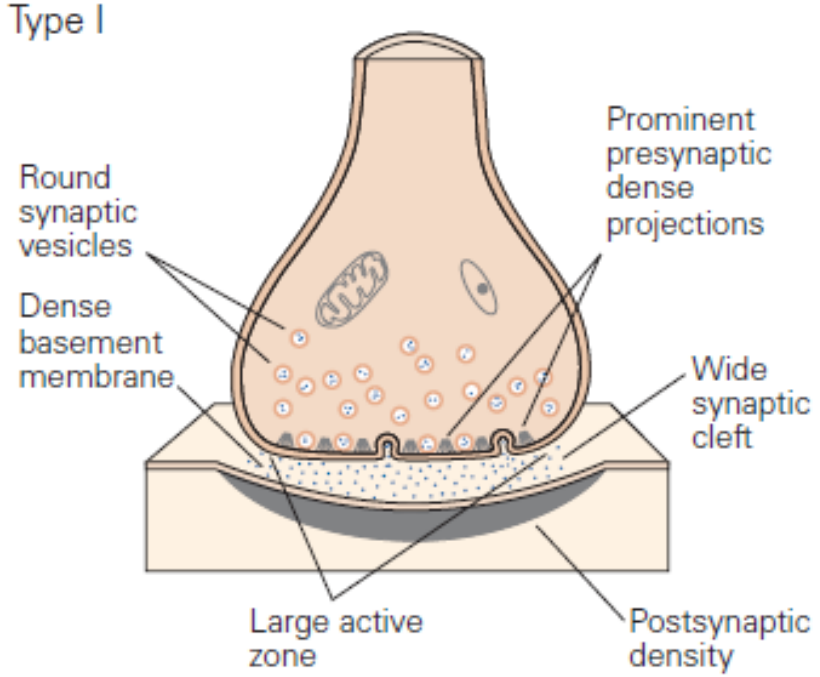
# Sinapsis Química

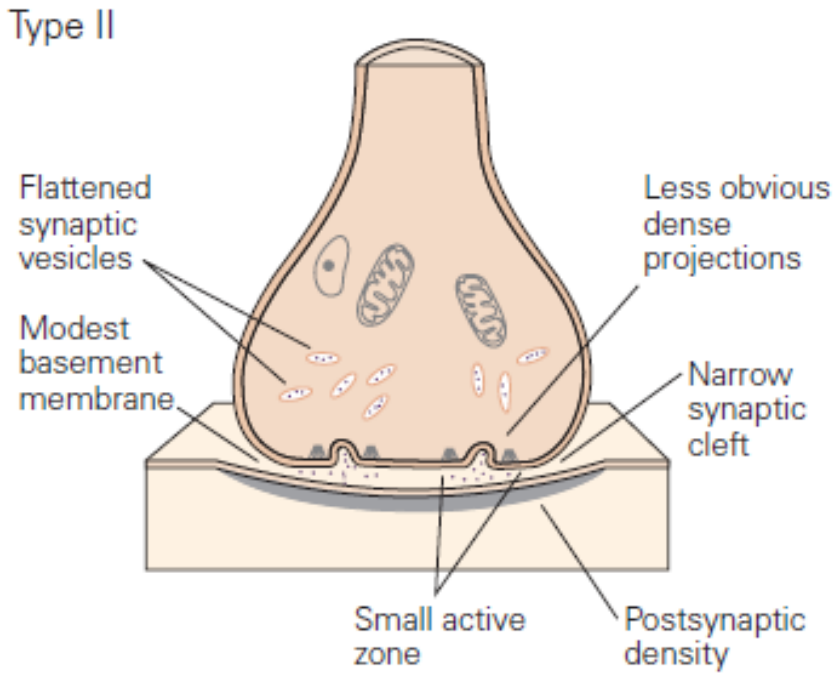

Síntesis/
Almacenamiento
Liberación
Interacción con el receptor
Reciclaje

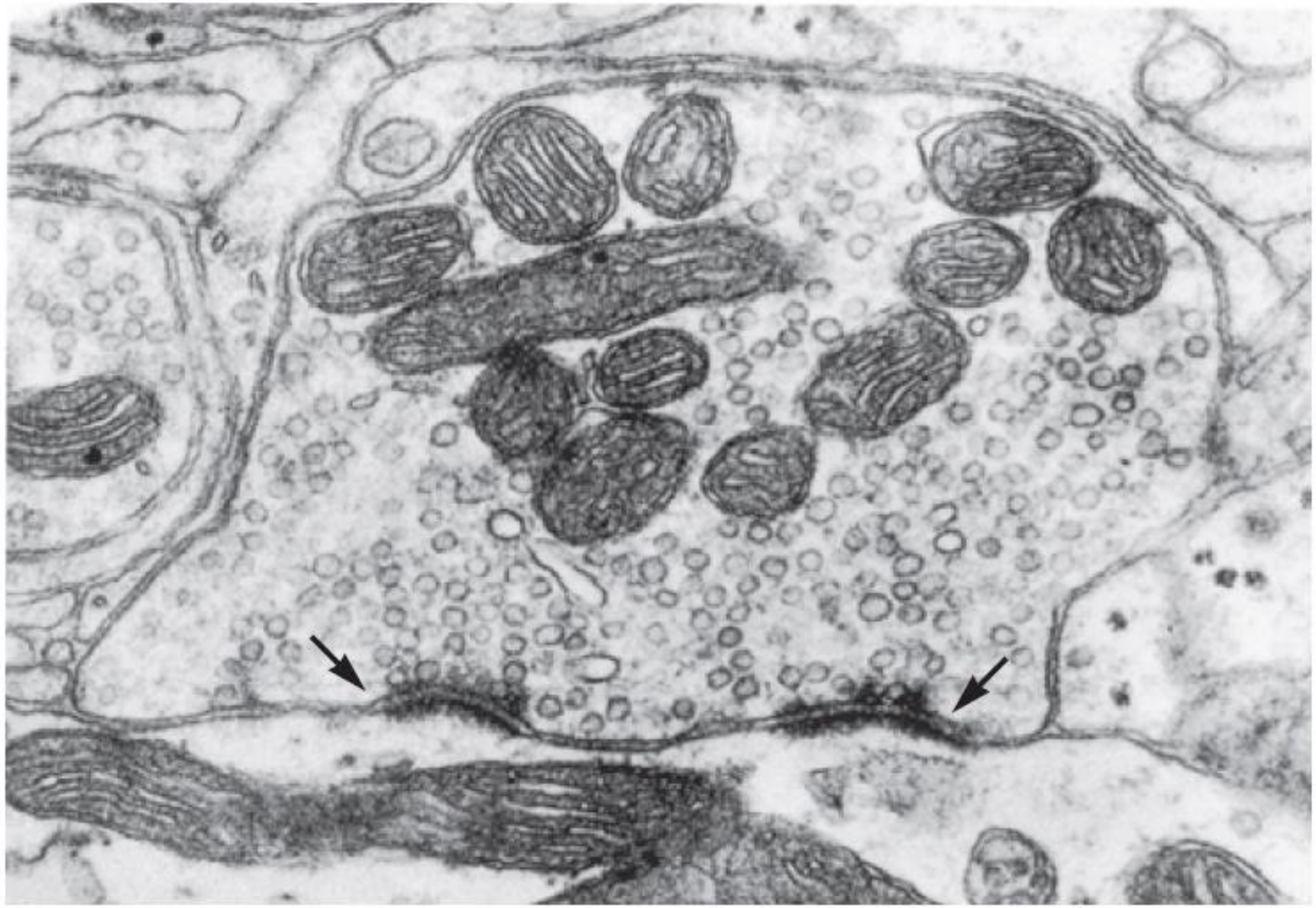
# Sinapsis Química

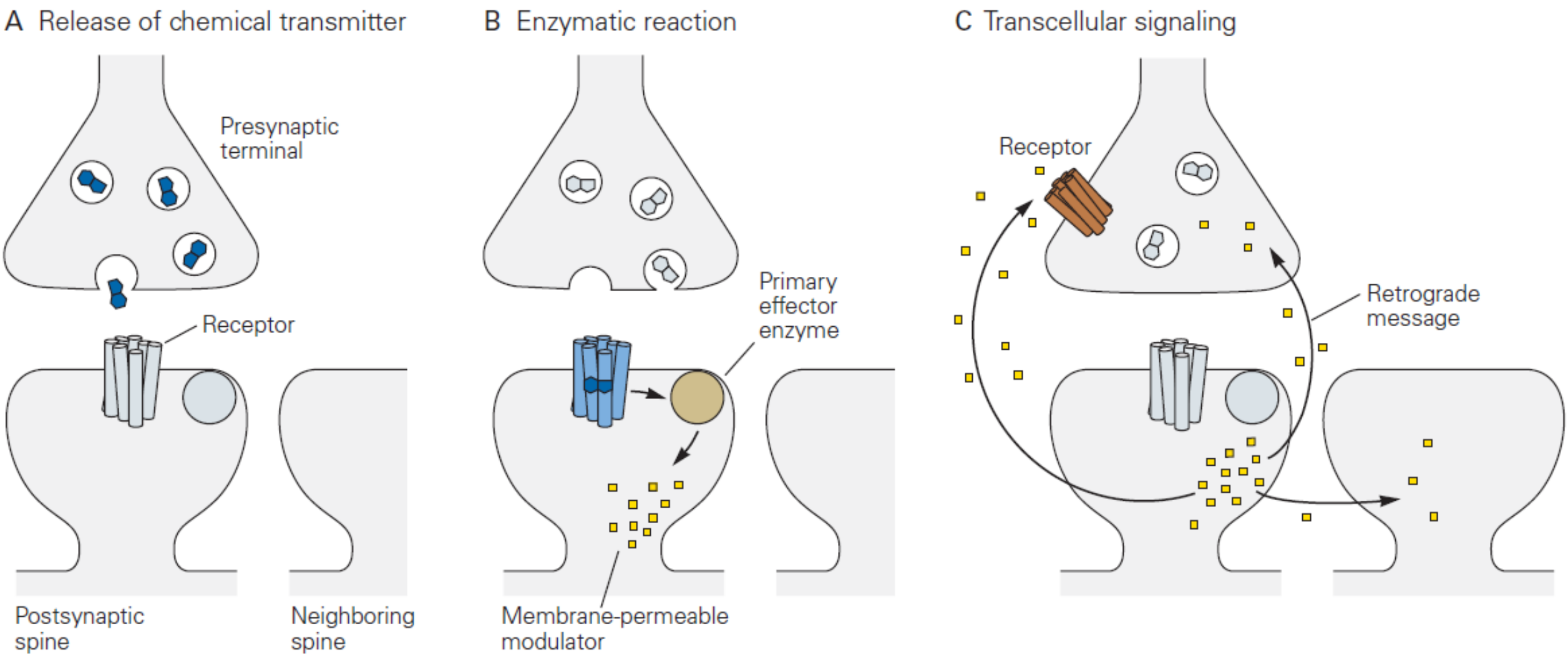



Spine
Type I
Spine synapse
Axodendritic
Shaft synapse
Type II
Type II
Axosomatic
Axosomatic synapse

