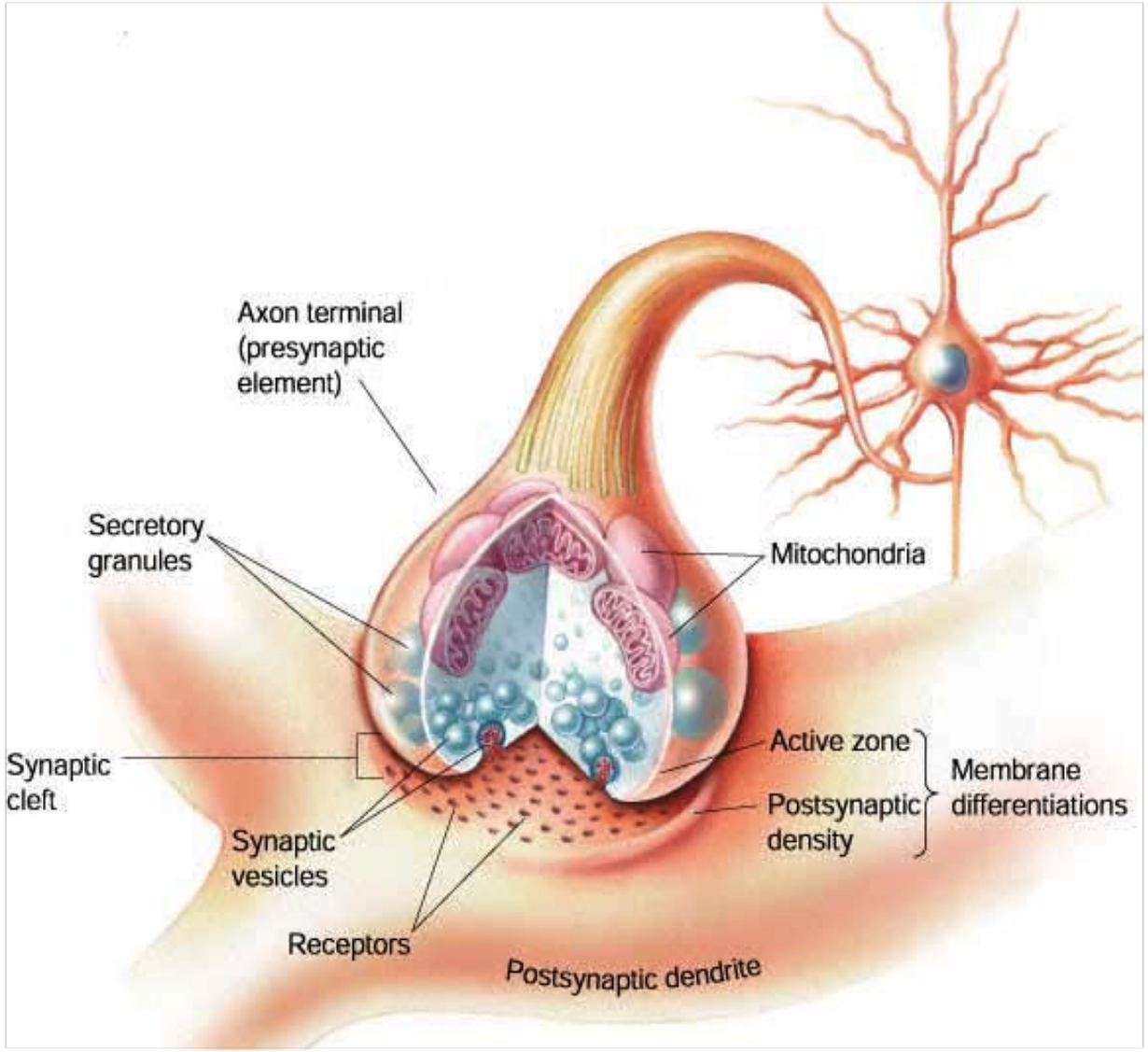
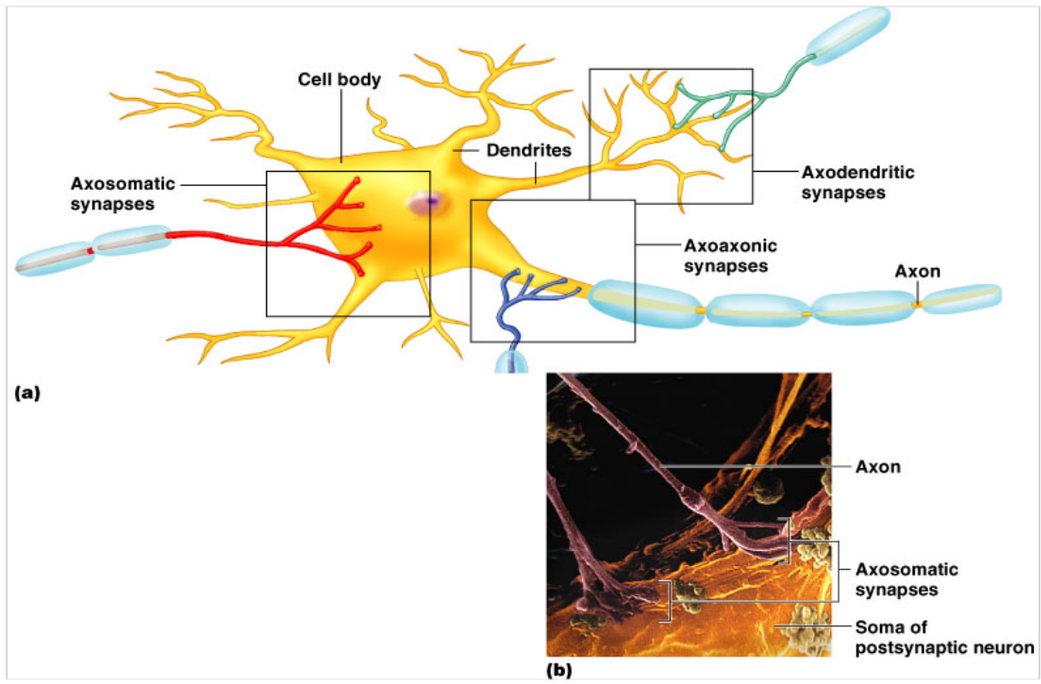
Chemical Signalling Between Neurons

The Synapse

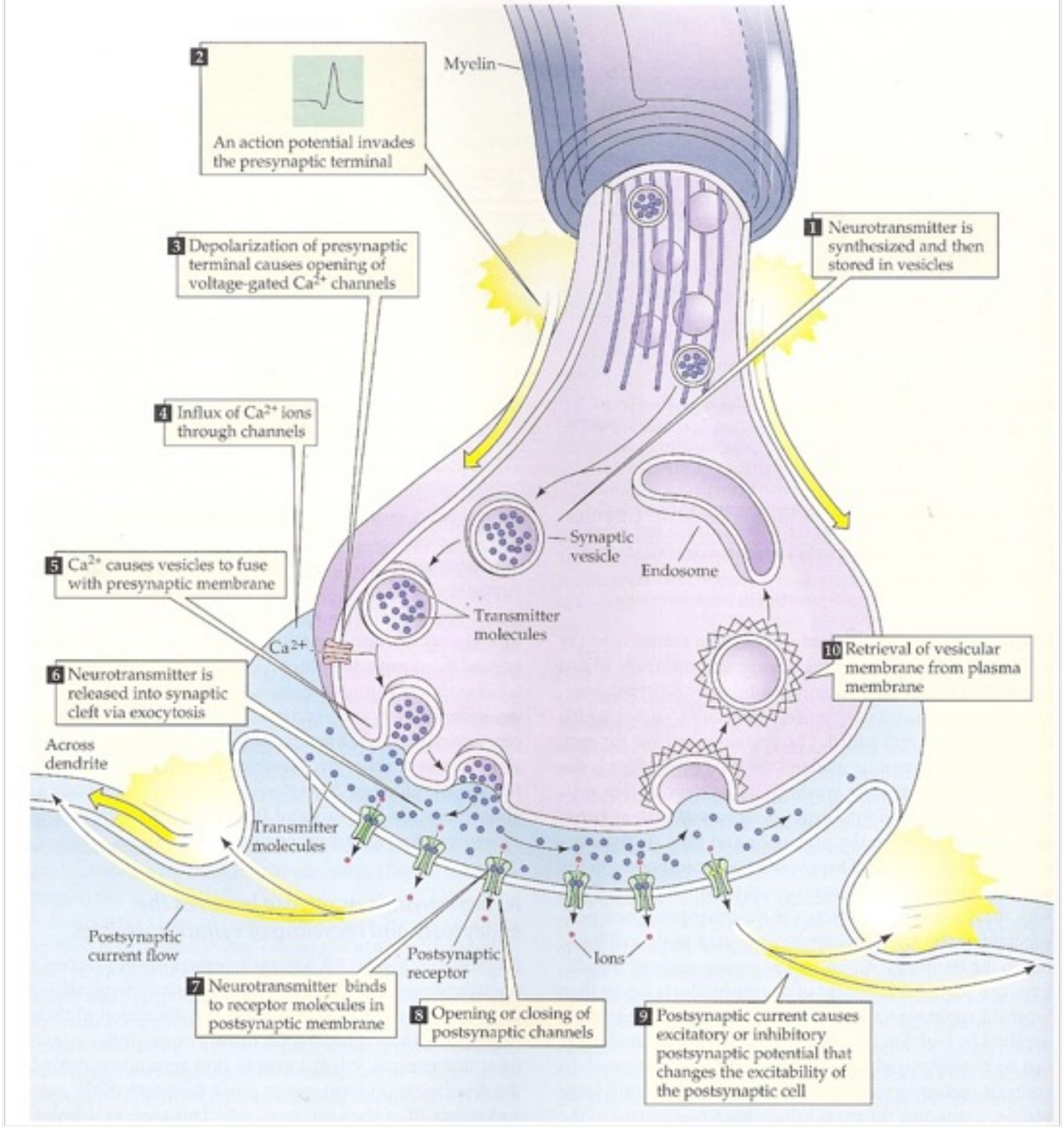


- Presynaptic & postsynaptic elements
- Synaptic cleft
- Vesicles
- Active zones
- Receptors

