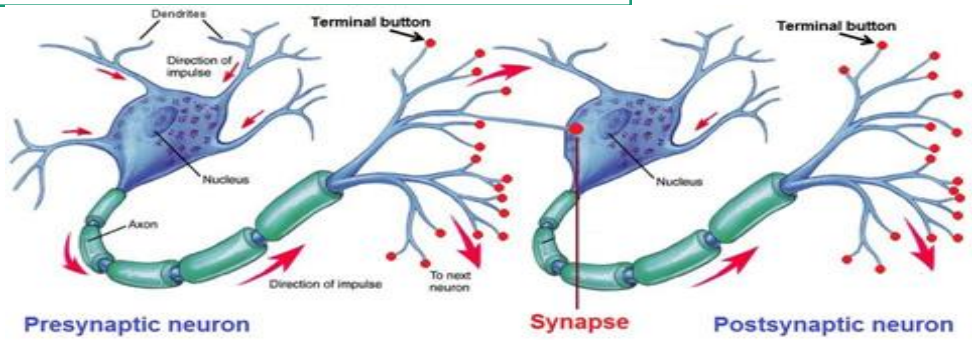
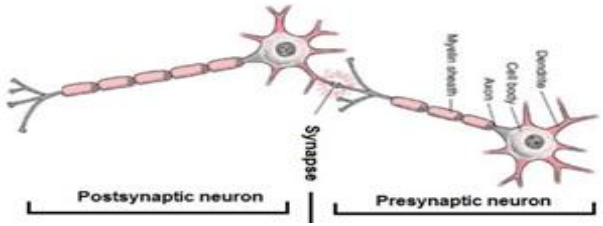
AL-Mustaqbal University College
Department of Pharmacy
physiology lec3/ 2nd stage

Synaptic Transmission

By: Dr. Weaam J. Abass





EXCITATION & CONDUCTION

- **Nerve cells have a low threshold for excitation. The stimulus may be electrical, chemical, or mechanical.**

- **Two types of physicochemical disturbances are produced:**
  1. **Local, nonpropagated potentials called, depending on their location, (synaptic, generator, or electrotonic potentials).**

  2. **Propagated potentials, the action potentials (or nerve impulses).**

Nerve Impulses (Nerve language)

- **These are the only electrical responses of neurons and other excitable tissues, and they are the main language of the nervous system.**

- **They are due to changes in the conduction of ions across the cell membrane that are produced by alterations in ion channels.**

- **The electrical events in neurons are rapid, being measured in milliseconds (ms); and the potential changes are small, being measured in millivolts (mV).**

Conduction

- **The impulse is normally transmitted (conducted) along the axon to its termination.**
- **Conduction is an active, self-propagating process, and the impulse moves along the nerve at a constant amplitude and velocity.**
- **The process is often compared to what happens when a match is applied to one end of a trail of gunpowder; by igniting the powder particles immediately in front of it, the flame moves steadily down the trail to its end as it is extinguished in its progression.**

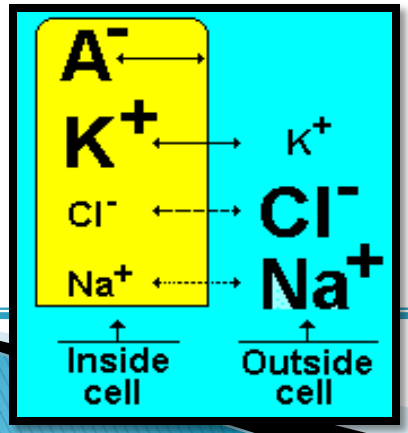
Salutatory Conduction

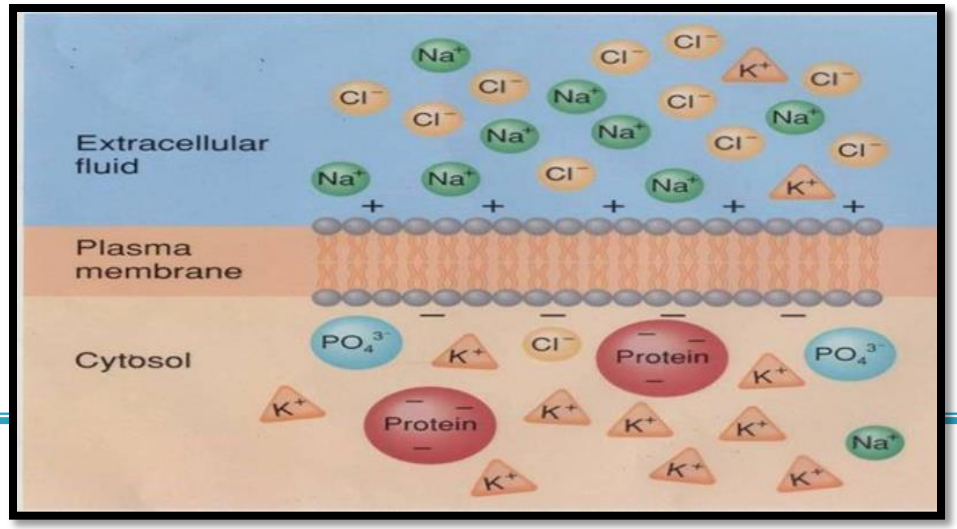
- **Conduction in myelinated axons involves depolarization in myelinated axons jumps from one node of Ranvier to the next.**
- **This jumping of depolarization from node to node is called salutatory conduction.**
- **It is a rapid process that allows myelinated axons to conduct up to 50 times faster than the unmyelinated fibers.**

Membrane Ionic Distribution & Membrane Potential

- Intracellular fluid and extracellular fluid are electrically neutral solutions, in that each has an equal number of positively and negatively charged ions.

- In an unstimulated or resting cell, a slight accumulation of negative charges (–) on the internal surface of the plasma membrane is attracted to an equal number of positive charges (+) that have accumulated on the external surface of the membrane.