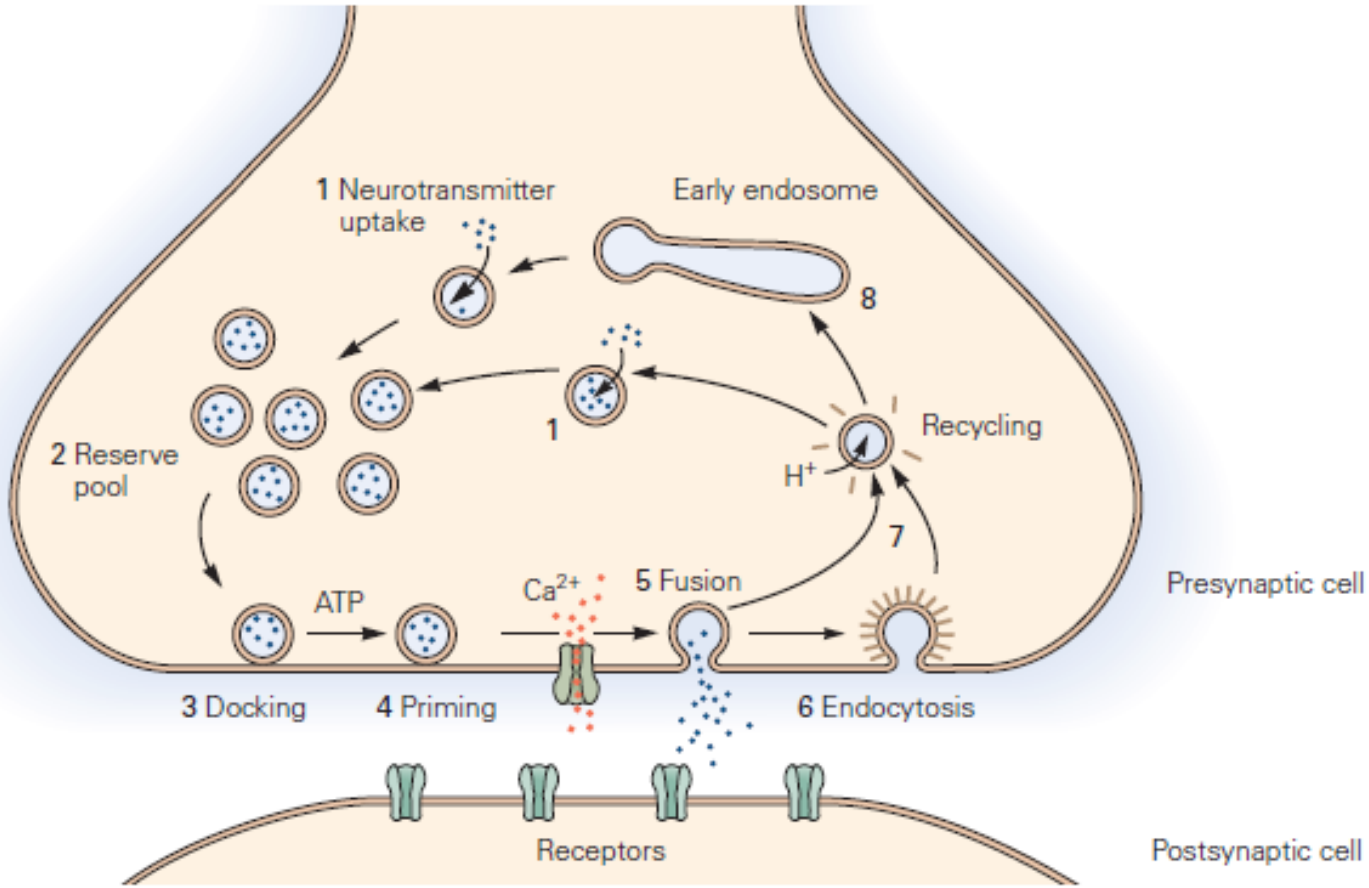

Type I
Round synaptic vesicles
Dense basement membrane
Prominent presynaptic dense projections
Wide synaptic cleft
Large active zone
Postsynaptic density


Type II
Flattened synaptic vesicles
Modest basement membrane
Less obvious dense projections
Narrow synaptic cleft
Small active zone
Postsynaptic density

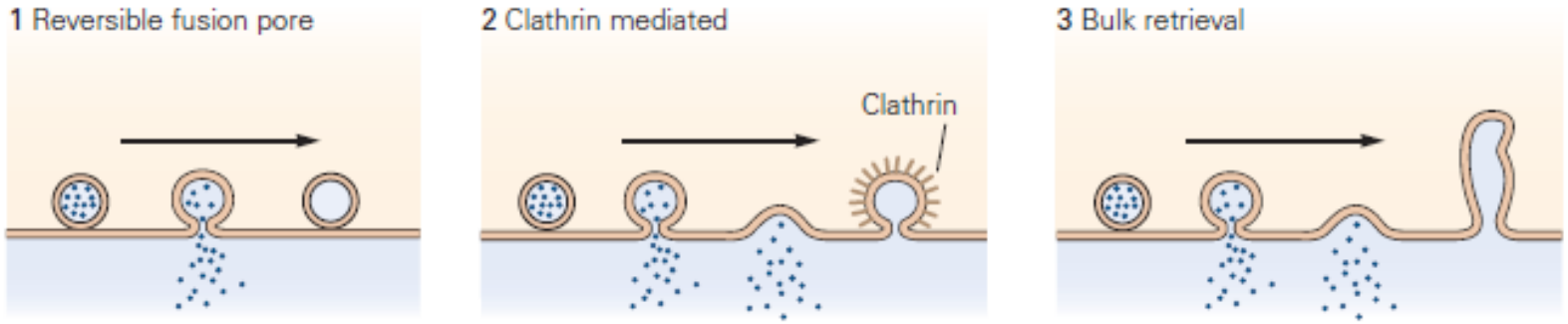


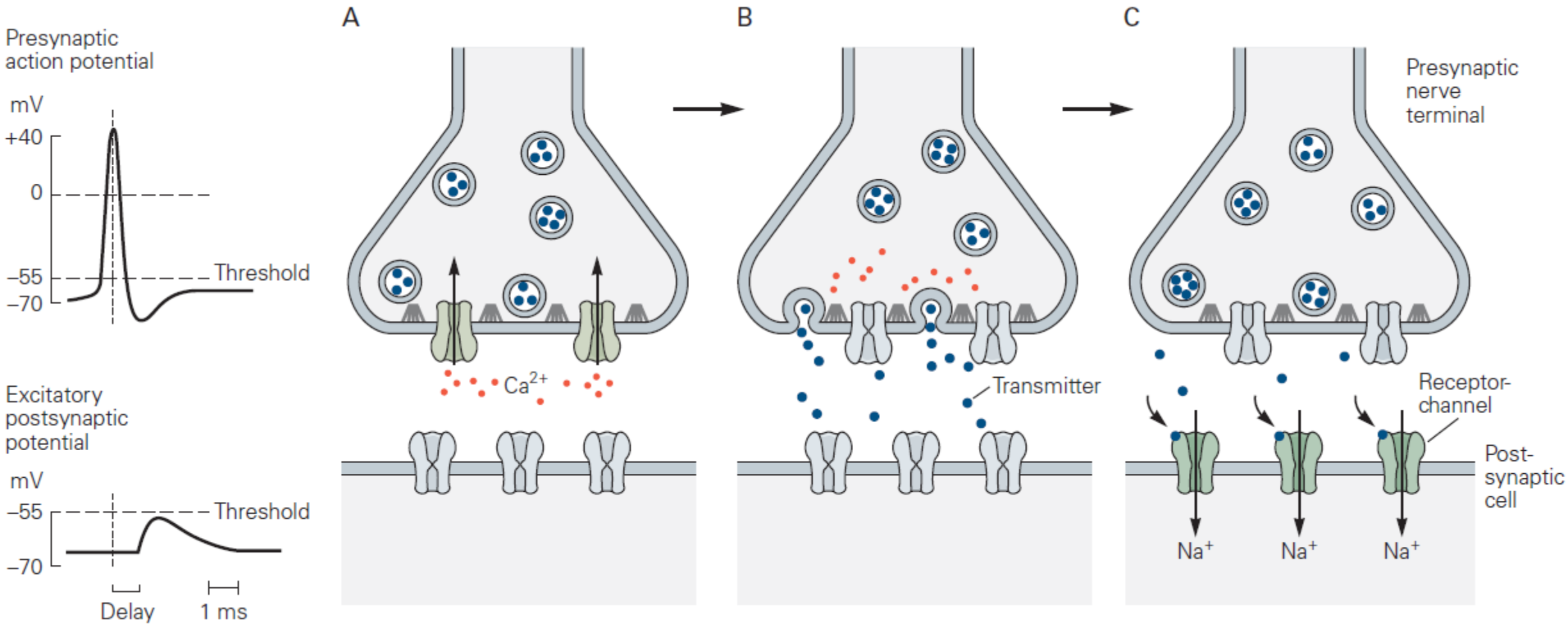

A Release of chemical transmitter
Presynaptic terminal
Receptor
Postsynaptic spine
Neighboring spine
B Enzymatic reaction
Primary effector enzyme
Membrane-permeable modulator
C Transcellular signaling
Receptor
Retrograde message

A Synaptic vesicle cycle

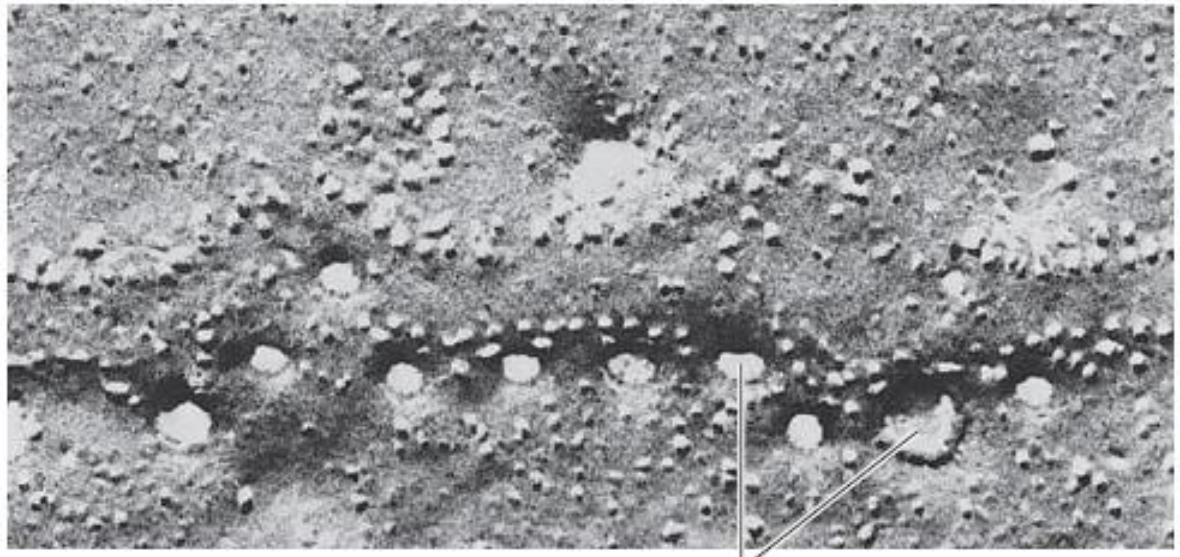



B Mechanisms for recycling synaptic vesicles

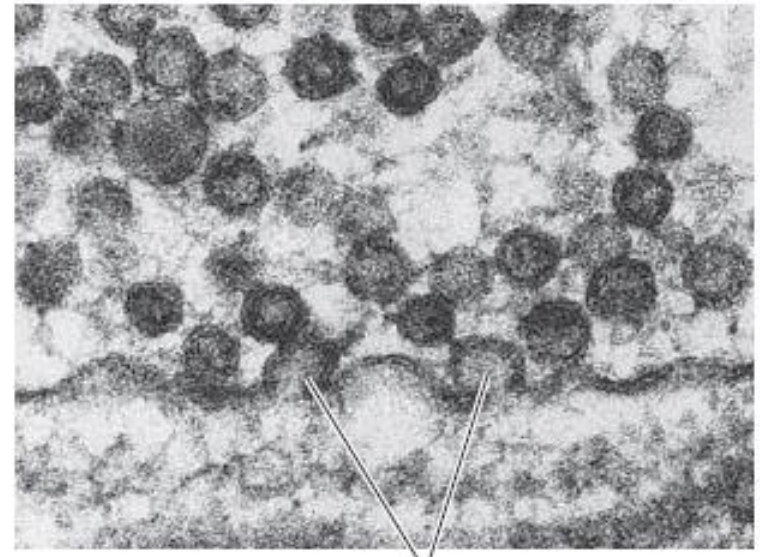



Presynaptic
action potential
mV
+40
0
–55
–70
Threshold
Excitatory
postsynaptic
potential
mV
–55
–70
Threshold
Delay
1 ms
A
B
C
Ca2+
Transmitter
Presynaptic
nerve
terminal
Receptor-
channel
Post-
synaptic
cell
Na+
Na+
Na+