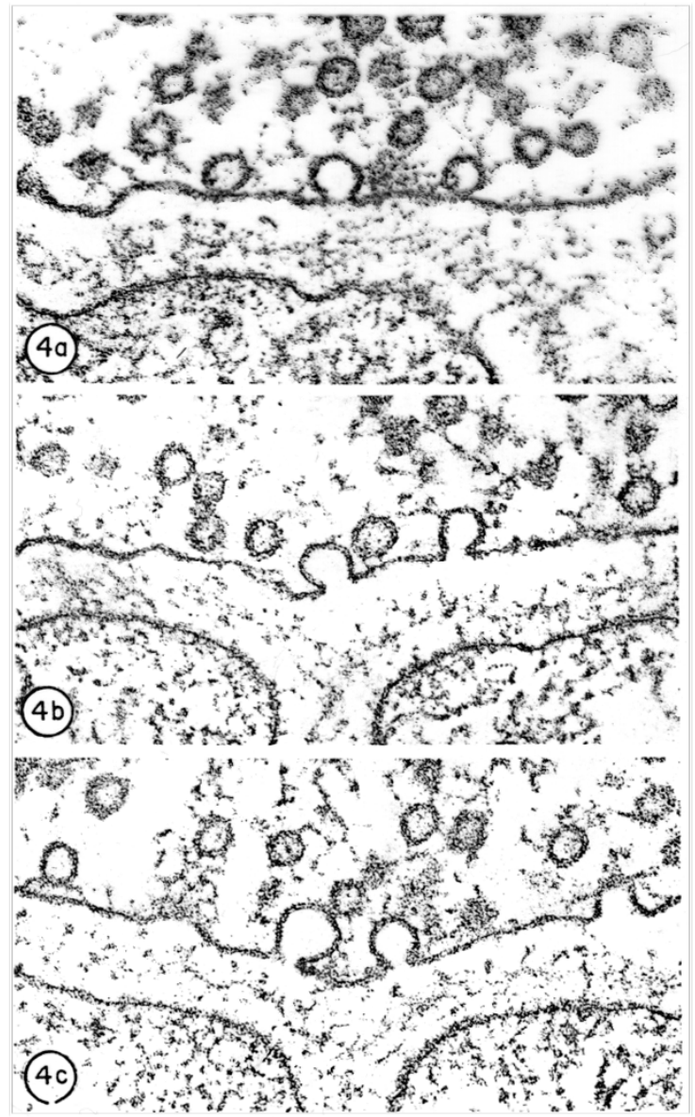
- Types of synaptic connection: axodendritic, axosomatic, axoaxonic



Synaptic Neurotransmitter Release



Exocytosis



Termination of Synaptic Transmission

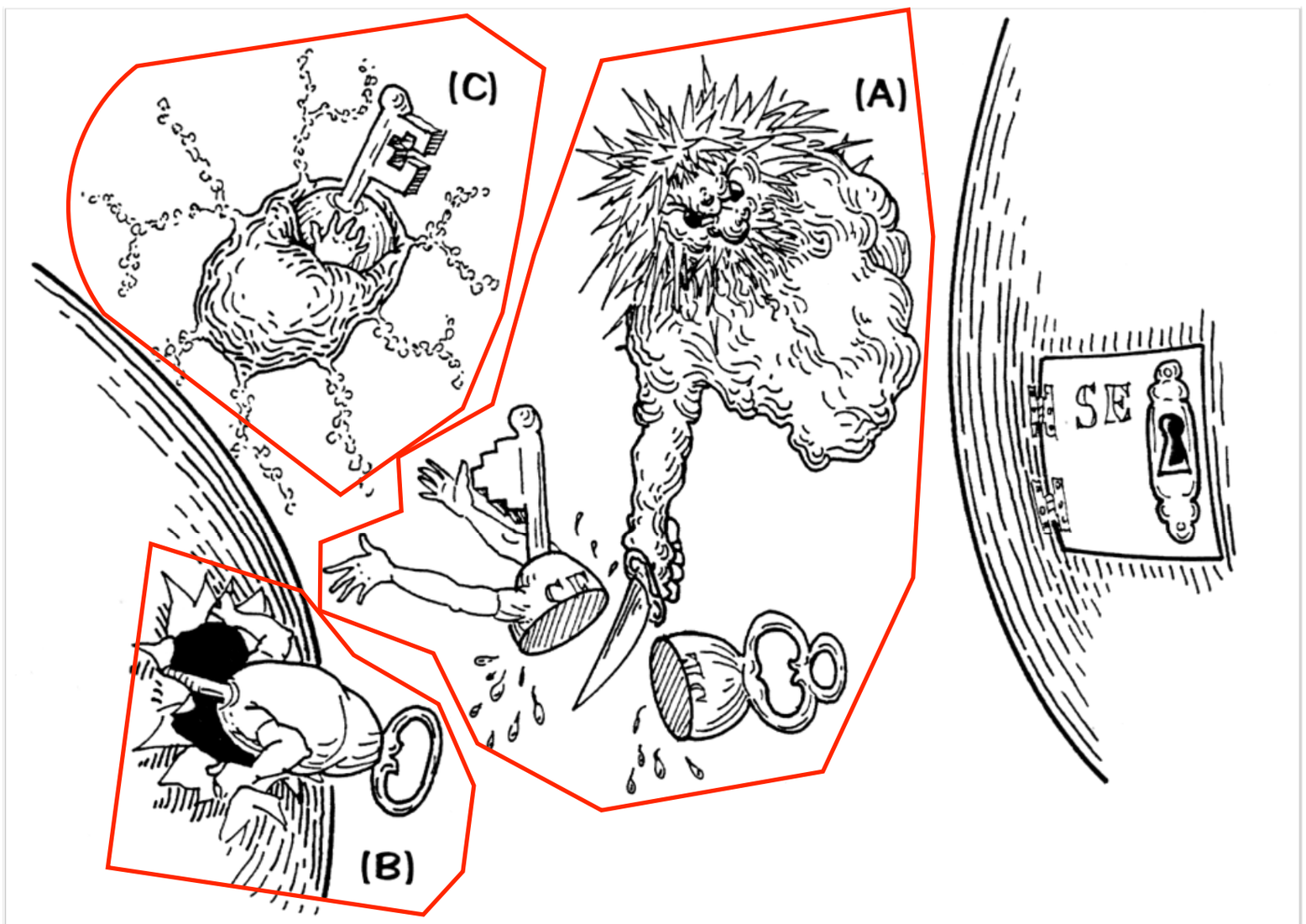


FIGURE 2-11 Neurotransmitters in the synaptic space are extracted from the synapse by three processes. The first consists of enzymes, which destroy the neurotransmitter molecule (A). The second consists of the reuptake of the neurotransmitters by the presynaptic neuron (B). The third consists of uptake of neurotransmitters by glial cells (C).