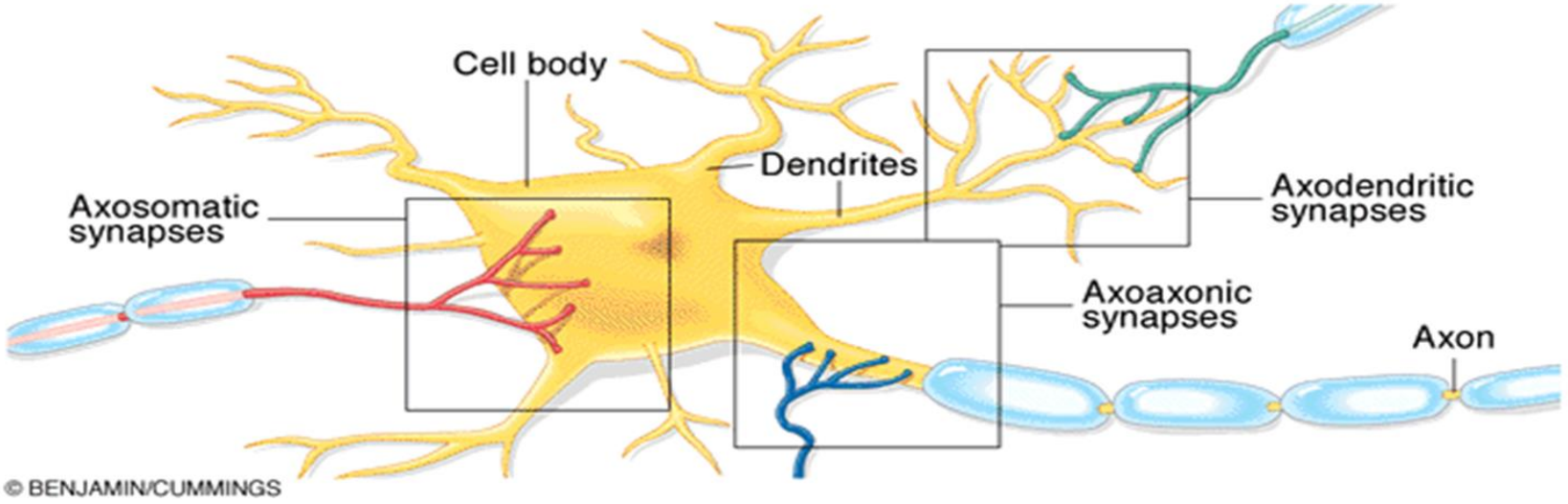


Synaptic Transmission

1.Chemical synapse (Classical Synapse)

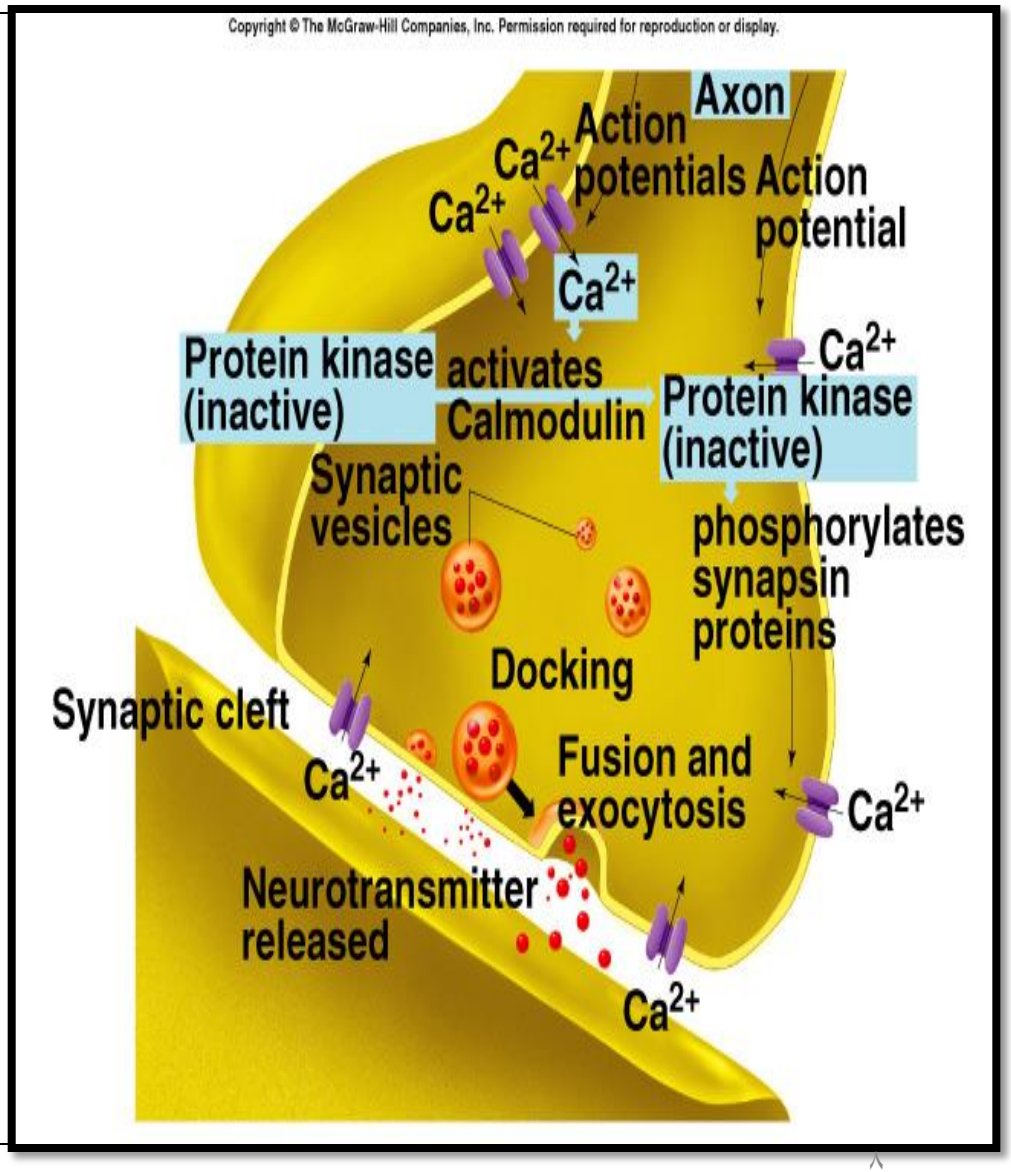
2.Non-synaptic chemical transmission

3.Electrical synapse



Chemical Synapse

- Terminal bouton is separated from postsynaptic cell by **synaptic cleft.**
- **Vesicles** fuse with axon membrane and NT released by exocytosis.
- Amount of NTs released depends upon **frequency of AP.**



Non-synaptic chemical transmission

The postganglionic neurons innervate the smooth muscles.