B Exocytosis

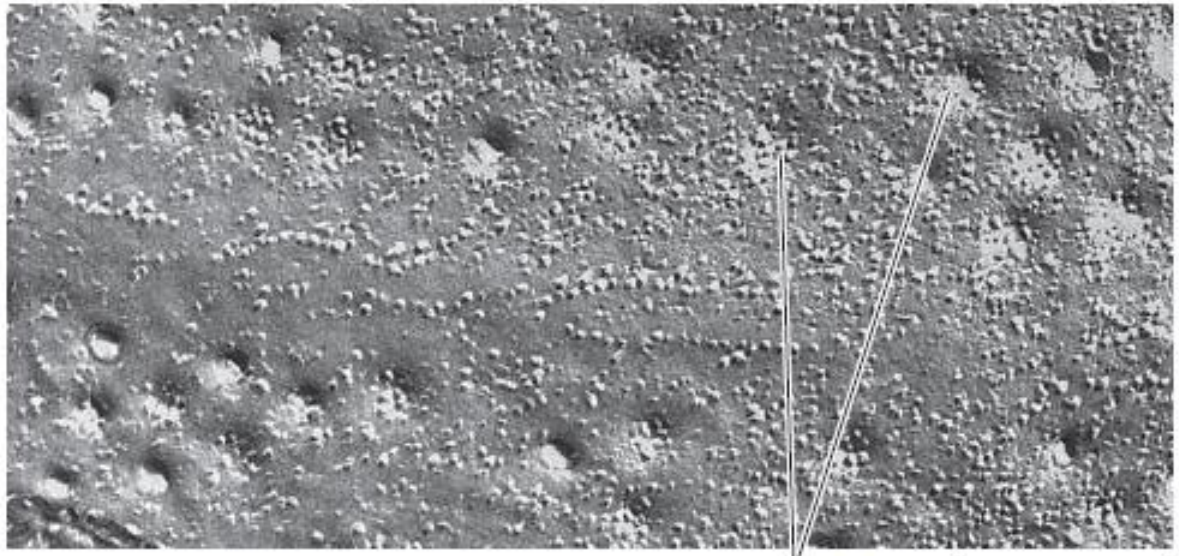


Vesicle fusions



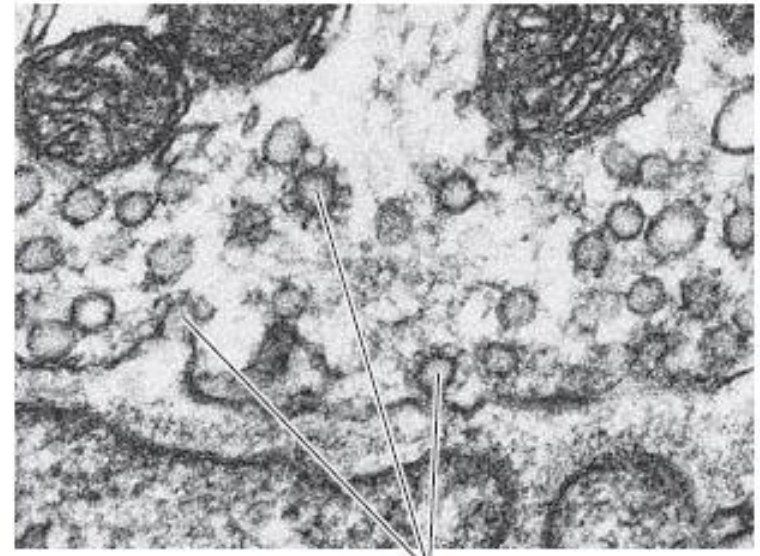
Vesicle fusions

C Endocytosis

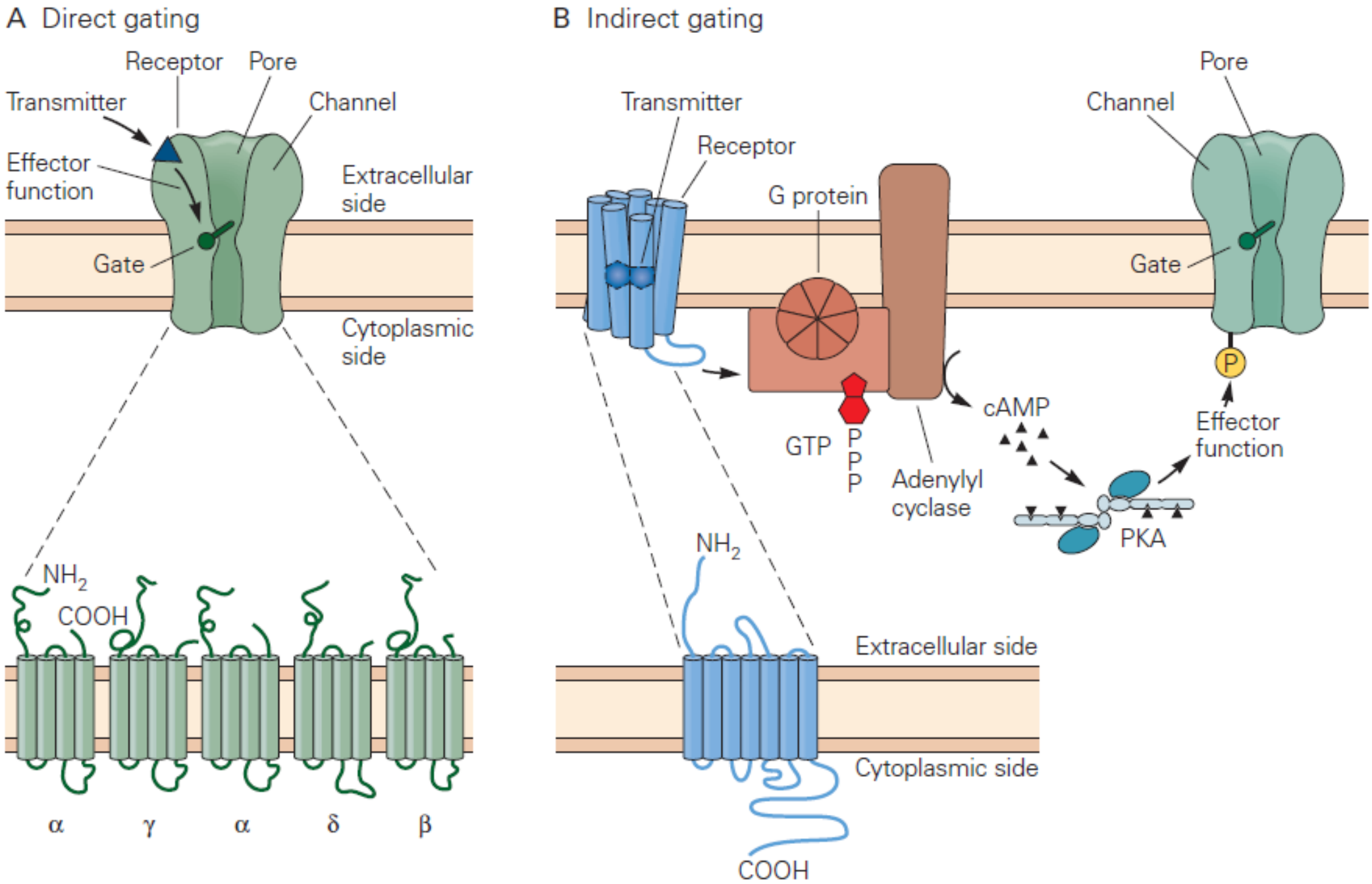


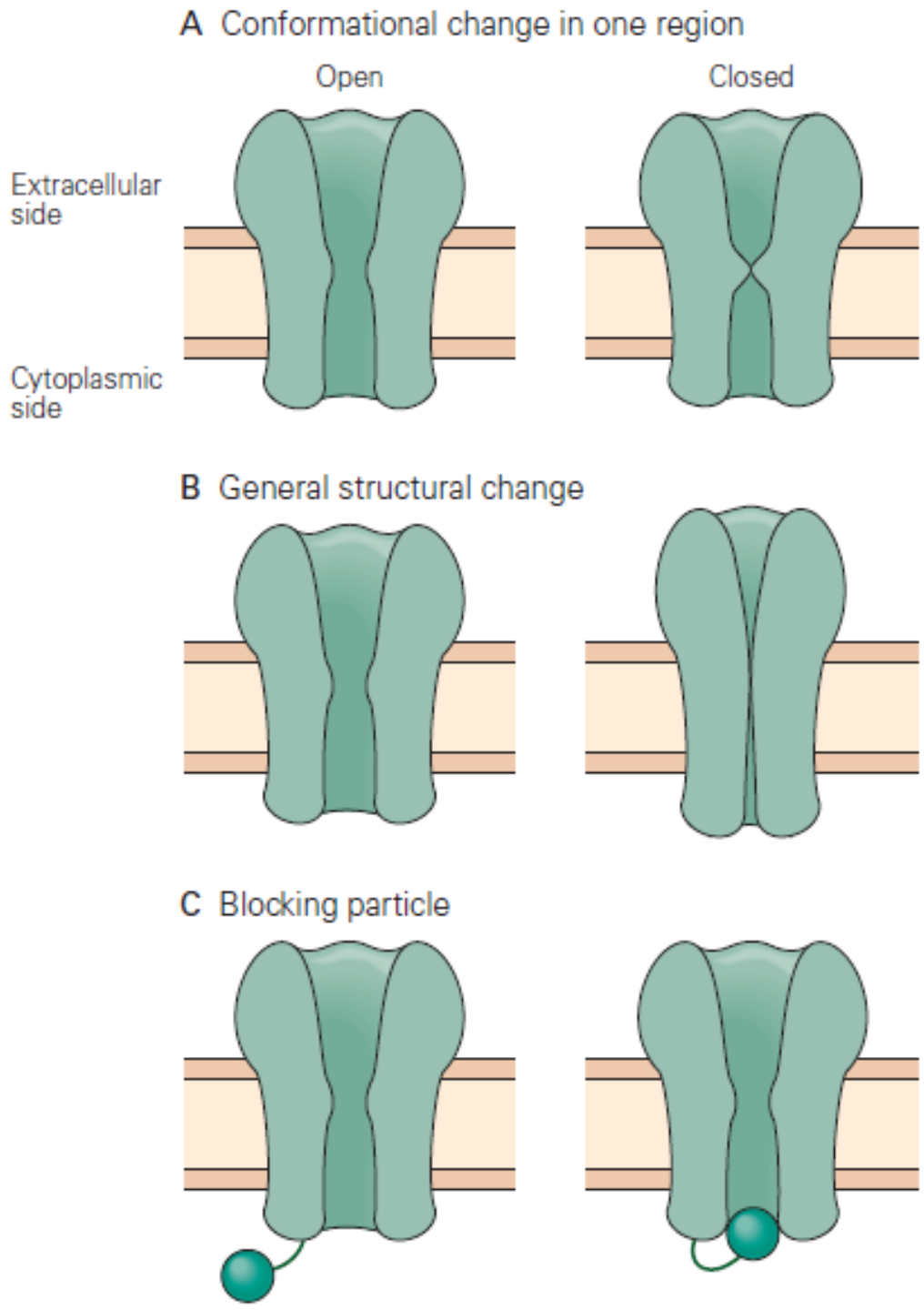
Coated pits

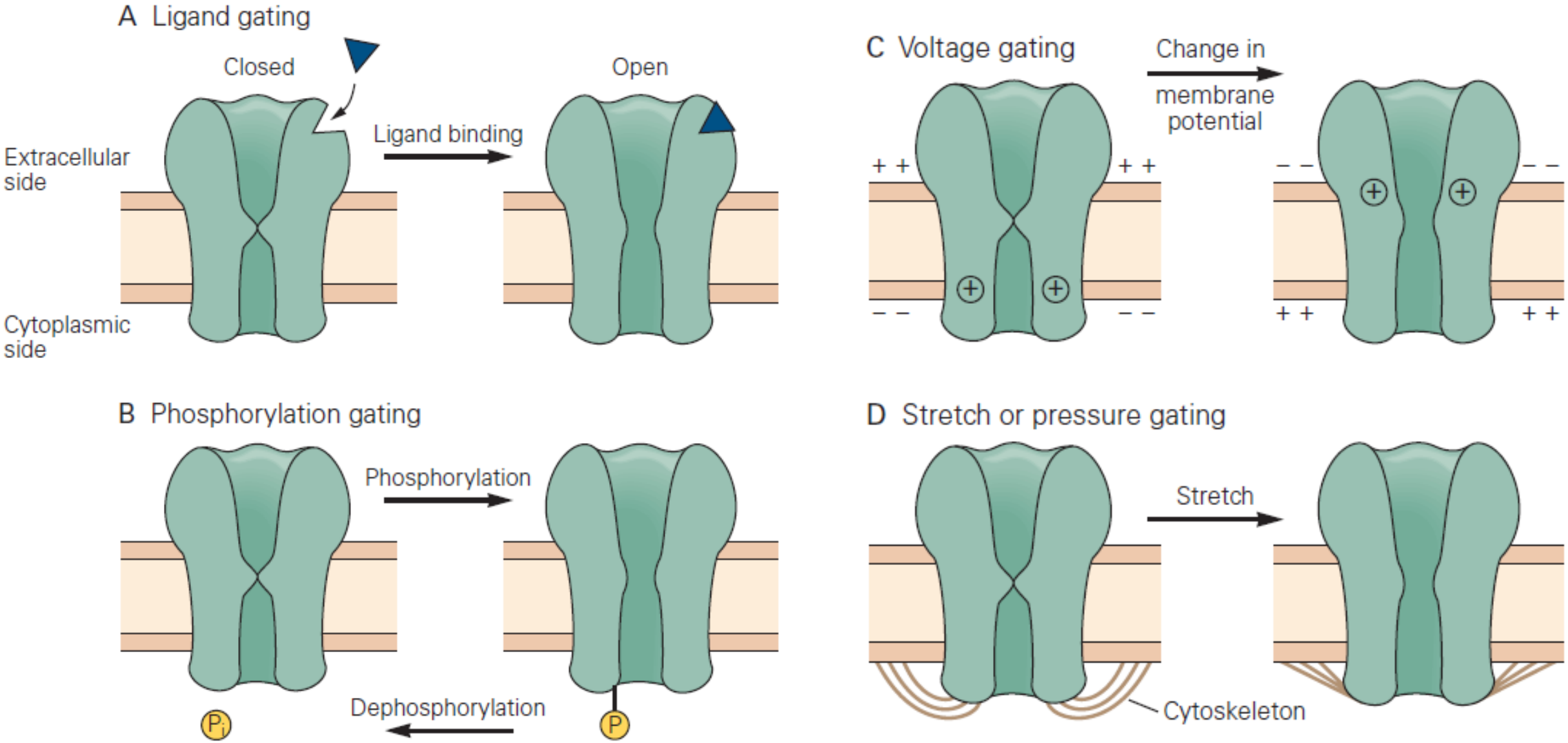
100 nm

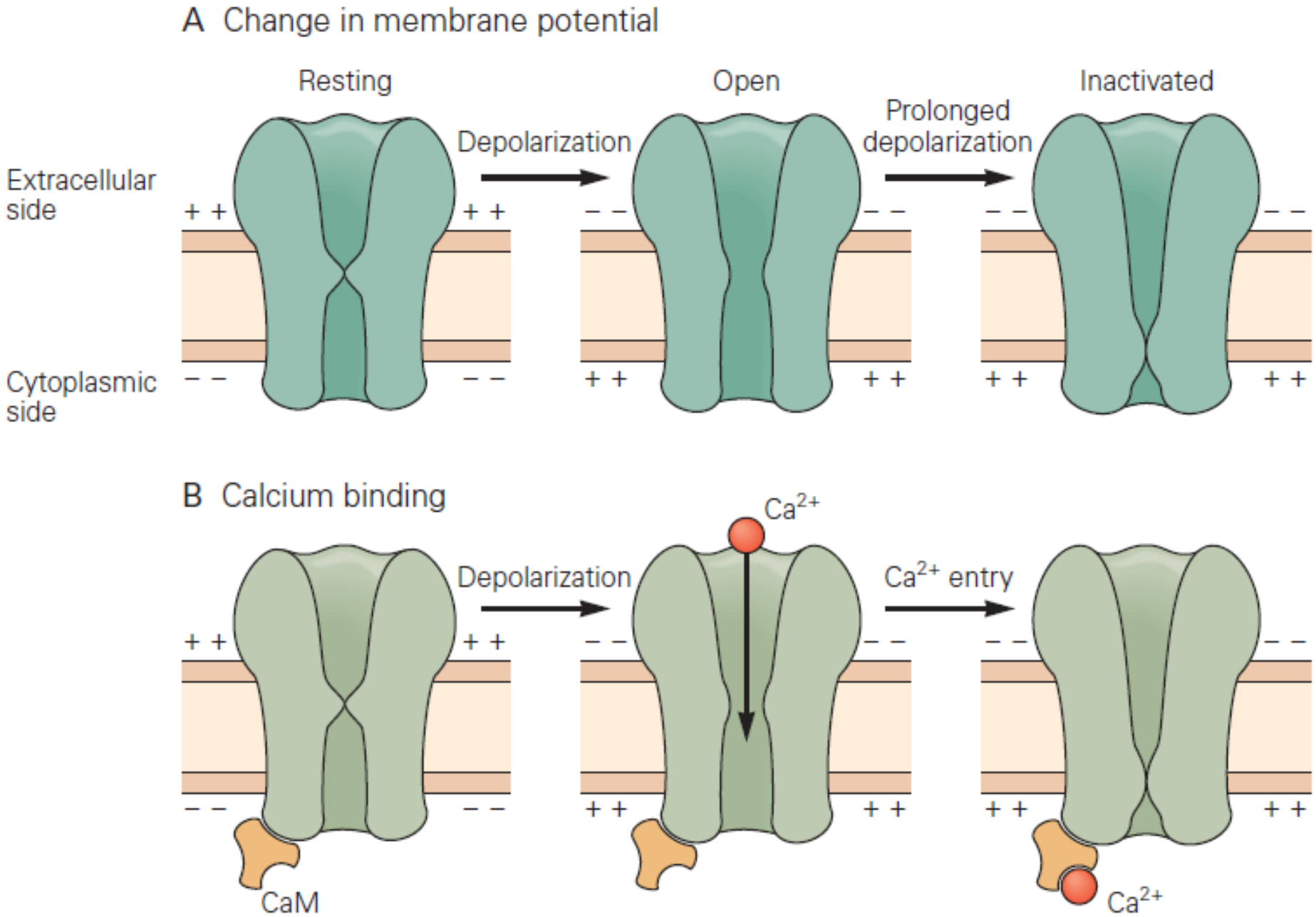


Coated vesicles and pits

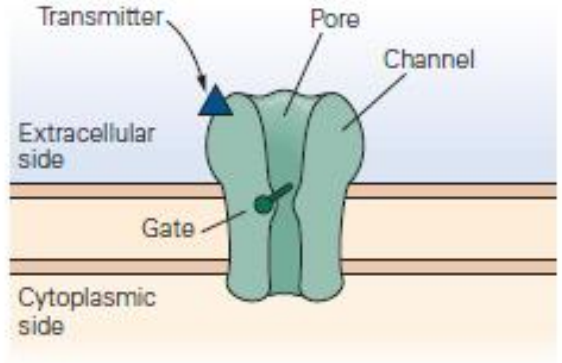

A Direct gating
Receptor
Pore
Transmitter
Channel
Effector function
Extracellular side
Gate
Cytoplasmic side
NH2
COOH
α
γ
α
δ
β
B Indirect gating
Transmitter
Receptor
G protein
Pore
Channel
Gate
P
Effector function
cAMP
GTP
P
P
P
Adenylyl cyclase
PKA
NH2