A. Enzymatic metabolism

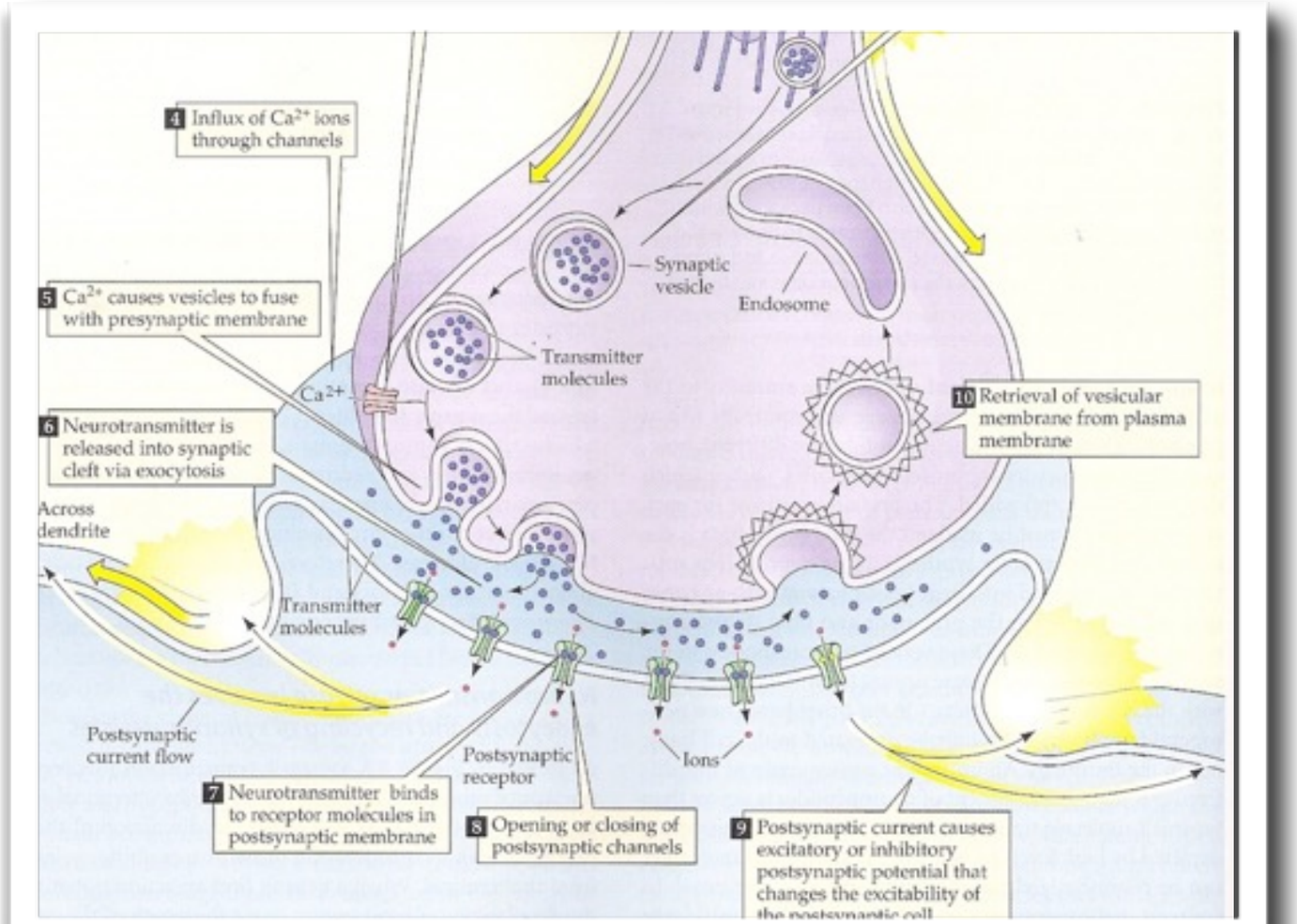
B. Reuptake

C. Uptake by glial cells

Synaptic Potentials

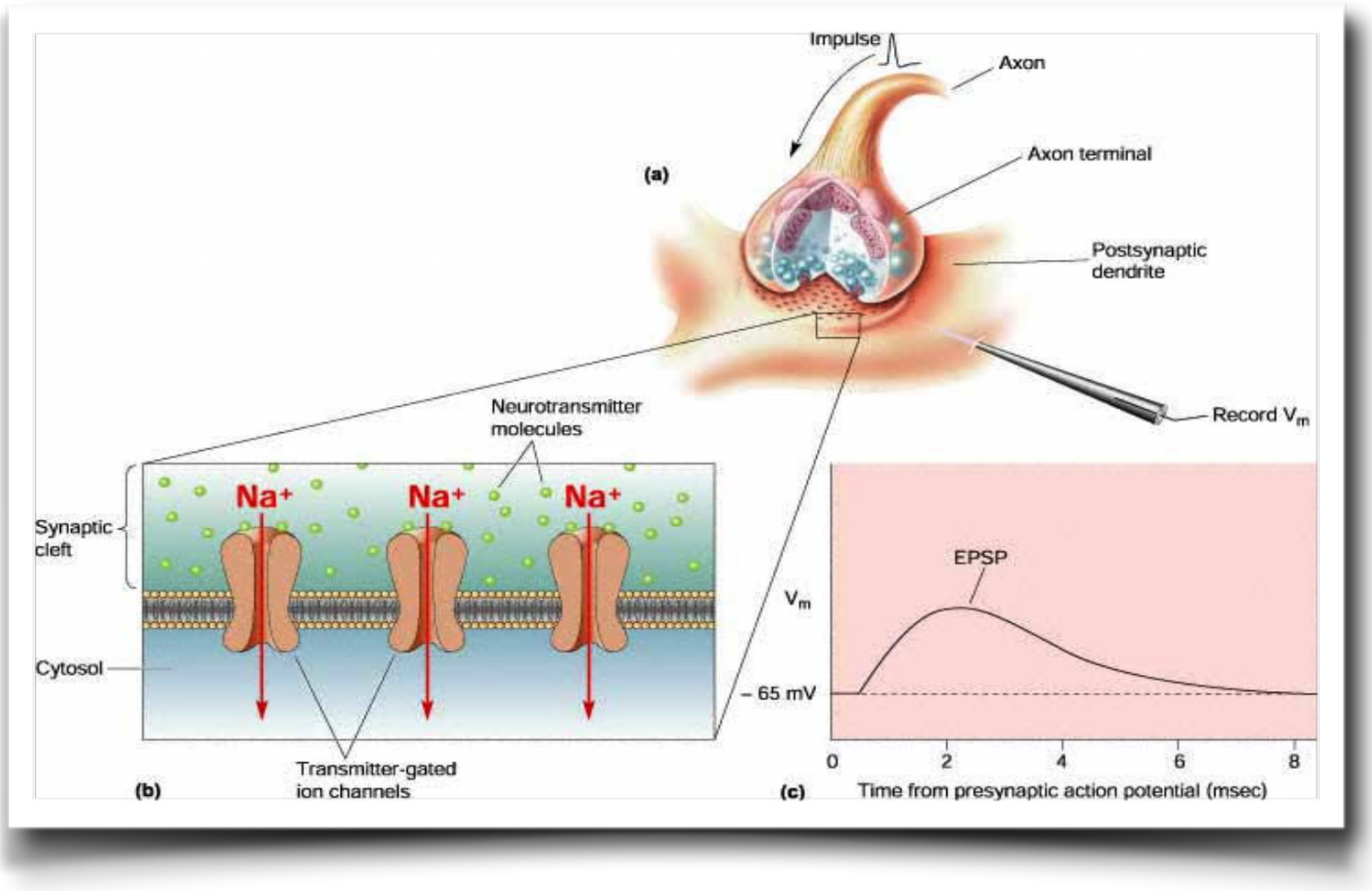
The synaptic response is a "Post-Synaptic Potential" (PSP)

- PSPs can be Excitatory or Inhibitory
  - Excitatory Postsynaptic Potentials (EPSPs)
  - Inhibitory Postsynaptic Potentials (IPSPs)



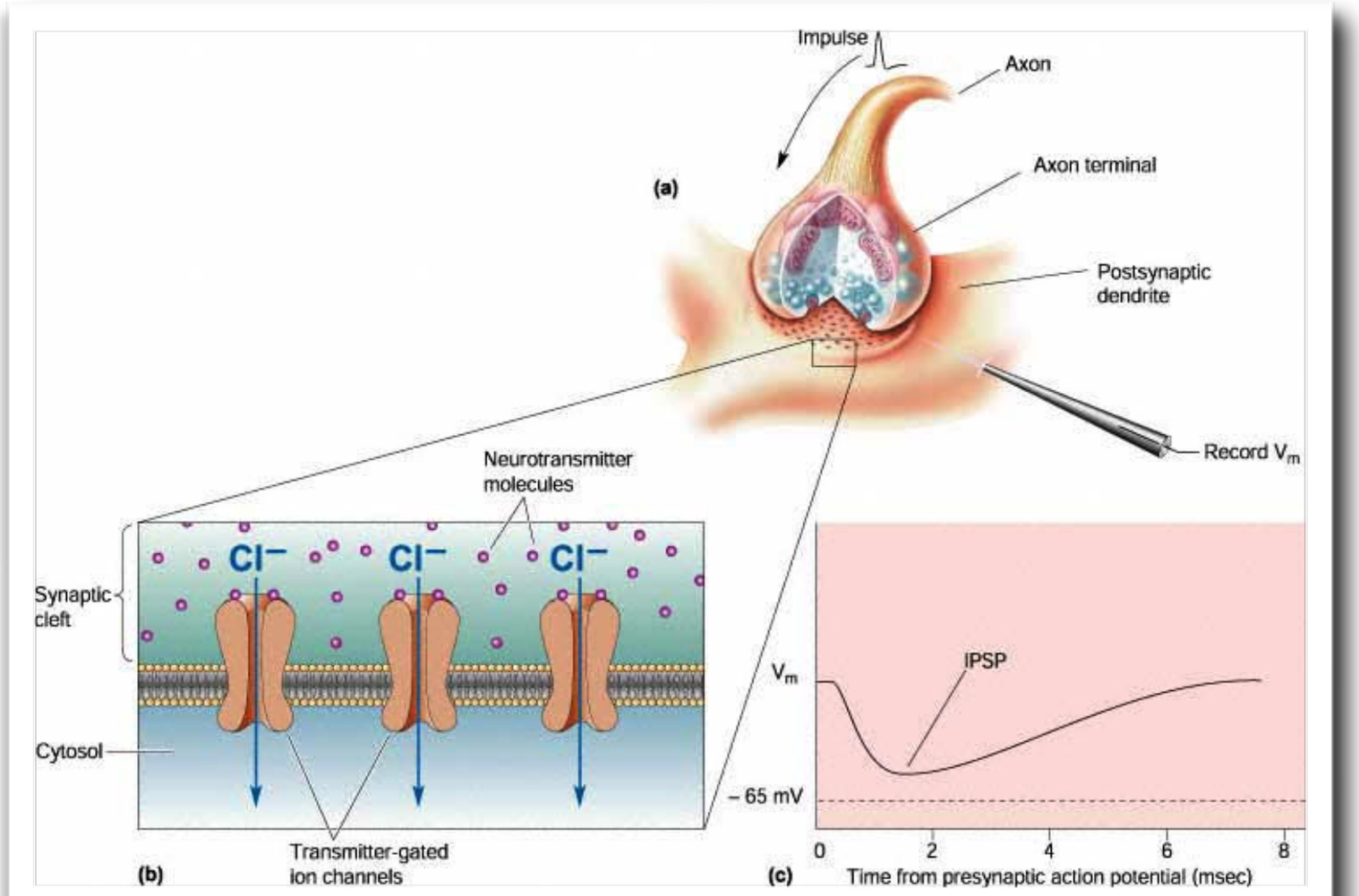
Two types of EPSPs

- Opening of channels permeable to Na^+
  - Na^+ enters the cell = Excitatory response
- Closing K^+ channels (K^+ cannot leave the cell)