- No recognizable endplates or other postsynaptic specializations;
- The multiple branches are beaded with enlargements (**varicosities**) that are not covered by Schwann cells and contain synaptic vesicles;

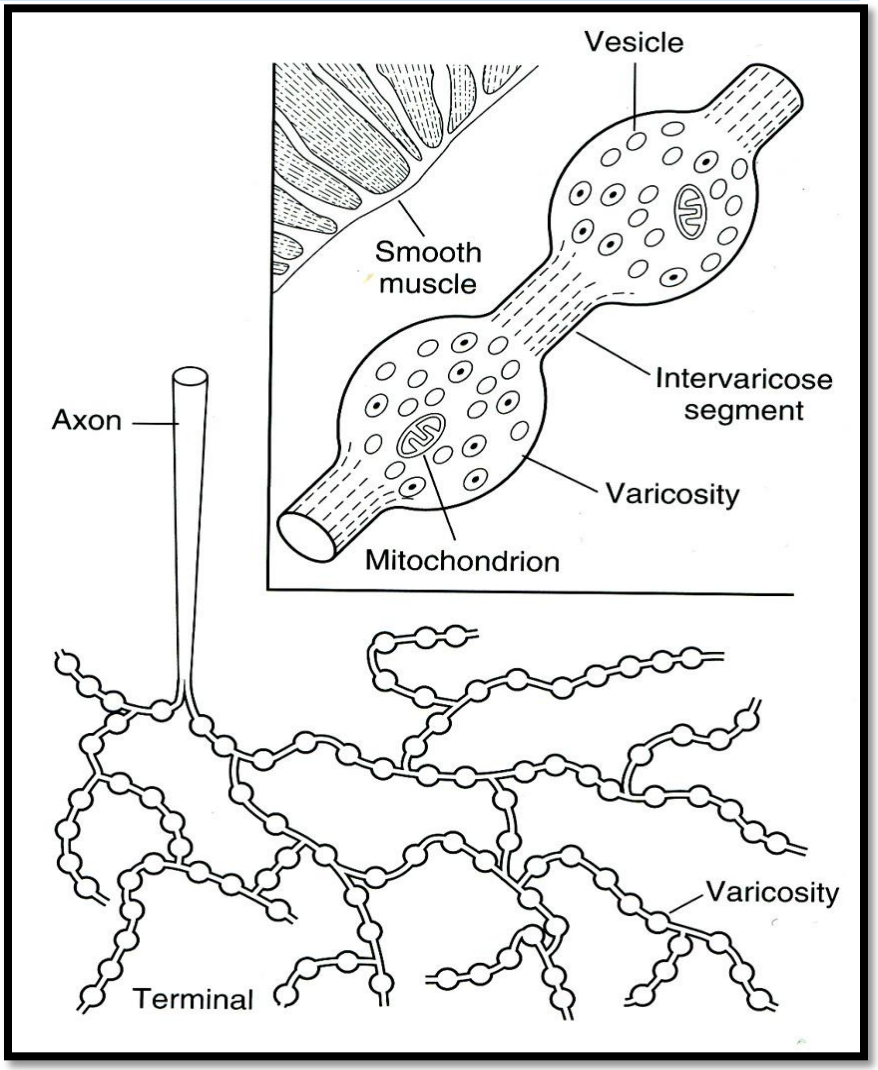


Fig. : Ending of postganglionic autonomic neurons on smooth muscle

Non-synaptic chemical transmission continued