Extracellular side
Cytoplasmic side
COOH


A Conformational change in one region
Open
Closed
Extracellular side
Cytoplasmic side
B General structural change
C Blocking particle


A Ligand gating
Closed
Open
Ligand binding
Extracellular side
Cytoplasmic side
B Phosphorylation gating
Phosphorylation
Dephosphorylation
Pi
P
C Voltage gating
Change in membrane potential
+ +
– –
D Stretch or pressure gating
Stretch
Cytoskeleton

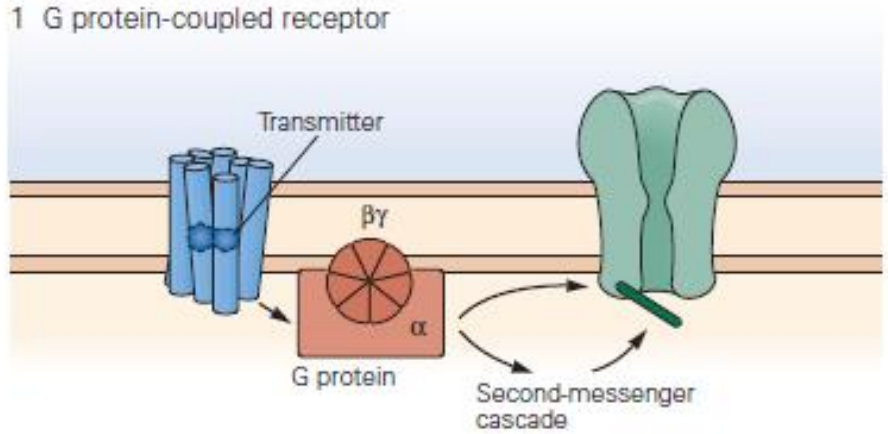

A Change in membrane potential
Resting
Open
Inactivated
Depolarization
Prolonged depolarization
Extracellular side
Cytoplasmic side
+ +
– –
B Calcium binding
Ca2+
Depolarization
Ca2+ entry
CaM
Ca2+