Two types of IPSPs

- Opening of channels permeable to Cl^-
  - Cl^- enters the cell = hyperpolarization
- Opening K^+ channels (more K^+ leaves the cell) = hyperpolarization

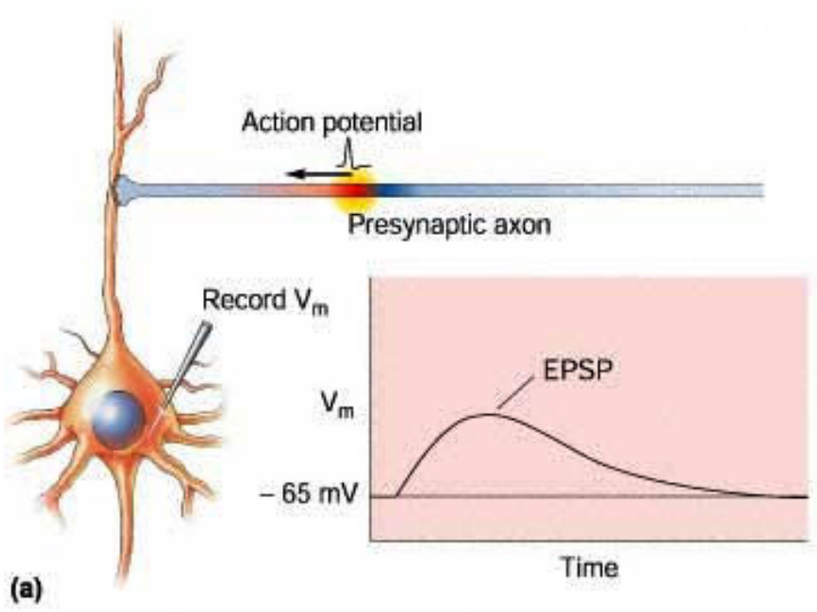


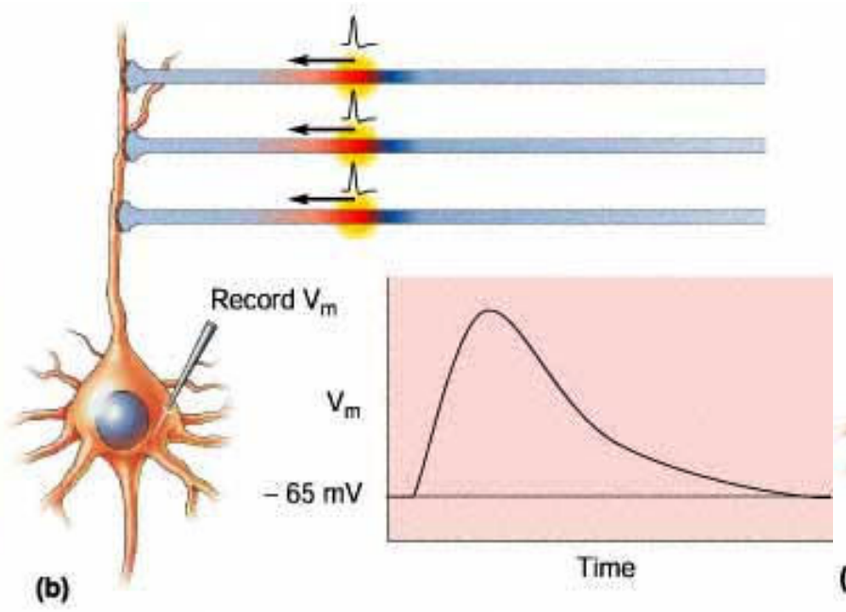
Synaptic Integration

A single EPSP is usually too small to make the cell fire an action potential

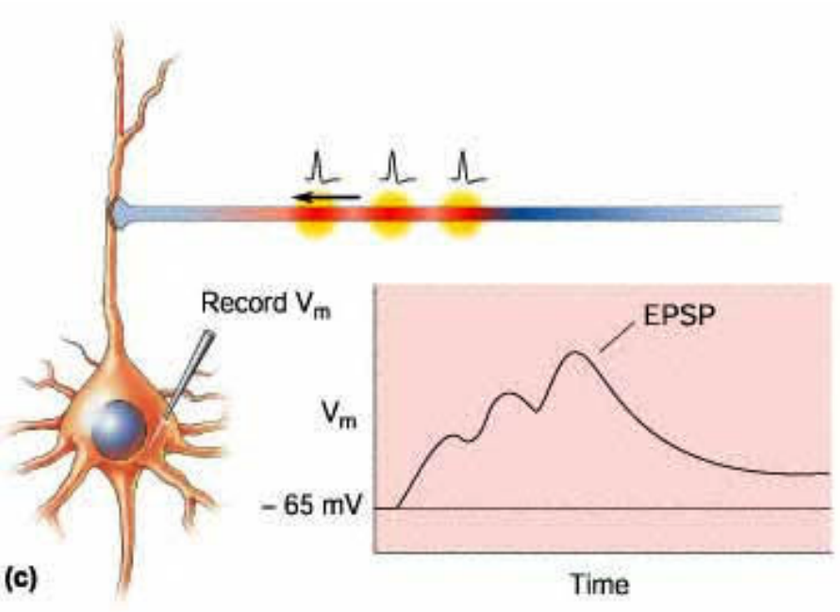
- The EPSPs have to be added together (summed)

Spatial





Temporal



Neurotransmitter Systems

Classical Neurotransmitters

- **Amino Acids**
  - Glutamate
  - γ-aminobutyric acid (GABA)
  - Glycine
- **Monoamines**
  - Dopamine (DA)
  - Norepinephrin (NE)
  - Serotonin (5-HT)

  (Dopamine, Norepinephrin: Catecholamines)
- **Acetylcholine**

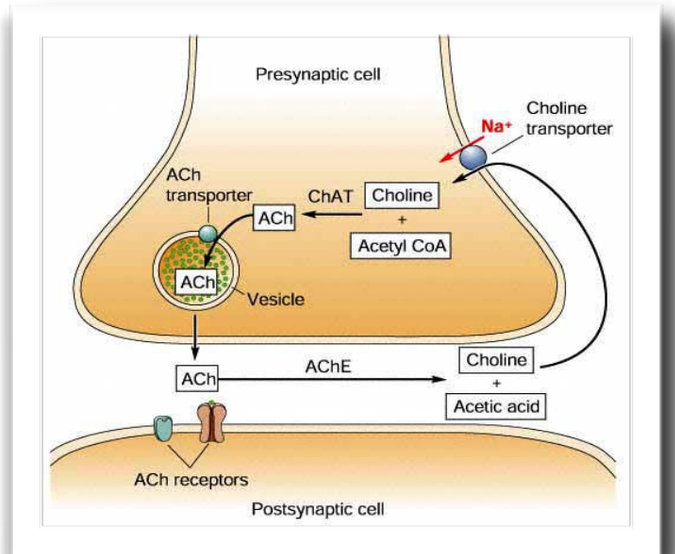
Non-Classical Neurotransmitters

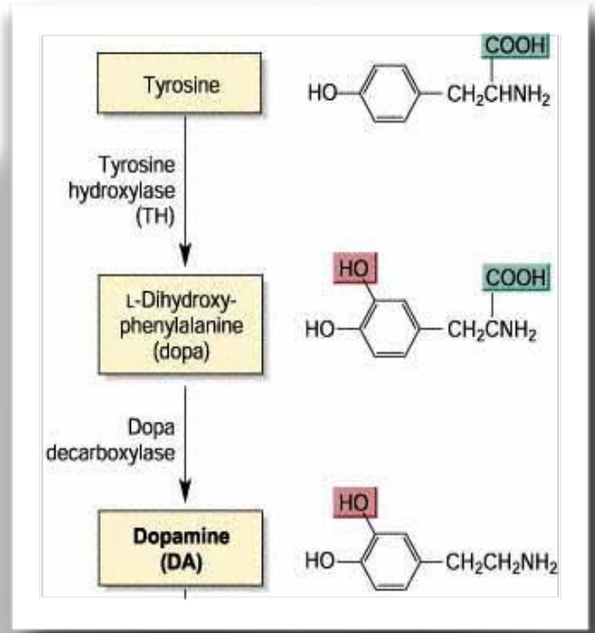
- **Neuropeptides**
  - Endorphins & enkephalins
  - Corticotropin-releasing factor (CRF)
  - Many more...
- **Lipids**
  - Anandamide
- **Gases**
  - Nitirc oxide (NO)