- In noradrenergic neurons, the varicosities are about 5μm, with up to 20,000 varicosities per neuron;
- Transmitter is apparently released at each varicosity, at many locations along each axon;
- One neuron innervate many effector cells.

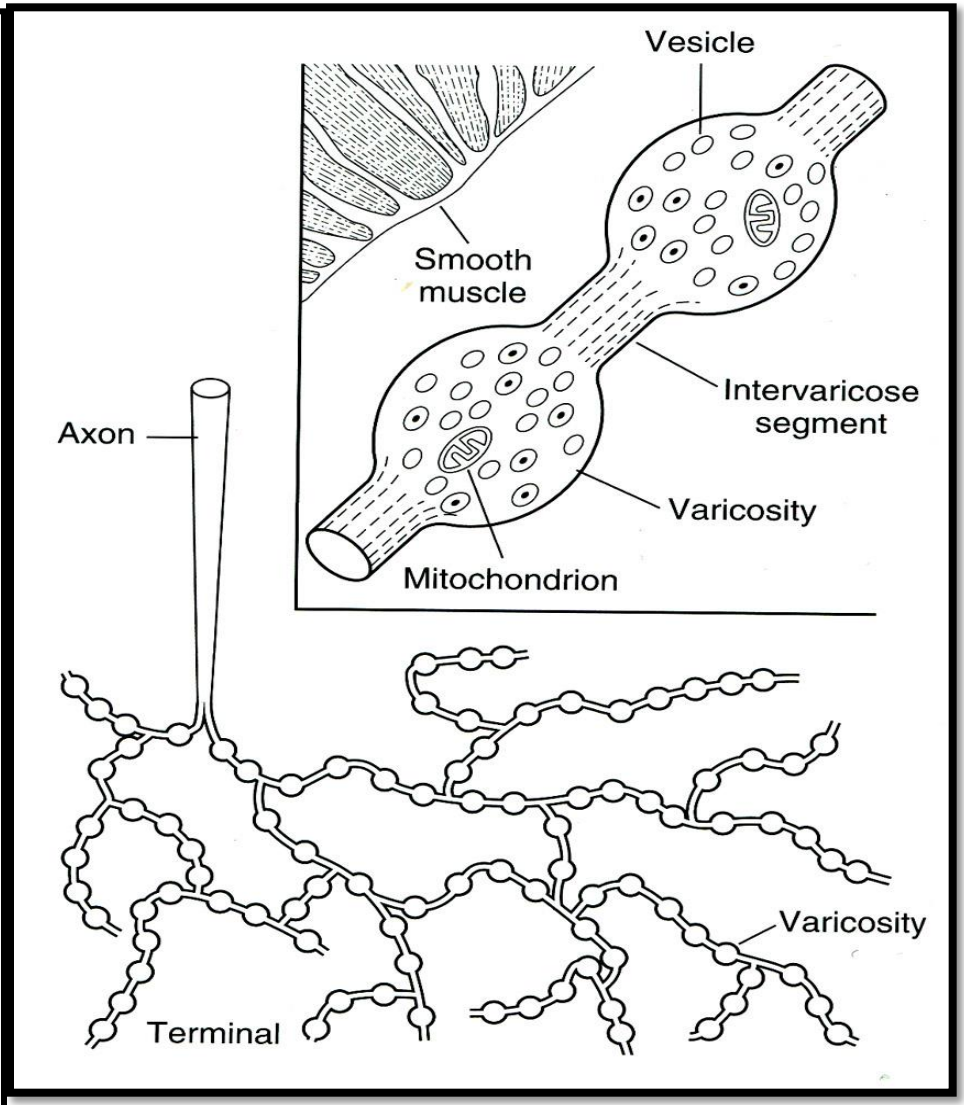
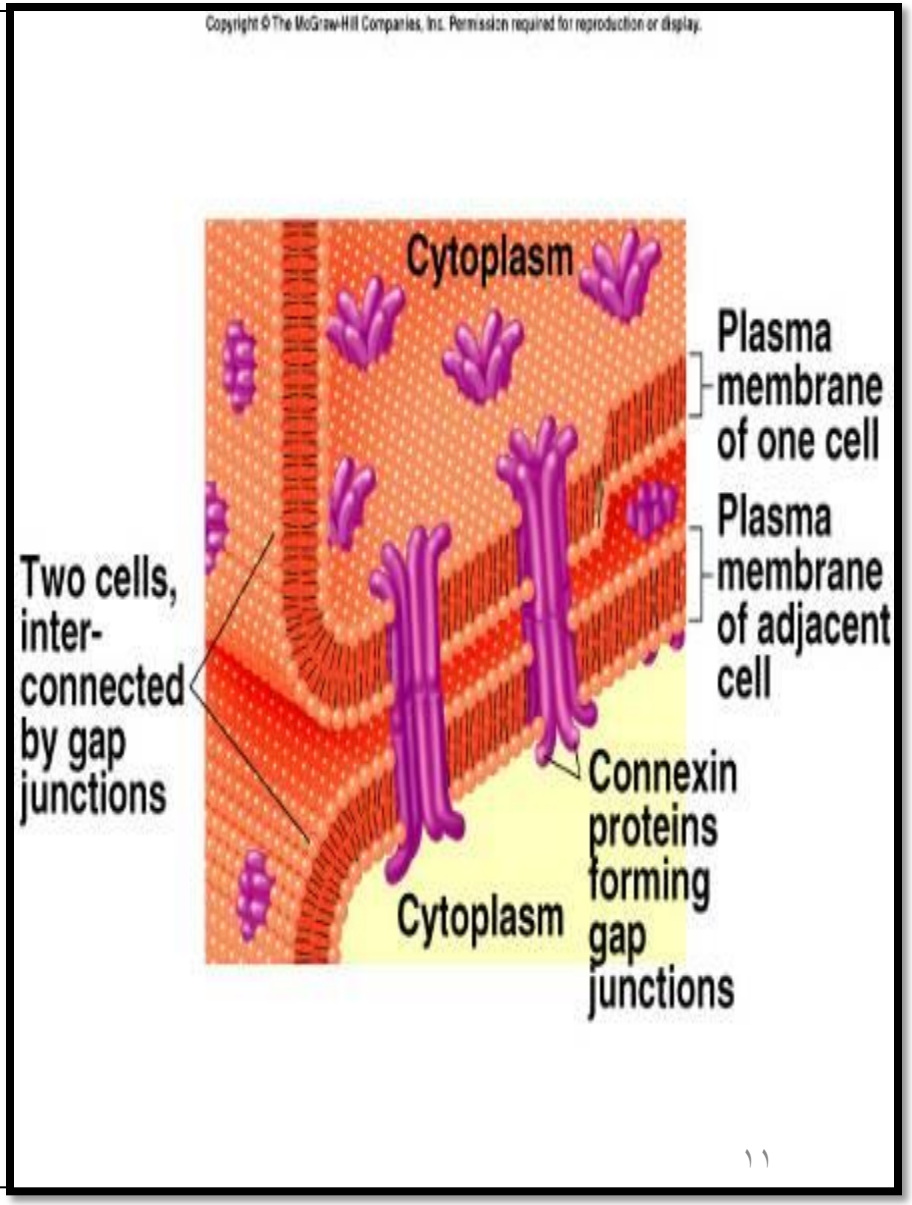