A Direct gating

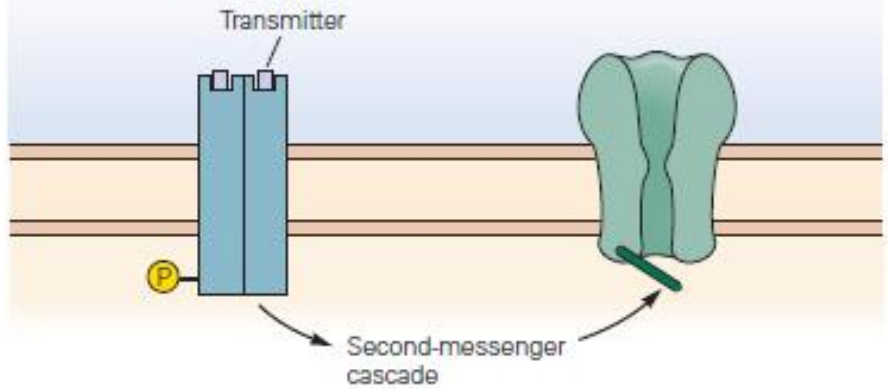


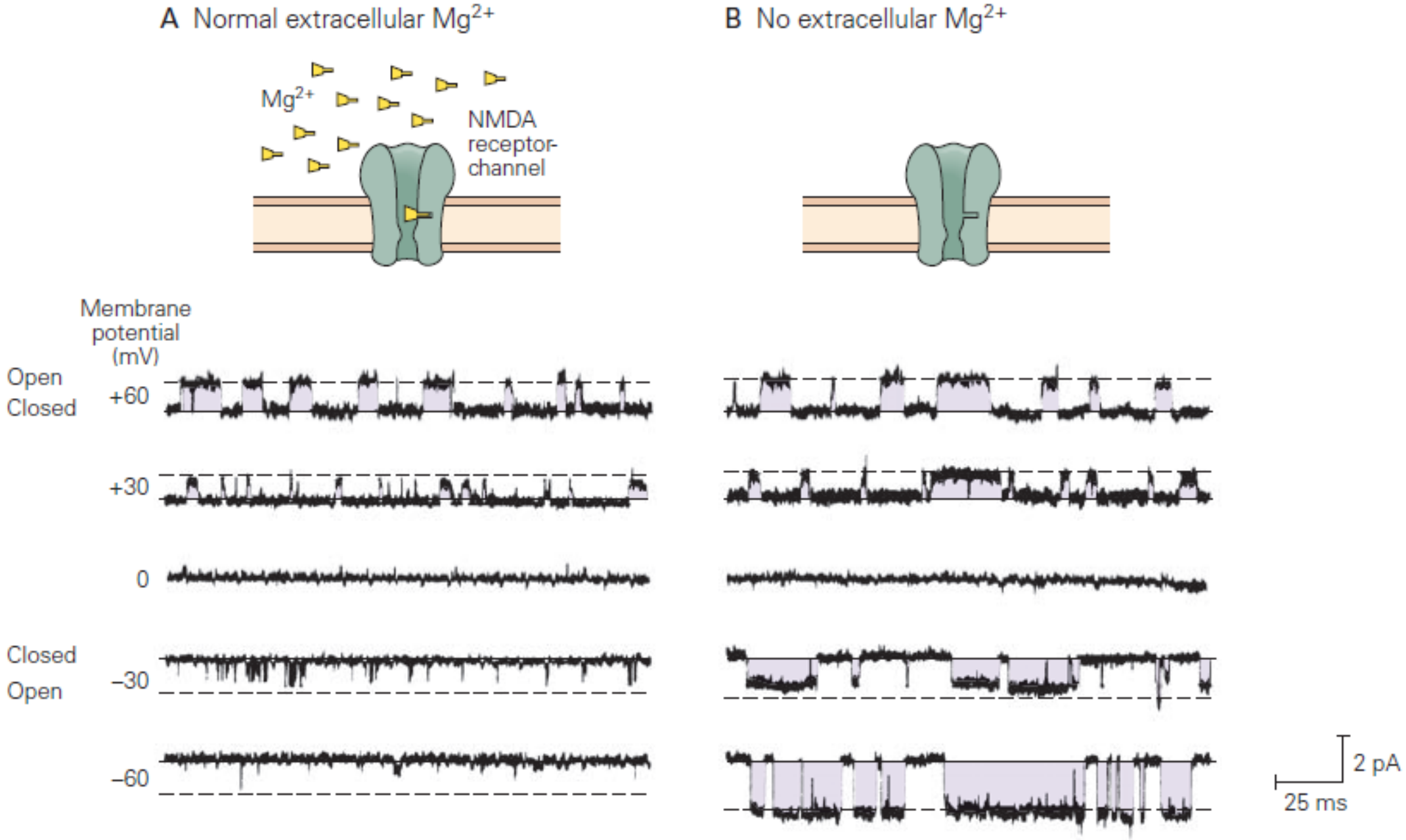

B Indirect gating

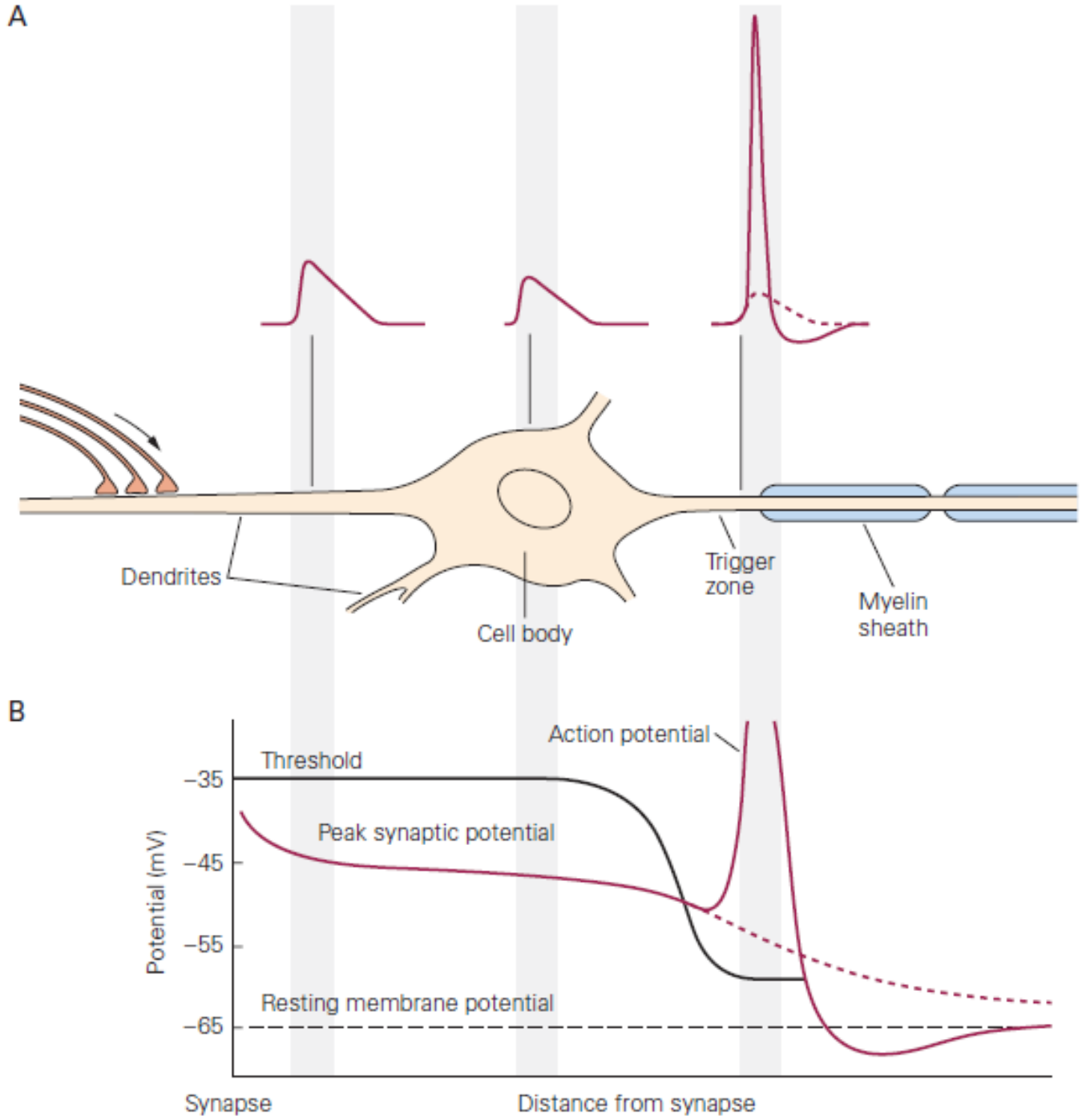
1 G protein-coupled receptor

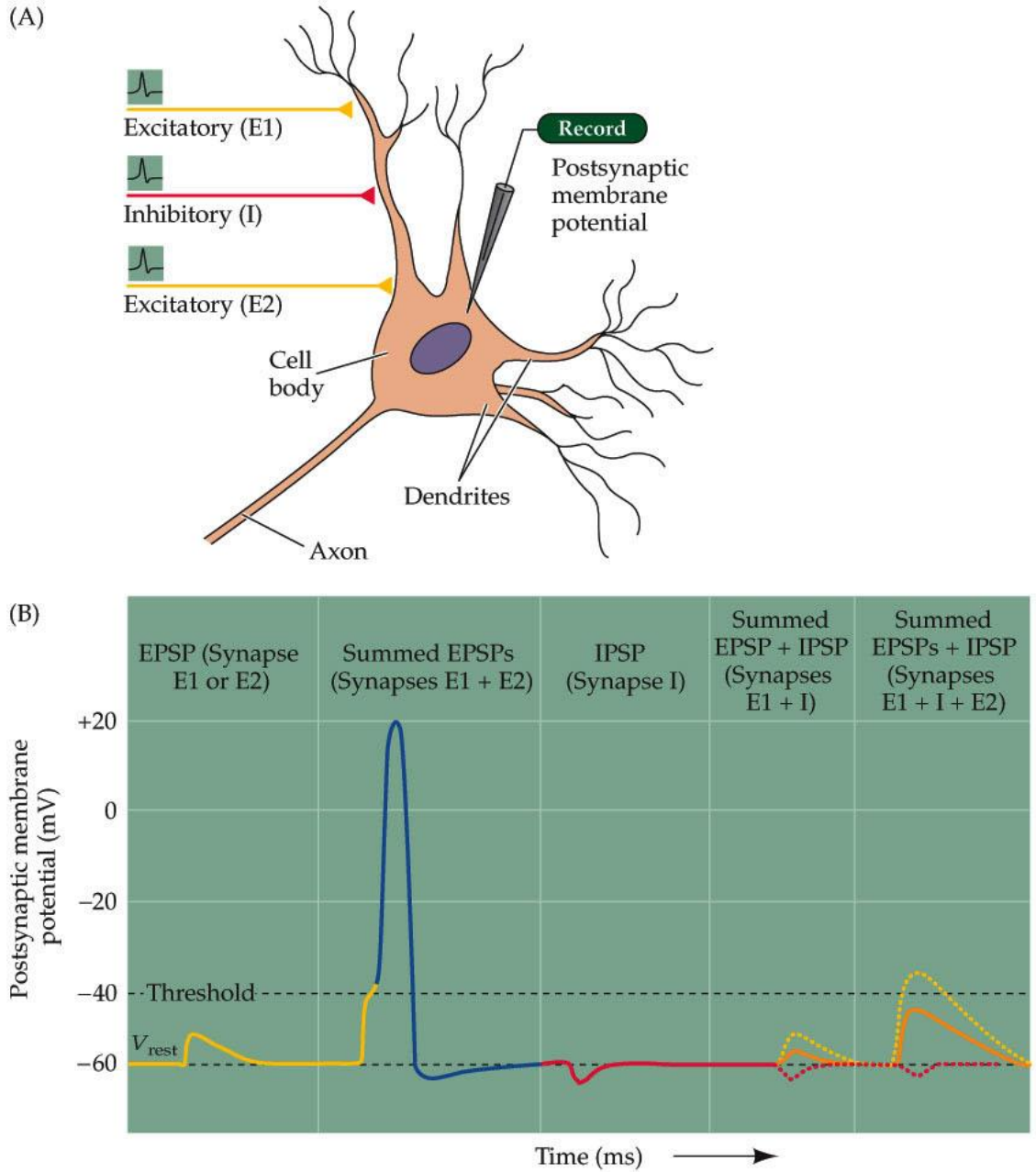



2 Receptor tyrosine kinase




A Normal extracellular $Mg^{2+}$
B No extracellular $Mg^{2+}$
$Mg^{2+}$
NMDA receptor-channel
Membrane potential (mV)
Open
Closed
+60
+30
0
Closed
Open
–30
–60
2 pA
25 ms


A
Dendrites
Cell body
Trigger zone
Myelin sheath
B
Action potential
Threshold
Peak synaptic potential
Resting membrane potential
Potential (mV)
−35
−45
−55
−65
Synapse
Distance from synapse