Neurotransmitter Systems

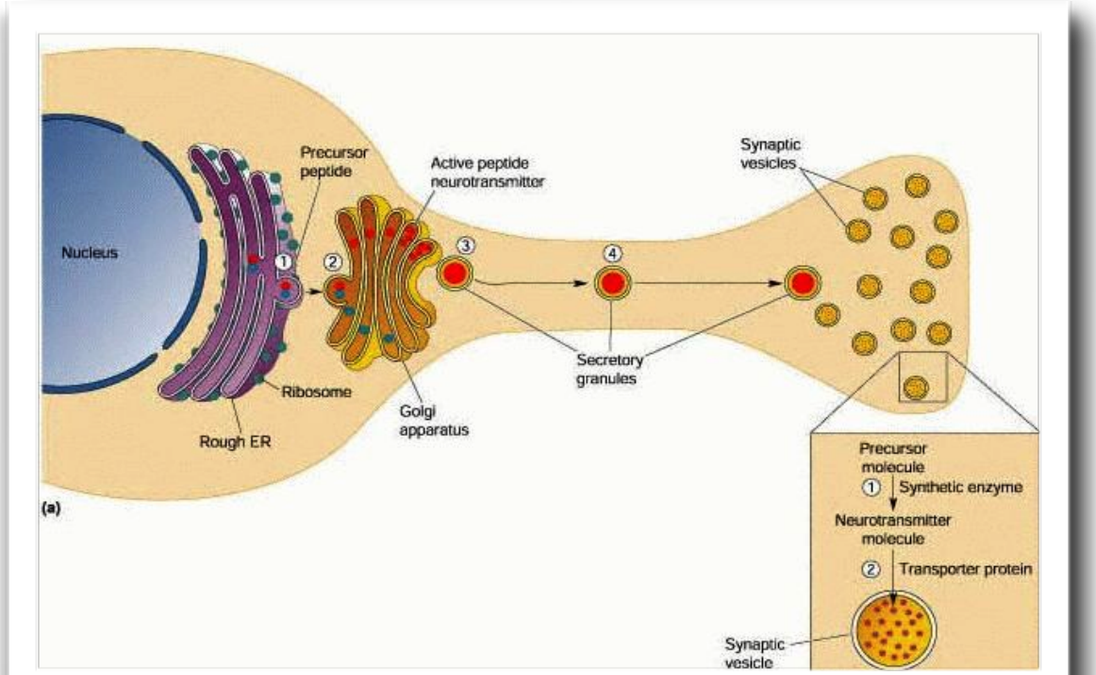
Neurotransmitter synthesis

- Typically, the necessary enzymes are transported to the terminal, where the synthesis is taking place (e.g., ACh, DA)



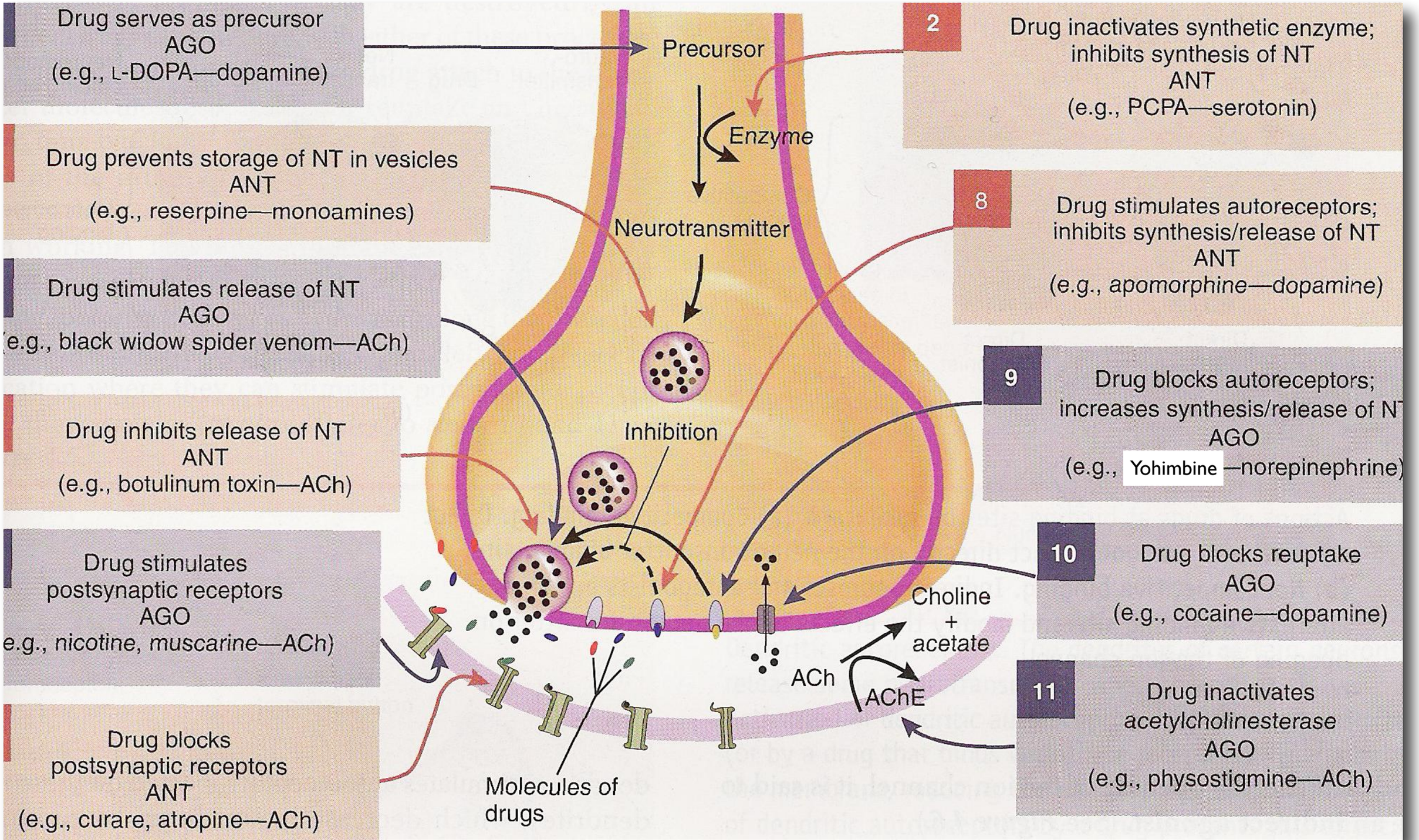


- Neuropeptides precursors are synthesized in the soma and carried with the proper enzymes inside large vesicles to the terminal (therefore, replenishment is slower)



Pharmacology of the Synapse

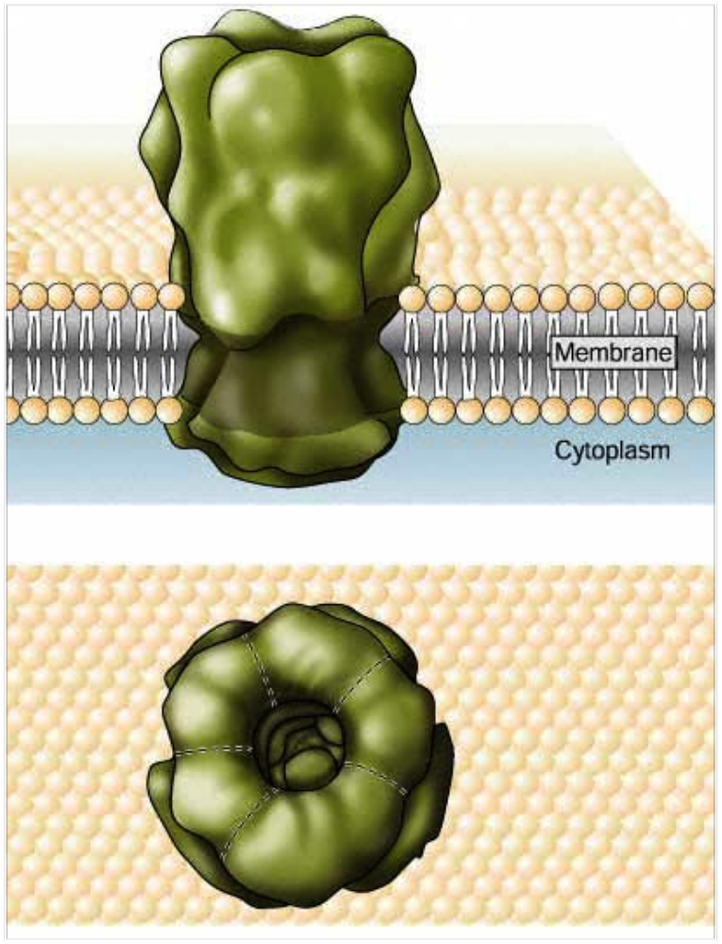
Agonist and antagonist action:

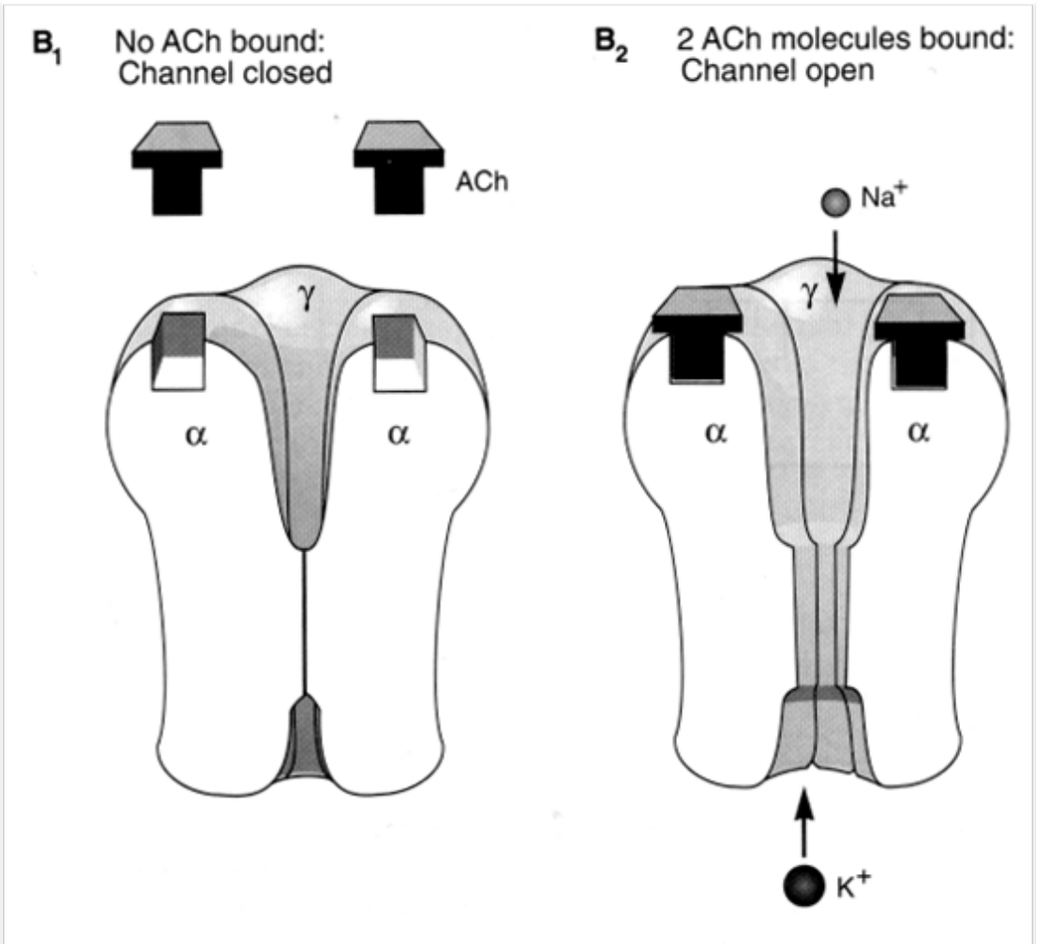


Receptors

1. Ionotropic (ligand-gated channel receptors)
   - Made of 4-5 subunits
   - At the centre of the receptor there is an ion channel or pore
   - Fast acting (opens fast, closes fast) = potential changes is fast and short-lived
   - Some are ion-specific

Acetylcholine (ACh) nicotinic receptor

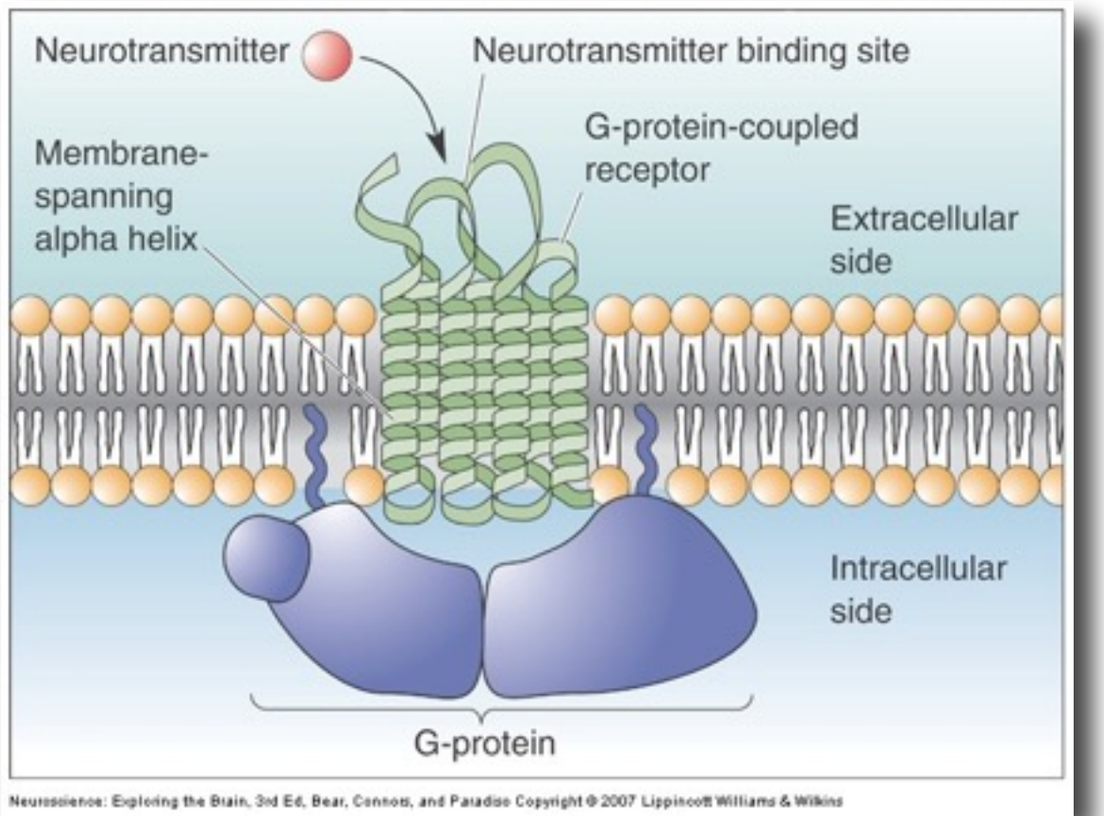


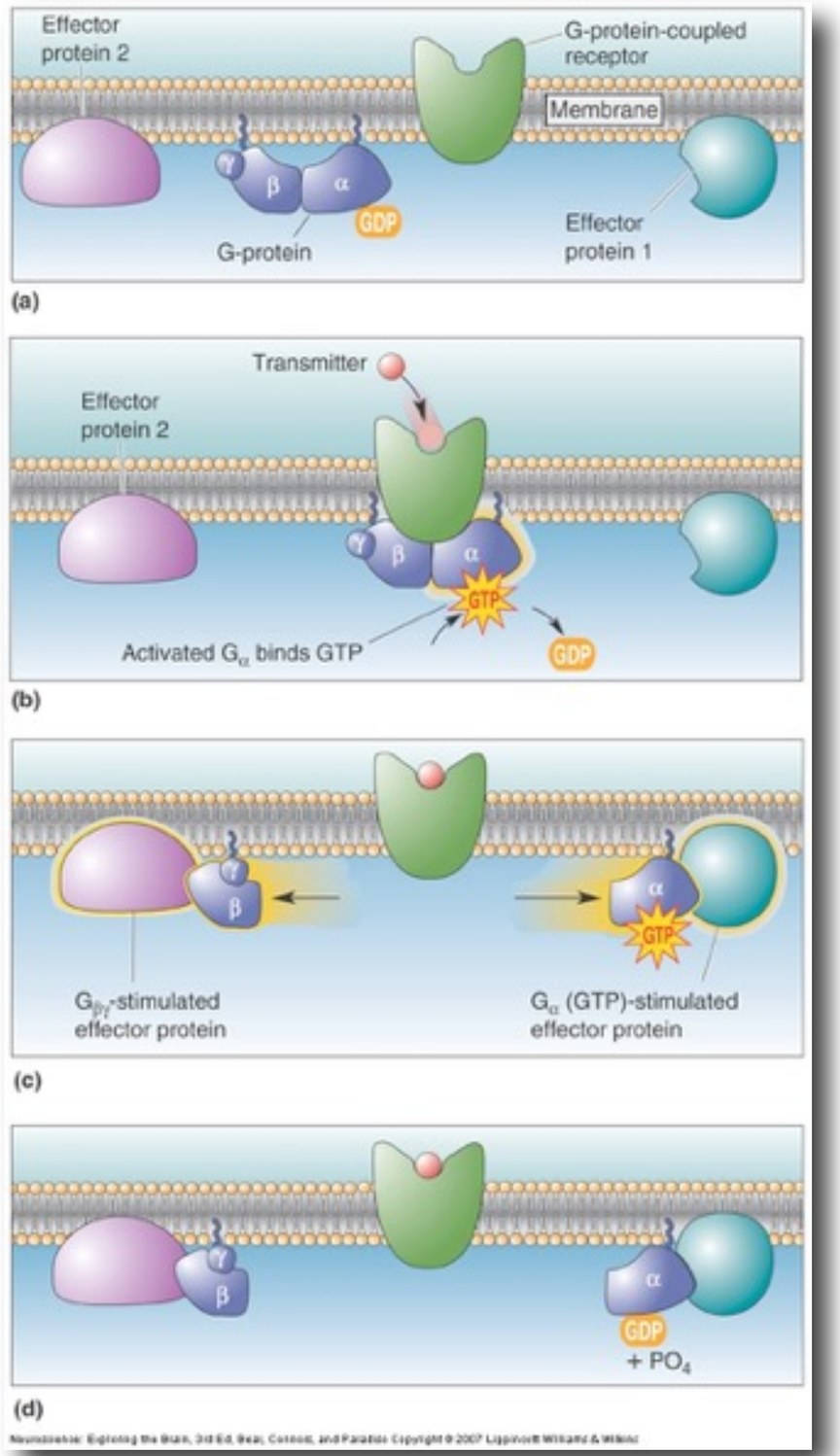


Receptors

2. Metabotropic (G protein-coupled receptors)

- Single protein
- No pore or channel! Activate intra-cellular proteins called **G-proteins**
- Take longer to induce post-synaptic response, but response is longer-lasting compared to ionotropic receptors
- Response is diverse - activates channels, enzymes, and/or changes gene expression