Fig. : Ending of postganglionic autonomic neurons on smooth muscle

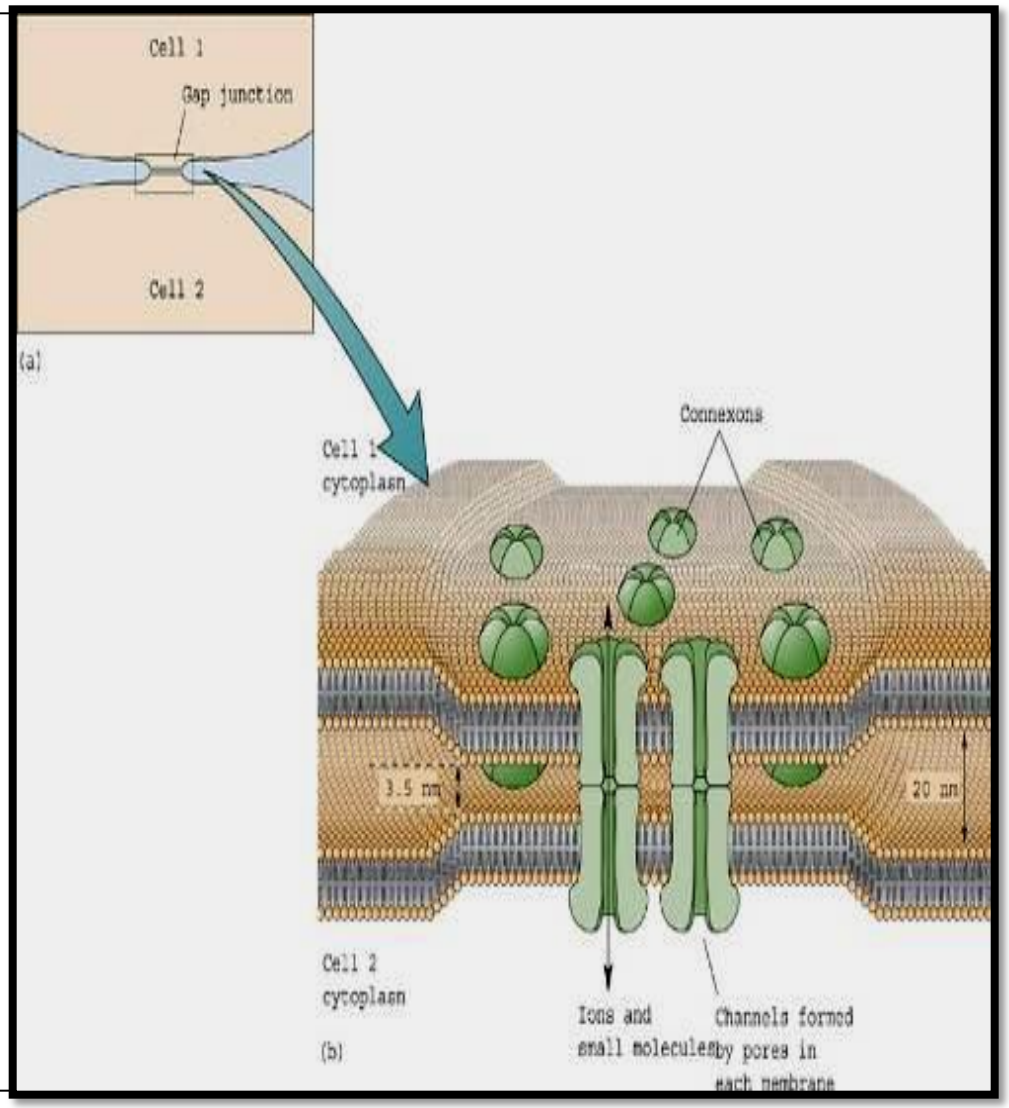
Electrical Synapse

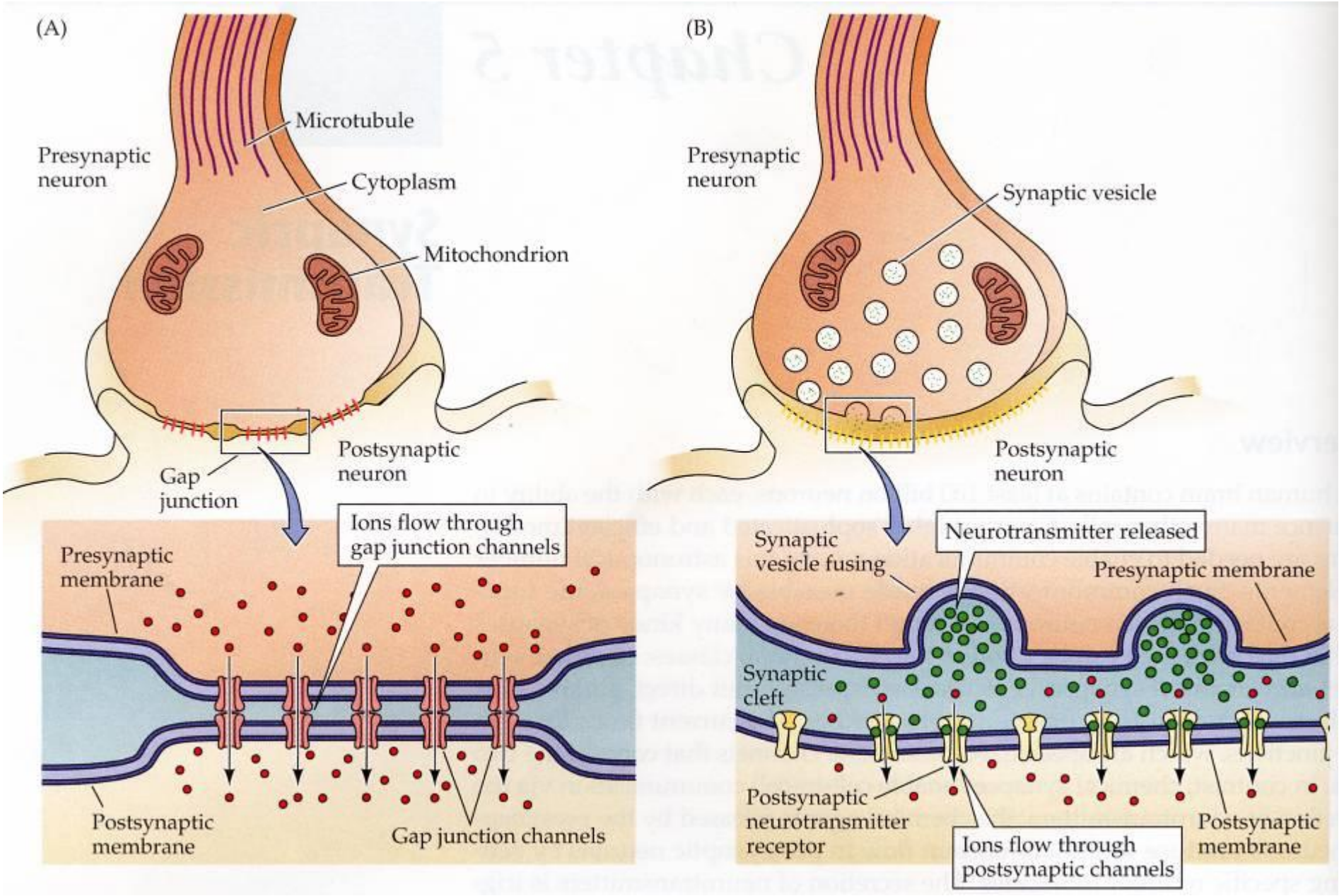
- Impulses can be regenerated **without** interruption in adjacent cells.
- **Gap junctions:**
  - Adjacent cells electrically coupled through a channel.
  - Each gap junction is composed of 12 connexin proteins.
- **Examples**: Smooth and cardiac muscles, brain, and glial cells.



Electrical Synapses

- **Electric current flow-** communication takes place by flow of electric current directly from one neuron to the other
- **No synaptic cleft or vesicles** cell membranes in direct contact
- **Communication not polarized-** electric current can flow between cells in either direction