***NEUROSCIENCE, Fourth Edition,* Figure 5.21**

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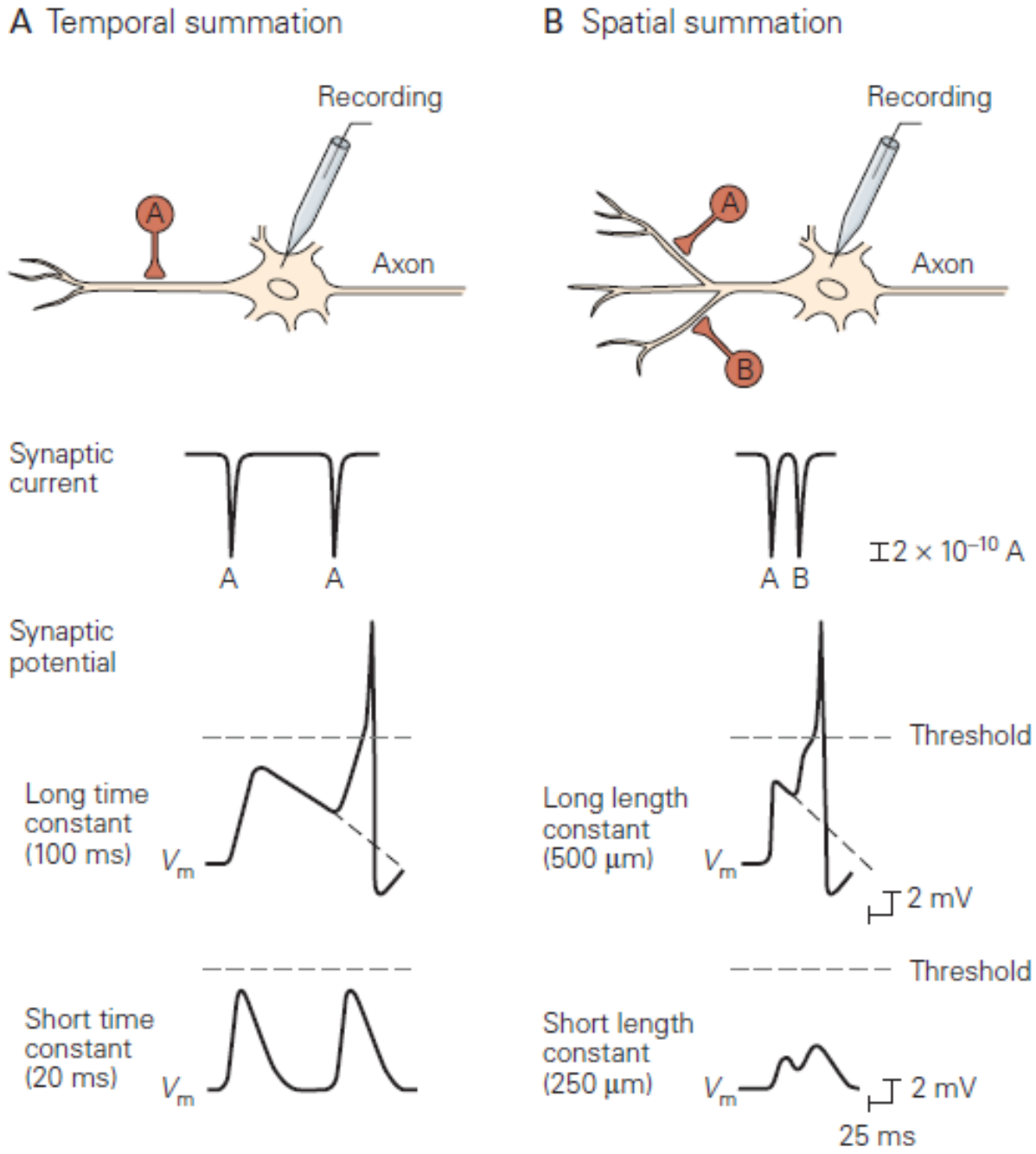
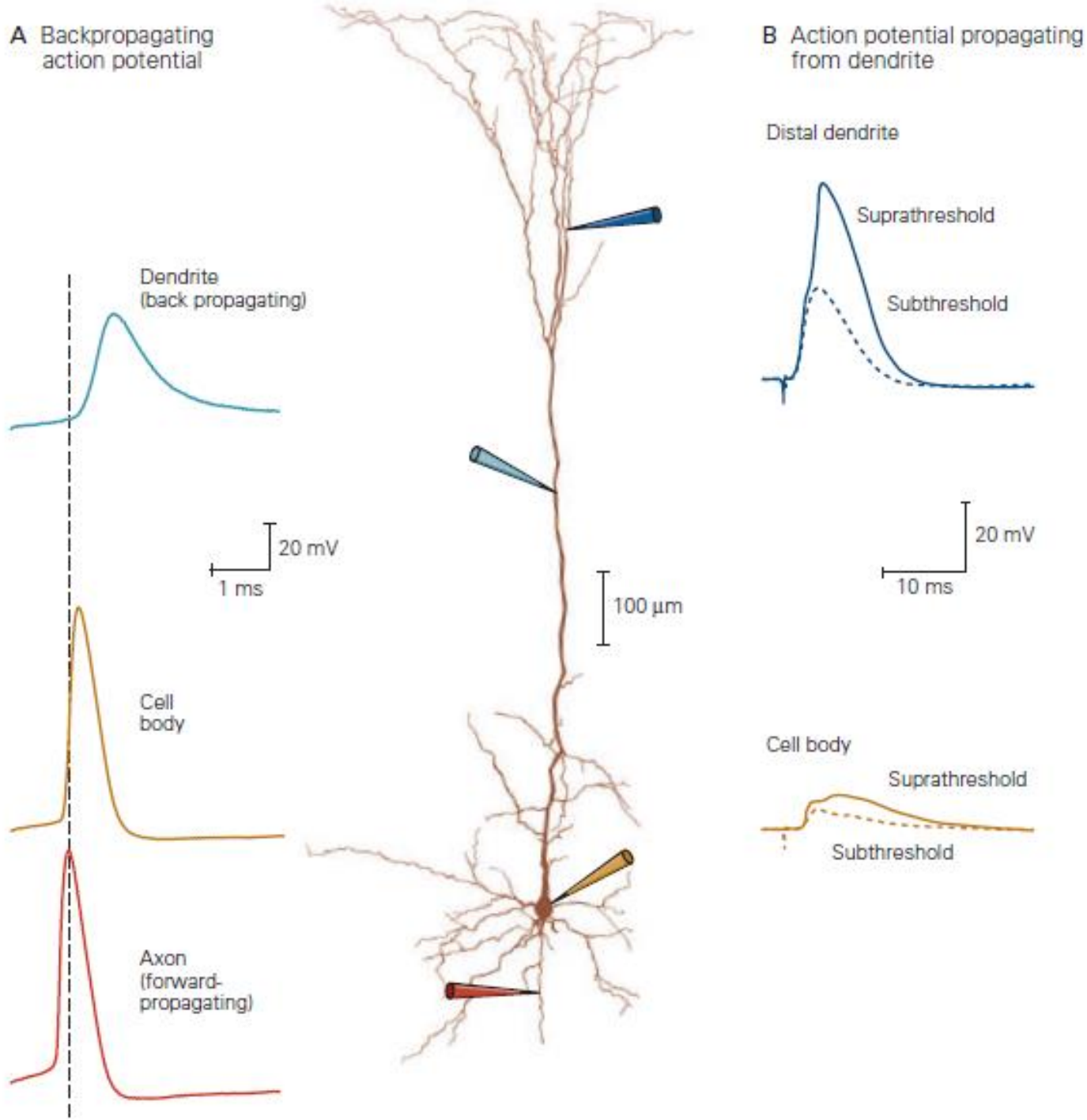
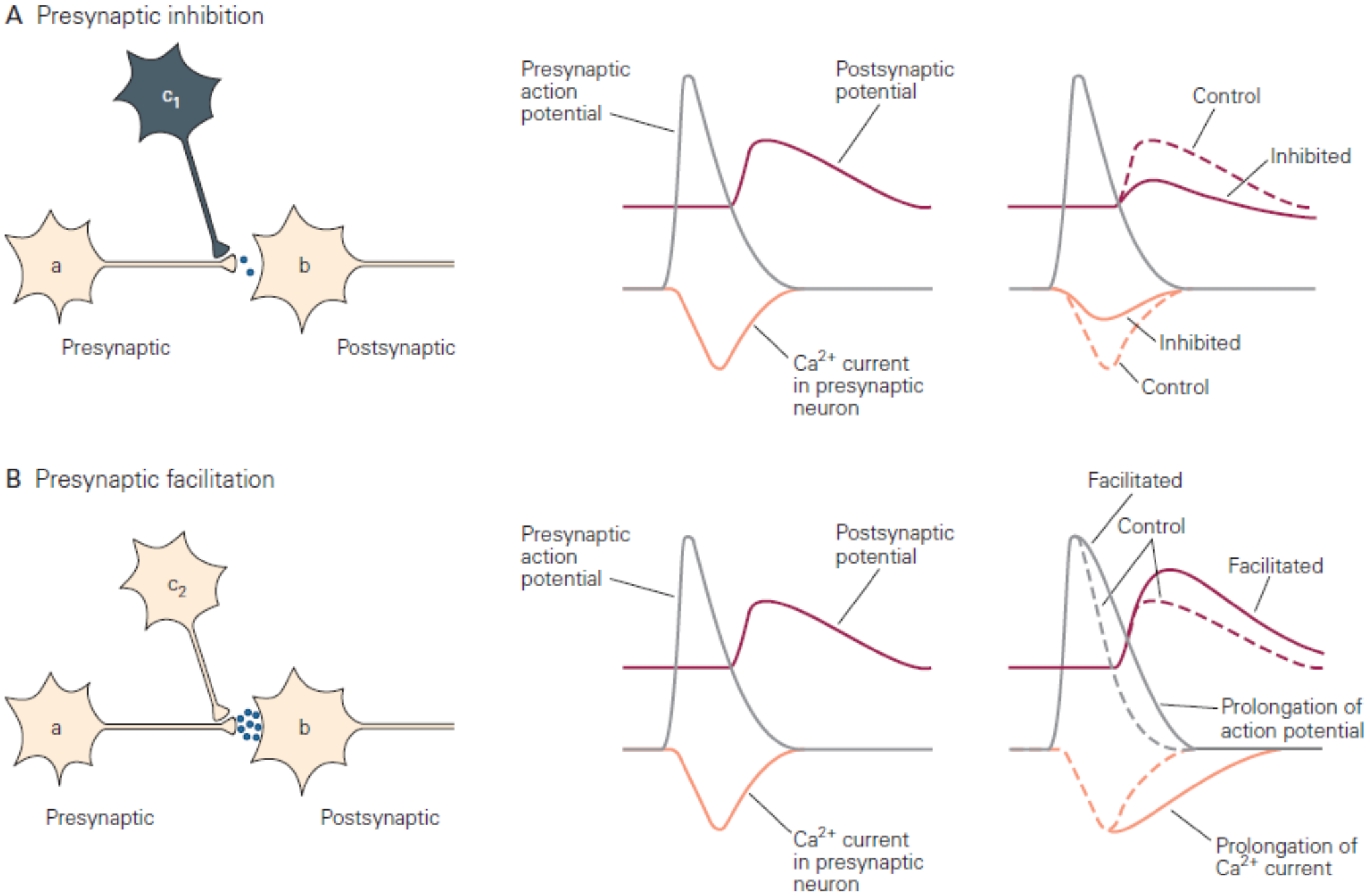

A Temporal summation
Recording
A
Axon
Synaptic current
A A
Synaptic potential
Long time constant (100 ms)
$V_m$
Short time constant (20 ms)
$V_m$
B Spatial summation
Recording
A
B
Axon
A B
2 × 10⁻¹⁰ A
Threshold
Long length constant (500 µm)
$V_m$
2 mV
Threshold
Short length constant (250 µm)
$V_m$
2 mV
25 ms


A Backpropagating action potential
Dendrite (back propagating)
20 mV
1 ms
Cell body
Axon (forward-propagating)
100 µm
B Action potential propagating from dendrite
Distal dendrite
Suprathreshold
Subthreshold
20 mV
10 ms
Cell body
Suprathreshold
Subthreshold


A Presynaptic inhibition
c1
a
b
Presynaptic
Postsynaptic
Presynaptic action potential
Postsynaptic potential
Ca2+ current in presynaptic neuron
Control
Inhibited
Inhibited
Control
B Presynaptic facilitation
c2
a
b
Presynaptic
Postsynaptic
Presynaptic action potential
Postsynaptic potential
Ca2+ current in presynaptic neuron
Facilitated
Control
Facilitated
Prolongation of action potential
Prolongation of Ca2+ current

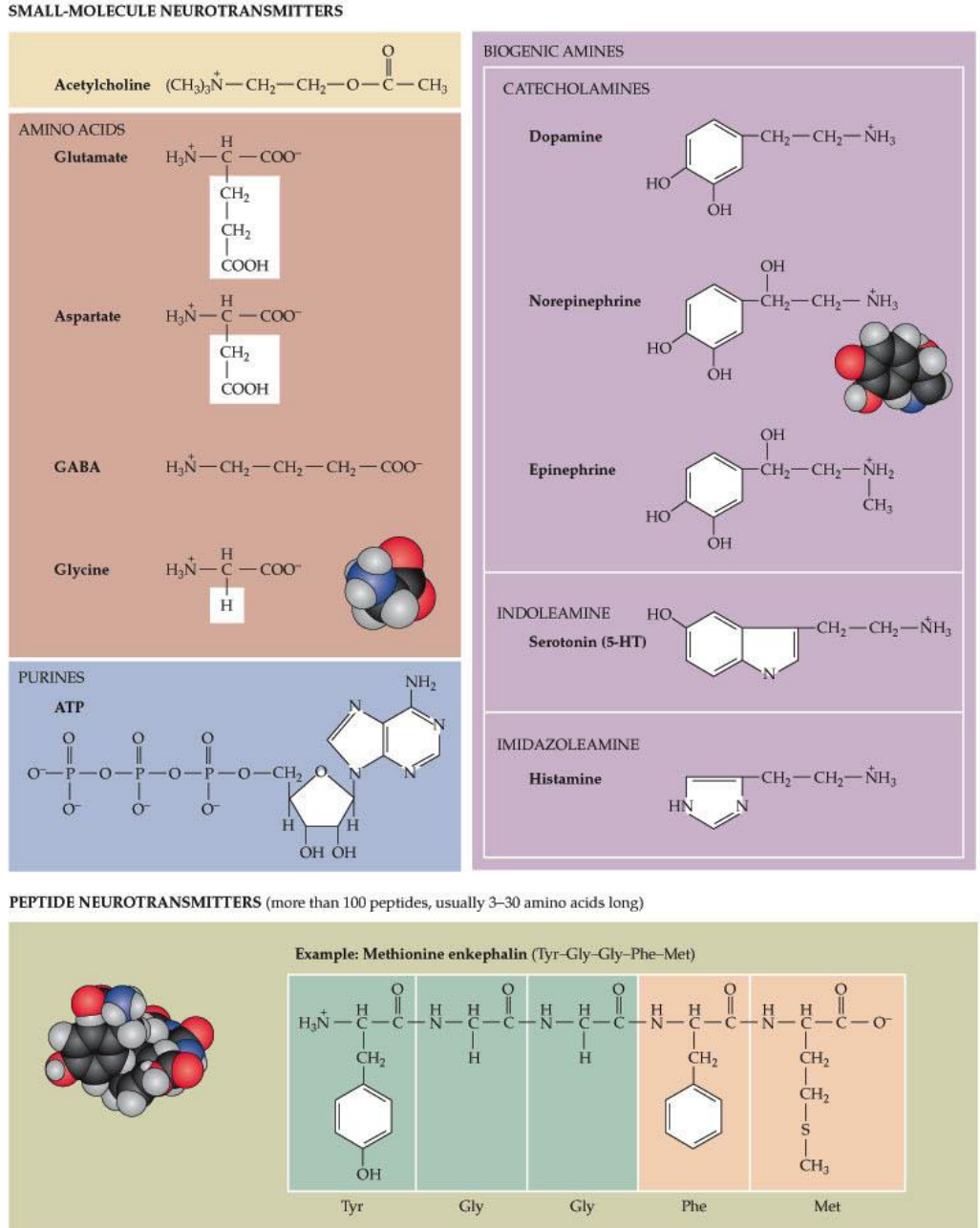
# Neurotransmisores

# Classic Characteristics:

- Synthesized in the neuron.
- Become localized in presynaptic terminal.
- Bind to receptor site on postsynaptic membrane.
- Removed by a specific mechanism from its specific site of action.