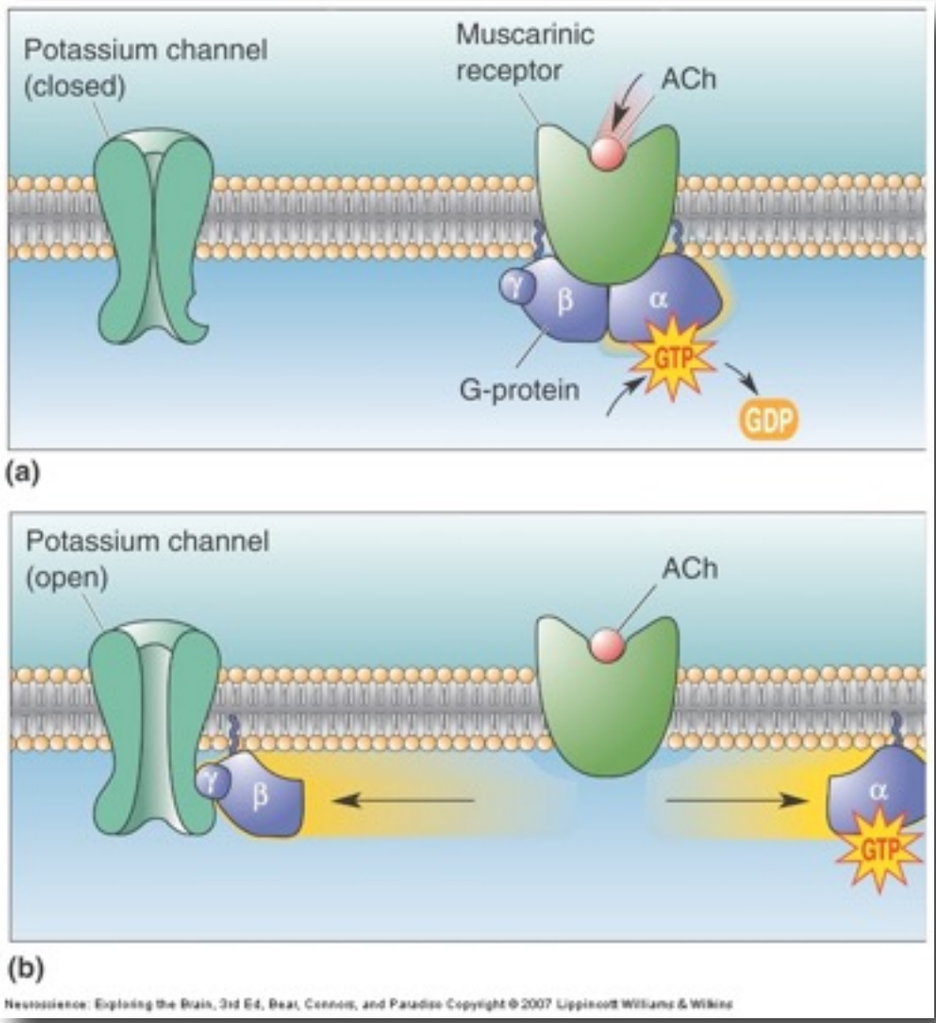


Receptors

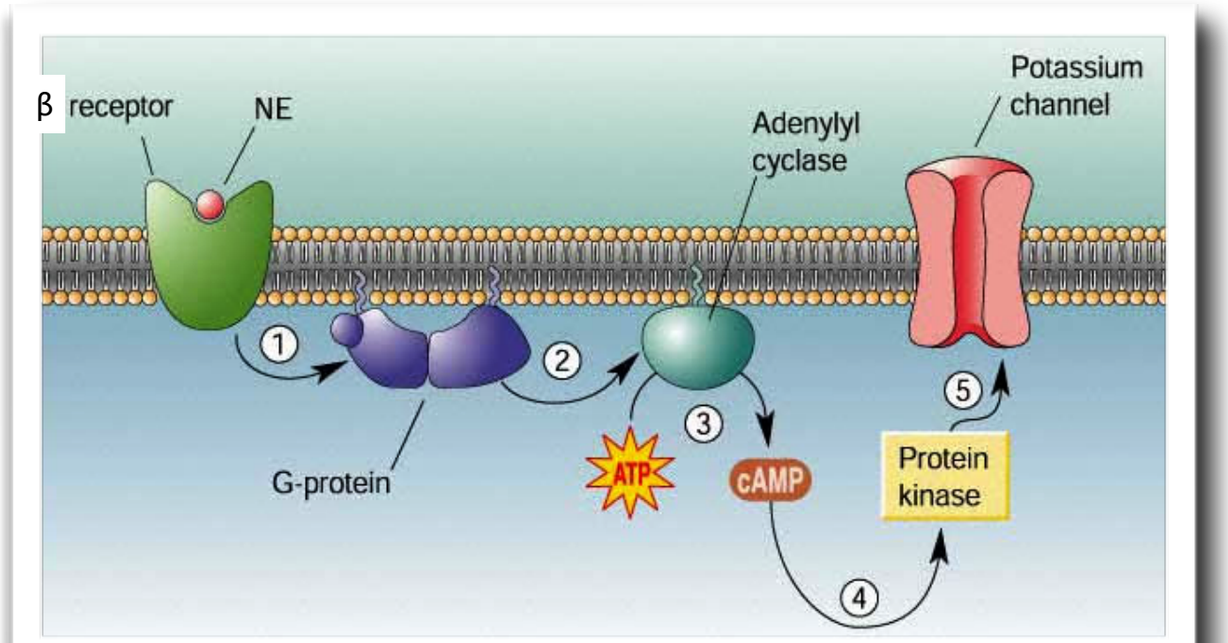
2. Metabotropic (G protein-coupled receptors)

- Two possible mechanisms:
  a. The G proteins stimulates or inhibits the opening of an ion channel ("short-cut")
  b. The G proteins modulate **effector enzymes** that synthesize or breakdown **second messenger** molecules

a.



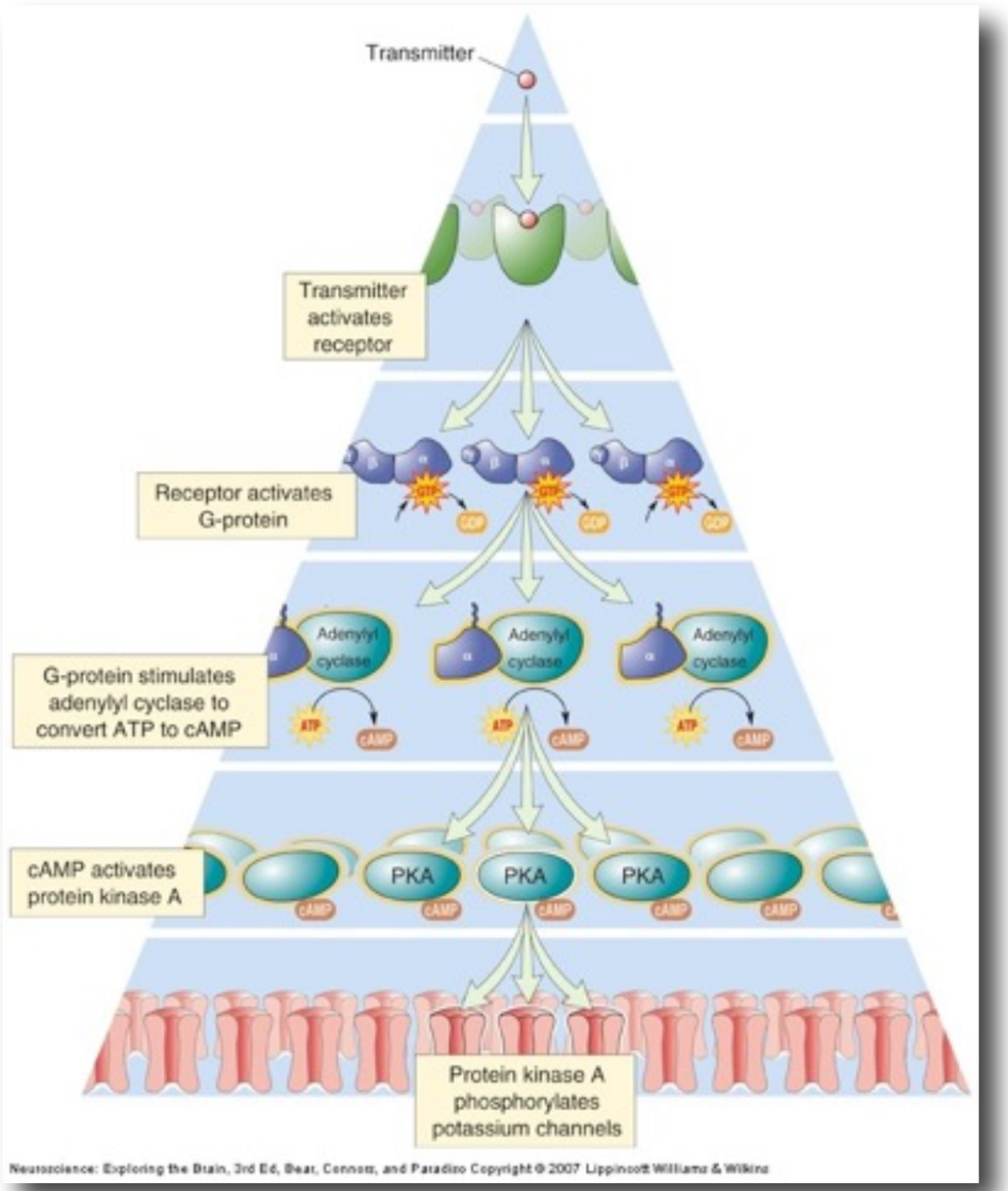
b.