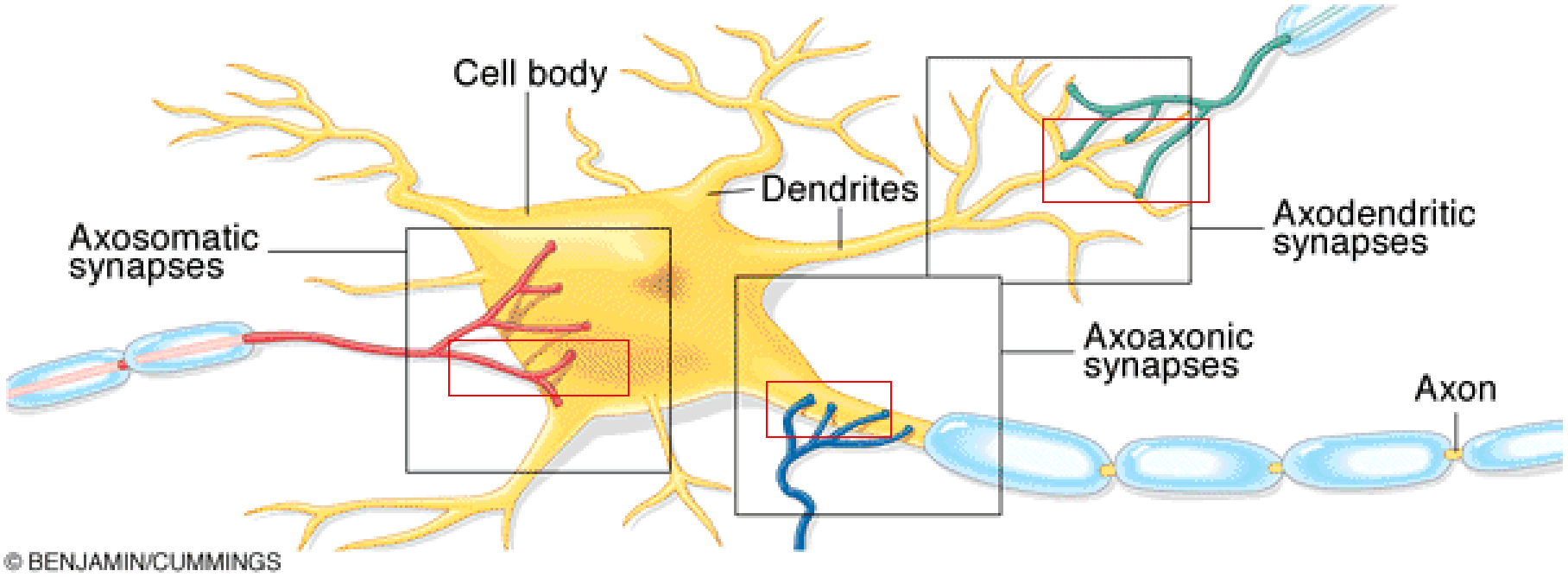
Electrical Synapse

Chemical Synapse

Purves, 2001

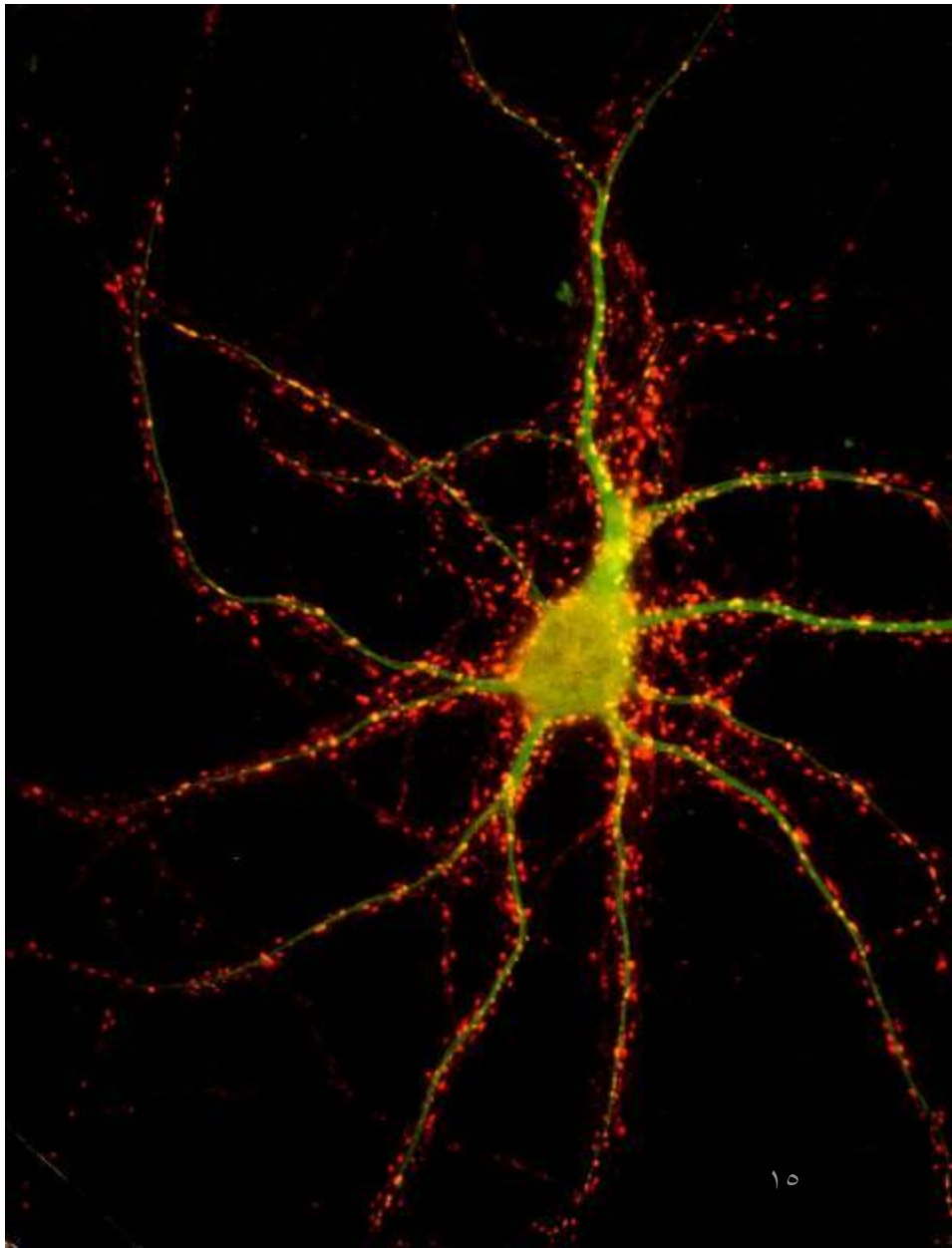
The Chemical Synapse and Signal Transmission

- The chemical **synapse** is a specialized junction that transfers nerve impulse information from a pre synaptic membrane to a postsynaptic



Synaptic connections

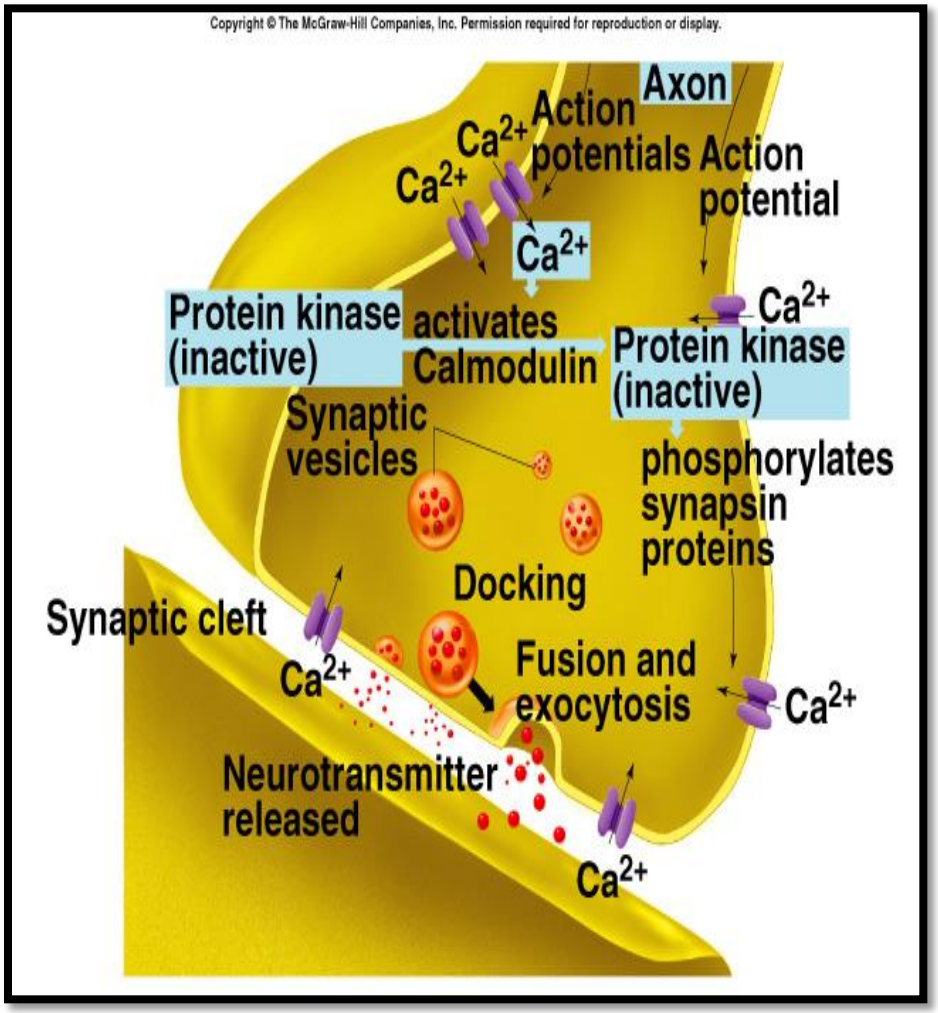
- ~100,000,000,000 neurons in human brain
- Each neuron contacts ~1000 cells
- Forms ~10,000 connections/cell
- How many synapses?