**Table 13–1** Small-Molecule Transmitter Substances and Their Precursors

| Transmitter | Precursor |
|---|---|
| Acetylcholine | Choline |
| Biogenic amines | |
| Dopamine | Tyrosine |
| Norepinephrine | Tyrosine |
| Epinephrine | Tyrosine |
| Serotonin | Tryptophan |
| Histamine | Histidine |
| Melatonin | Serotonin |
| Amino acids | |
| Aspartate | Oxaloacetate |
| γ-Aminobutyric acid | Glutamine |
| Glutamate | Glutamine |
| Glycine | Serine |
| ATP | ADP |
| Adenosine | ATP |
| Arachidonic acid | Phospholipids |
| Carbon monoxide | Heme |
| Nitric oxide | Arginine |




**NEUROSCIENCE, Fourth Edition, Figure 6.1**

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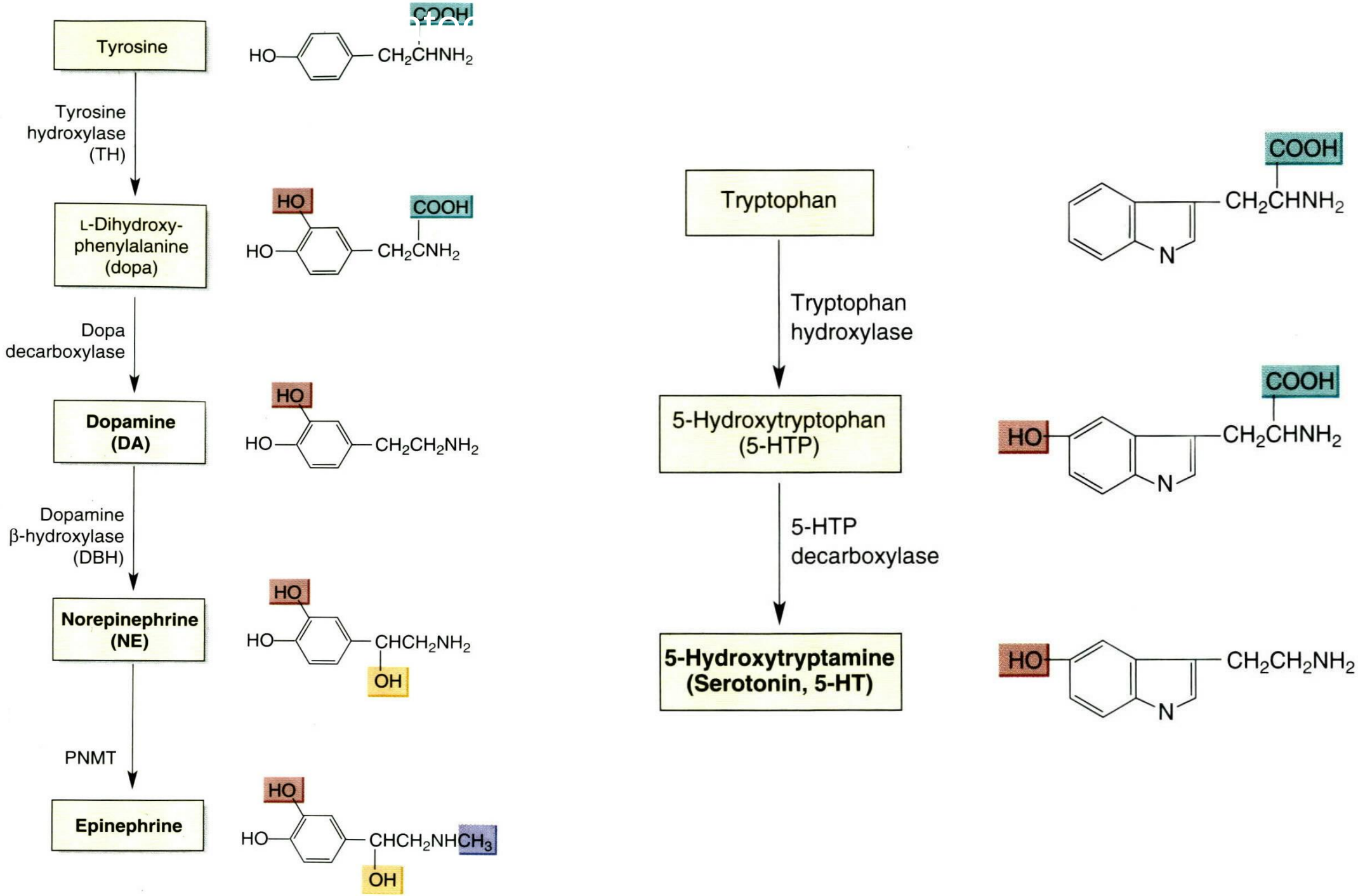

Tyrosine
Tyrosine hydroxylase (TH)
L-Dihydroxy-phenylalanine (dopa)
Dopa decarboxylase
Dopamine (DA)
Dopamine β-hydroxylase (DBH)
Norepinephrine (NE)
PNMT
Epinephrine
Tryptophan
Tryptophan hydroxylase
5-Hydroxytryptophan (5-HTP)
5-HTP decarboxylase
5-Hydroxytryptamine (Serotonin, 5-HT)

# Classification

- Small molecule transmitters:
    - Amino acids:
        - Dietary amino acids.
        - GABA
    - Monoamines:
        - Catecholamines.
        - Indoleamines.
- Acetylcholine.

# Amino Acids

- Dietary:

  Aspartate.

  Glycine.
- Gamma aminobutyric acid (GABA):

  From decarboxylation of glutamate.

# Monoamines

- Catecholamines:

  Derived from tyrosine.

  Include:

    Dopamine.

    Norepinephrine.

    Epinephrine.

# Monoamines

- Indoleamine:

  Derived from tryptophan.

  Includes:

    Serotonin.

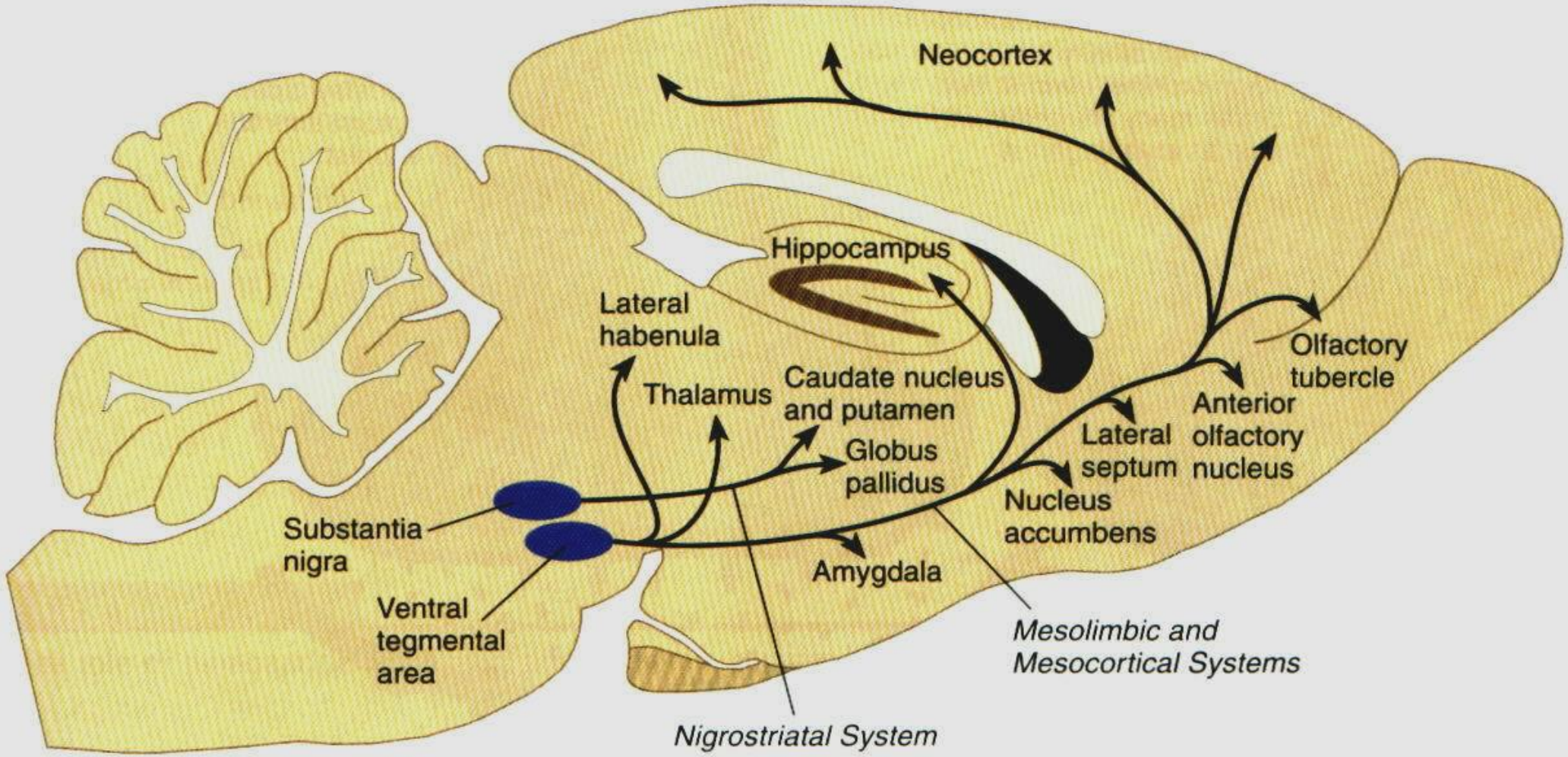



**figure 4.13**

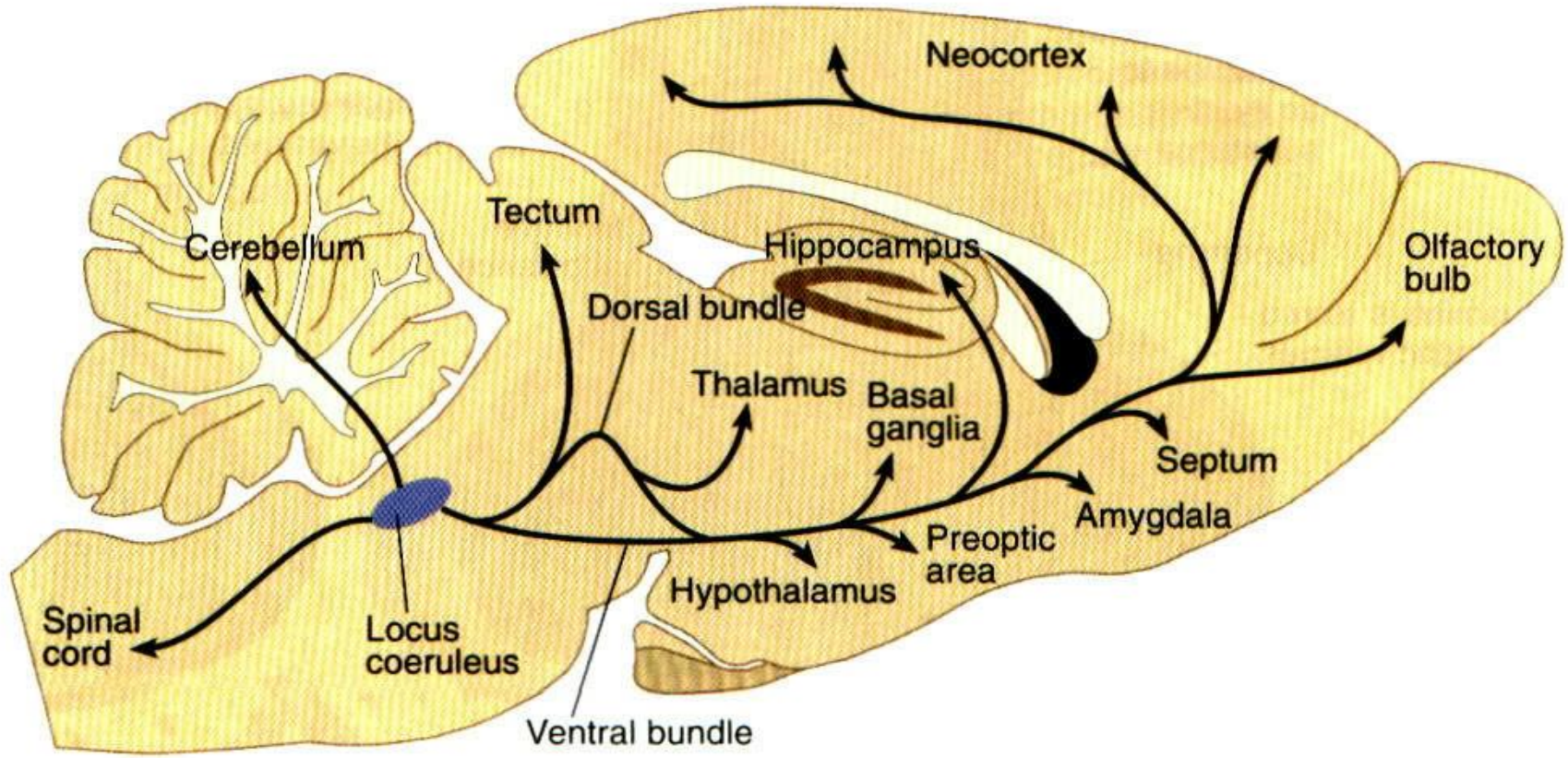
A schematic midsagittal section of a rat brain, showing the locations of the most important groups of dopaminergic neurons and the distribution of their axons and terminal buttons.