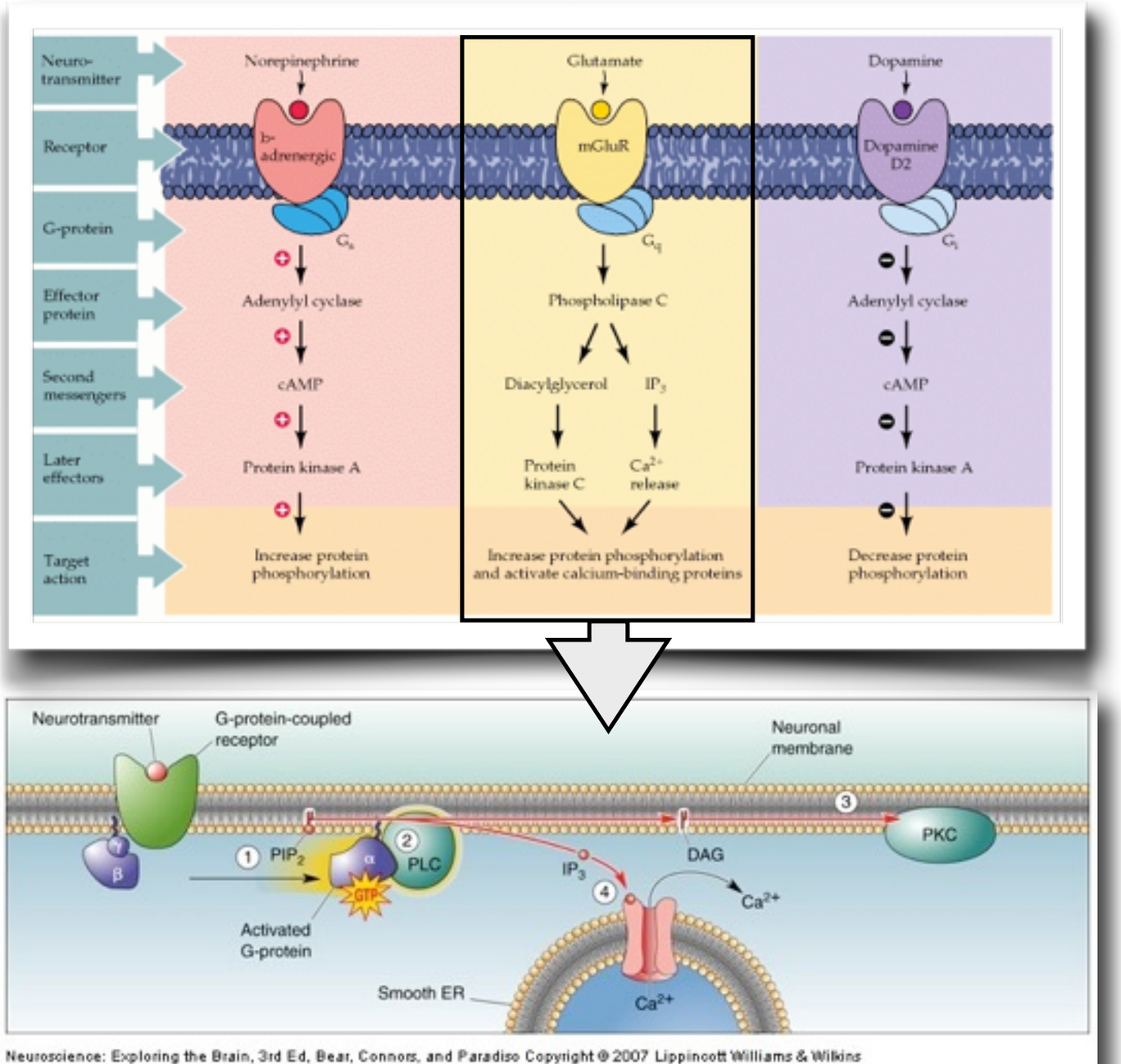


Receptors

2. Metabotropic (G protein-coupled receptors)

- The cascade results in amplification of the signal
- Second messengers and protein kinases have many targets, the particular pathway activated by a receptor is determined by the specific G-protein subunits





Receptors

2. Metabotropic (G protein-coupled receptors)

- Second messengers and protein kinases have many targets

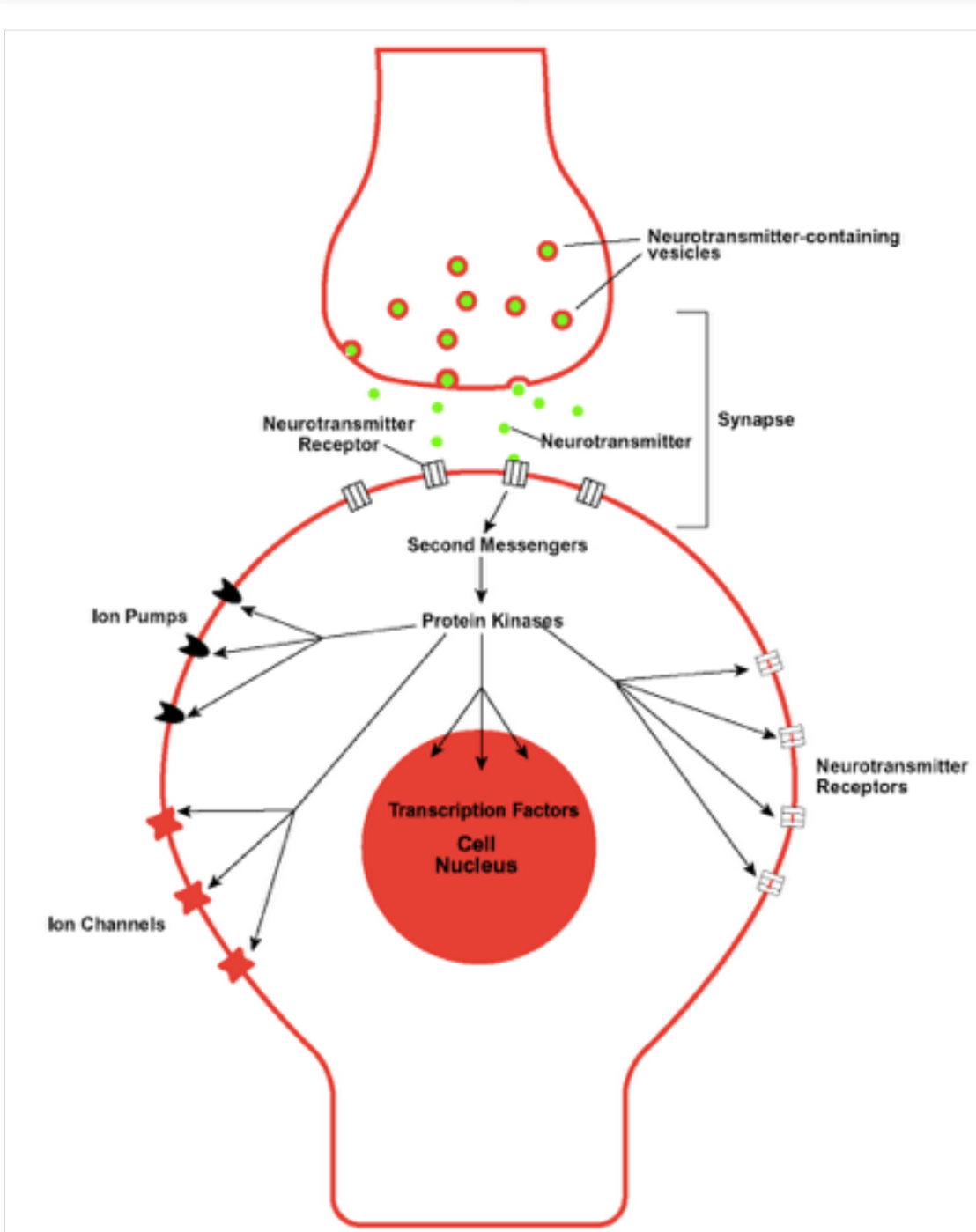


Fig. 1. Some of the signaling pathways of slow synaptic transmission.