Chemical Synapses

- **Neurotransmitter-** communication via a chemical intermediary called a **neurotransmitter**, released from one neuron and influences another

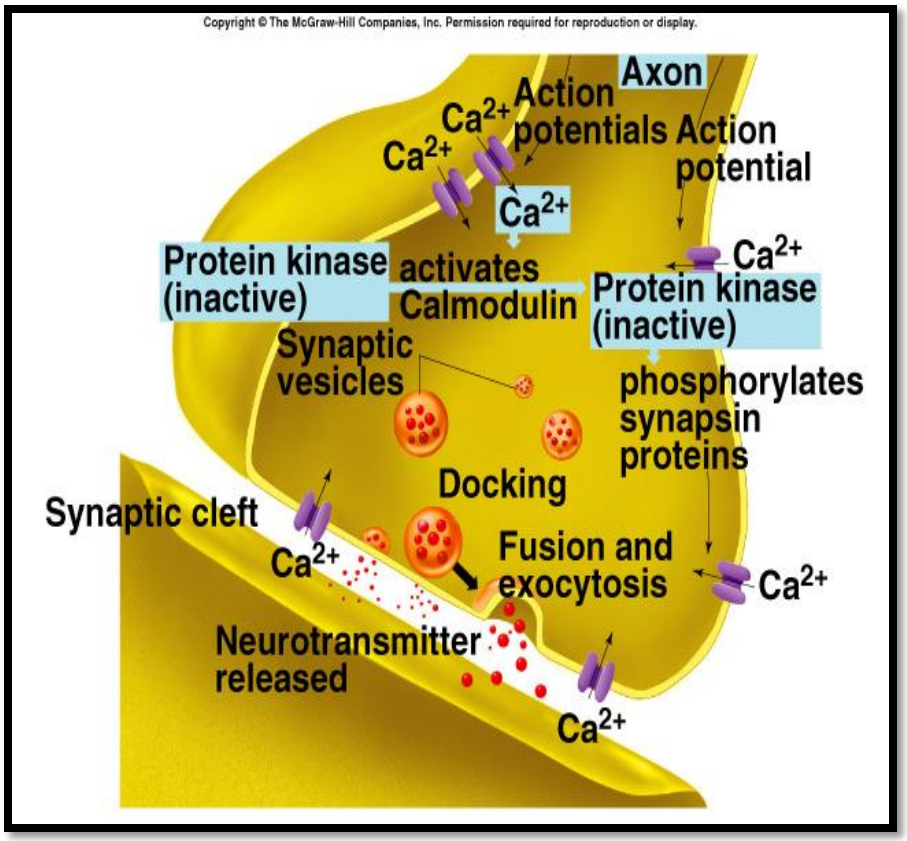
- **Synaptic cleft-** a small gap between the sending (presynaptic) and the receiving



Chemical Synapses

- **Synaptic vesicles-** small spherical or oval organelles contain chemical transmitter used in transmission

- **Polarization-** communication occurs in only one direction, from sending presynaptic site, to receiving postsynaptic site



Synaptic Transmission Model

- Precursor transport
- NT synthesis
- Storage
- Release
- Activation
- Termination ~diffusion, degradation, uptake, autoreceptors

Synaptic Transmission

- AP travels down axon to bouton.
- VG Ca^{2+} channels open.
  - Ca^{2+} enters bouton down concentration gradient.
  - Inward diffusion triggers rapid fusion of synaptic vesicles and release of NTs.
- Ca^{2+} activates calmodulin, which activates protein kinase.
- Protein kinase phosphorylates synapsins.
  - Synapsins aid in the fusion of synaptic vesicles.

Synaptic Transmission (continued)

- NTs are released and diffuse across synaptic cleft.
- NT (ligand) binds to specific receptor proteins in postsynaptic cell membrane.
- Chemically-regulated gated ion channels open.
  - EPSP: depolarization.
  - IPSP: hyperpolarization.
- Neurotransmitter inactivated to end transmission.

Neurotransmitters and receptors

Neuro-transmitter:

- Endogenous signaling **molecules** that **alter** the behaviour of neurons or effector cells.

Neuro-receptor:

- **Proteins** on the cell membrane or in the cytoplasm that could bind with specific neurotransmitters and **alter** the behavior of neurons of effector cells