(Adapted from Fuxe et al., 1985.)

**figure 4.16**

A schematic midsagittal section of a rat brain, showing the locations of the most important groups of noradrenergic neurons and the distribution of their axons and terminal buttons.

(Adapted from Cotman and McGaugh, 1980.)



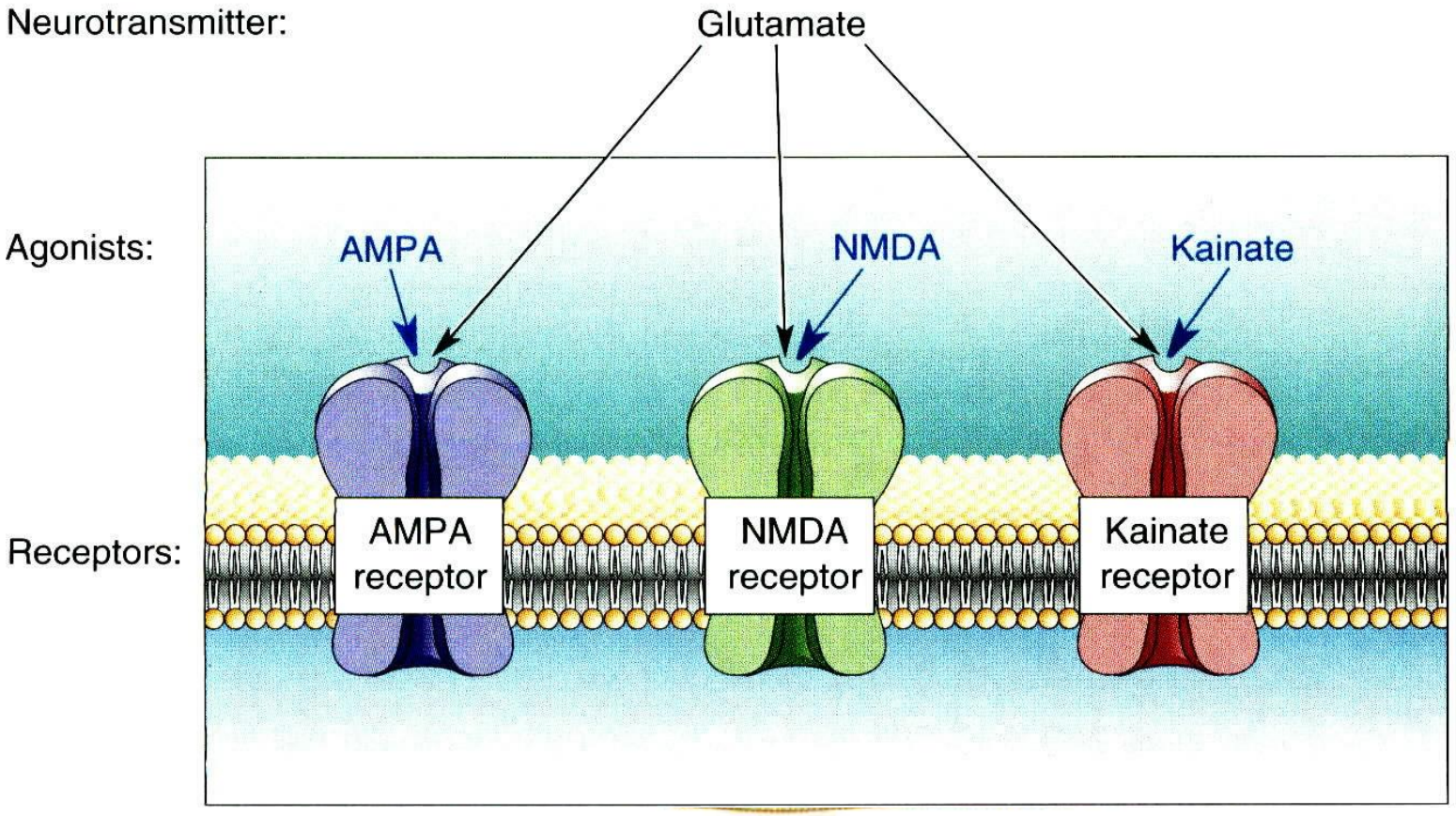
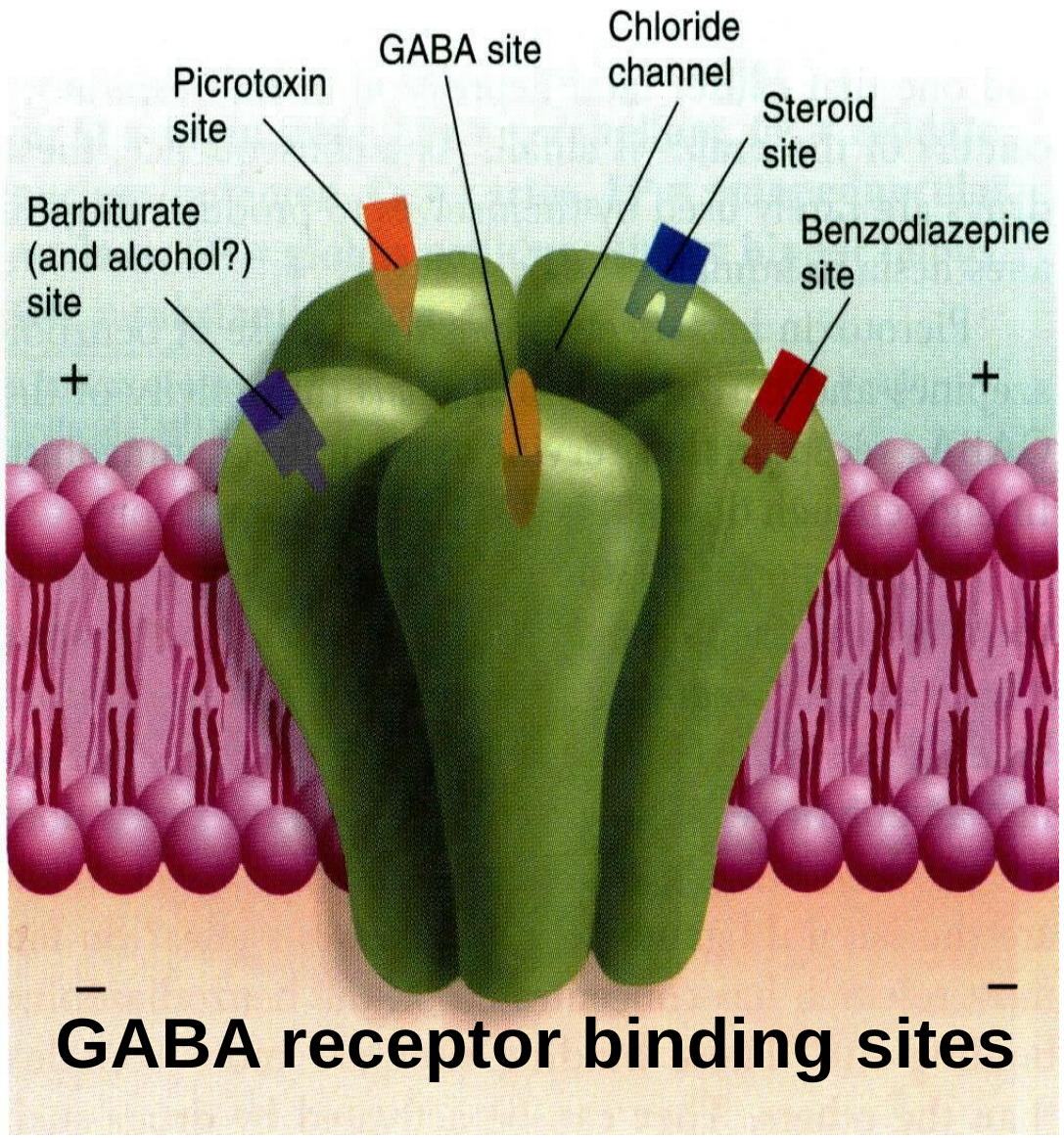



**Figure 6.8**

**The neuropharmacology of glutamatergic synaptic transmission.** There are three main subtypes of glutamate receptors, each of which binds glutamate and each of which is activated selectively by a different agonist.

**A schematic illustration of a $GABA_A$ receptor, with its binding sites.**




# GABA receptor binding sites

**Table 15-3** Some Families of Neuroactive Peptides

| Family | Peptide members |
|---|---|
| Opioids | Opiocortins, enkephalins, dynorphin, FMRFamide |
| Neurohypophyseal hormones | Vasopressin, oxytocin, neurophysins |
| Tachykinins | Substance P, physalaemin, kassinin, uperolein, eledoisin, bombesin, substance K |
| Secretins | Secretin, glucagon, vasoactive intestinal peptide, gastric inhibitory peptide, growth hormone–releasing factor, peptide histidine isoleucineamide |
| Insulins | Insulin, insulin-like growth factors I and II |
| Somatostatins | Somatostatins, pancreatic polypeptide |
| Gastrins | Gastrin, cholecystokinin |

(C)

| Receptor | AMPA | NMDA | Kainate | GABA | Glycine | nACh | Serotonin | Purines |
|---|---|---|---|---|---|---|---|---|
| Subunits (combination of 4 or 5 required for each receptor type) | Glu R1 | NR1 | Glu R5 | $\alpha_{1-7}$ | α1 | $\alpha_{2-9}$ | 5-$HT_3$ | $P_{2X1}$ |
| | Glu R2 | NR2A | Glu R6 | $\beta_{1-4}$ | α2 | $\beta_{1-4}$ | | $P_{2X2}$ |
| | Glu R3 | NR2B | Glu R7 | $\gamma_{1-4}$ | α3 | γ | | $P_{2X3}$ |
| | Glu R4 | NR2C | KA1 | δ | α4 | δ | | $P_{2X4}$ |
| | | NR2D | KA2 | ε | β | | | $P_{2X5}$ |
| | | | | $\rho_{1-3}$ | | | | $P_{2X6}$ |
| | | | | | | | | $P_{2X7}$ |

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(B)

| Receptor class | Glutamate | $GABA_B$ | Dopamine | NE, Epi | Histamine | Serotonin | Purines | Muscarinic |
|---|---|---|---|---|---|---|---|---|
| Receptor subtype | Class I | $GABA_B$ R1 | $D1_A$ | α1 | H1 | 5-HT 1 | A type | M1 |
| | mGlu R1 | $GABA_B$ R2 | $D1_B$ | α2 | H2 | 5-HT 2 | A1 | M2 |
| | mGlu R5 | | D2 | β1 | H3 | 5-HT 3 | A2a | M3 |
| | Class II | | D3 | β2 | | 5-HT 4 | A2b | M4 |
| | mGlu R2 | | D4 | β3 | | 5-HT 5 | A3 | M5 |
| | mGlu R3 | | | | | 5-HT 6 | P type | |
| | Class III | | | | | 5-HT 7 | P2x | |
| | mGlu R4 | | | | | | P2y | |
| | mGlu R6 | | | | | | P2z | |
| | mGlu R7 | | | | | | P2t | |
| | mGlu R8 | | | | | | P2u | |

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