Neurotransmitters and receptors

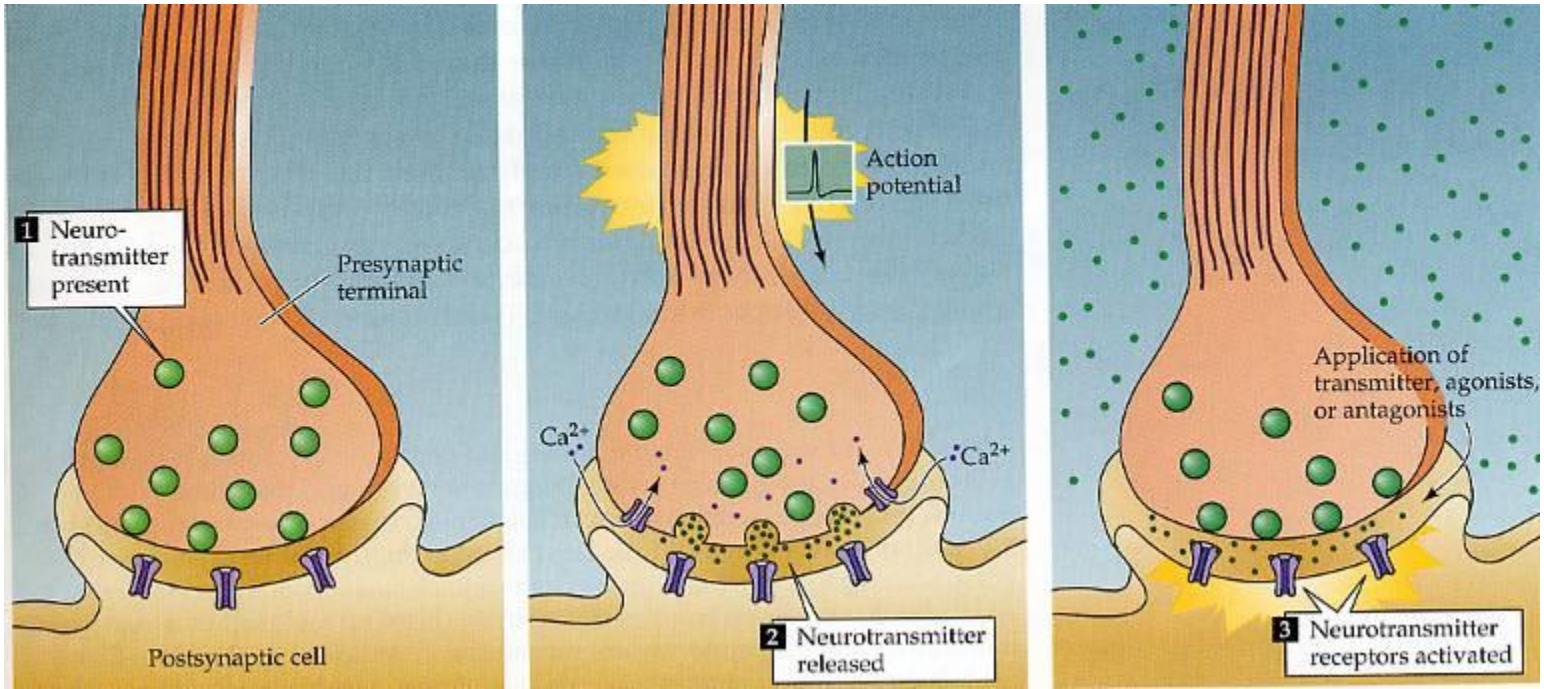
- Different molecules serve as neurotransmitters

- The properties of the ***transmitter*** **do not** determine its effects on the postsynaptic cells

- The properties of the ***receptor*** determine whether a transmitter is excitatory or inhibitory

A neurotransmitter must (classical definition)

- Be synthesized and released from neurons
- Be found at the presynaptic terminal
- Have same effect on target cell when applied externally
- Be blocked by same drugs that block synaptic transmission
- Be removed in a specific way



Purves, 2001

Classical Transmitters (small-molecule transmitters)

- Biogenic Amines
  - Acetylcholine
  - Catecholamines
    - Dopamine
    - Norepinerphrine
    - Epinephrine
  - Serotonin
- Amino Acids
  - Glutamate
  - GABA (γ-amino butyric acid)
  - Glycine

Non-classical Transmitters

- Neuropeptides
- Neurotrophins
- Gaseous messengers
  - –Nitric oxide
  - –Carbon Monoxide
- D-serine

Agonist

A substance that mimics a specific neurotransmitter,

is able to attach to that neurotransmitter's receptor

and thereby produces the same action that the neurotransmitter usually produces.

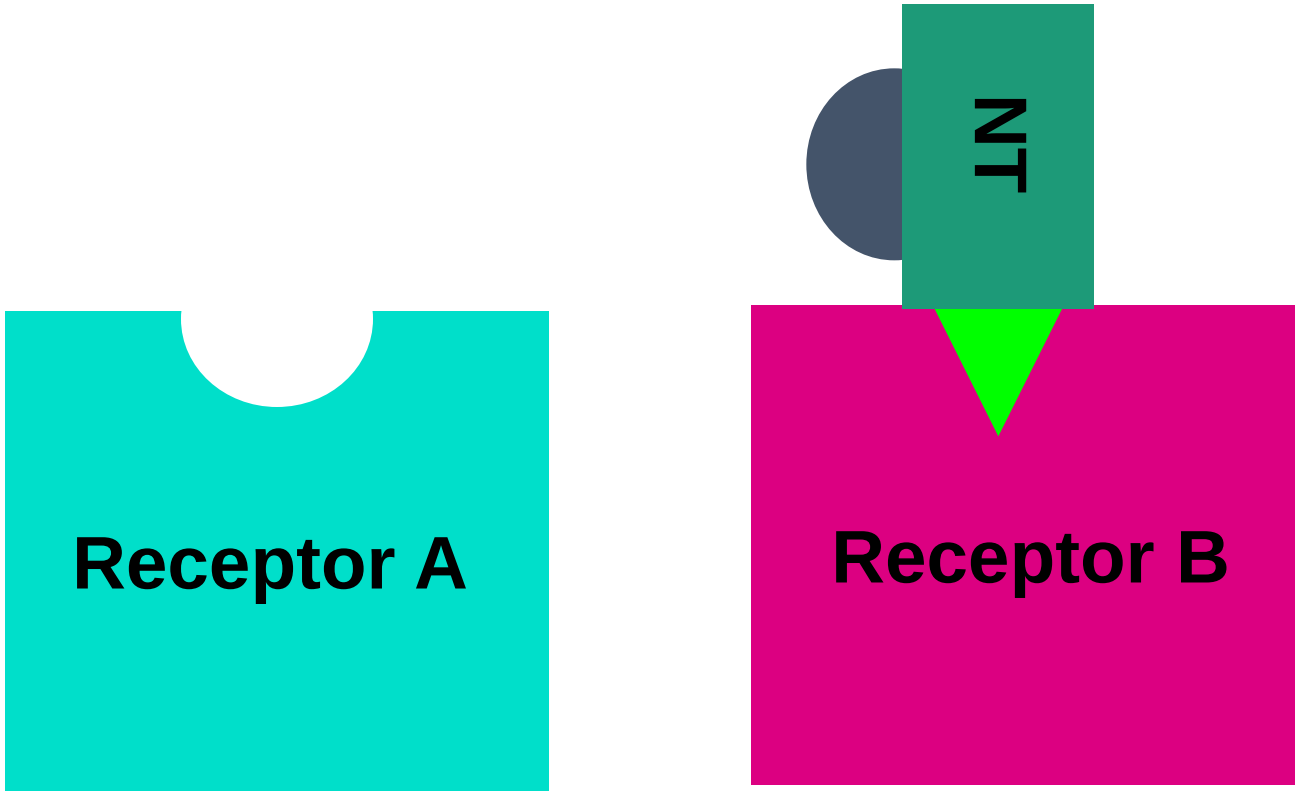
Drugs are often designed as receptor agonists to treat a variety of diseases and disorders when the original chemical substance is missing or depleted.

Antagonist

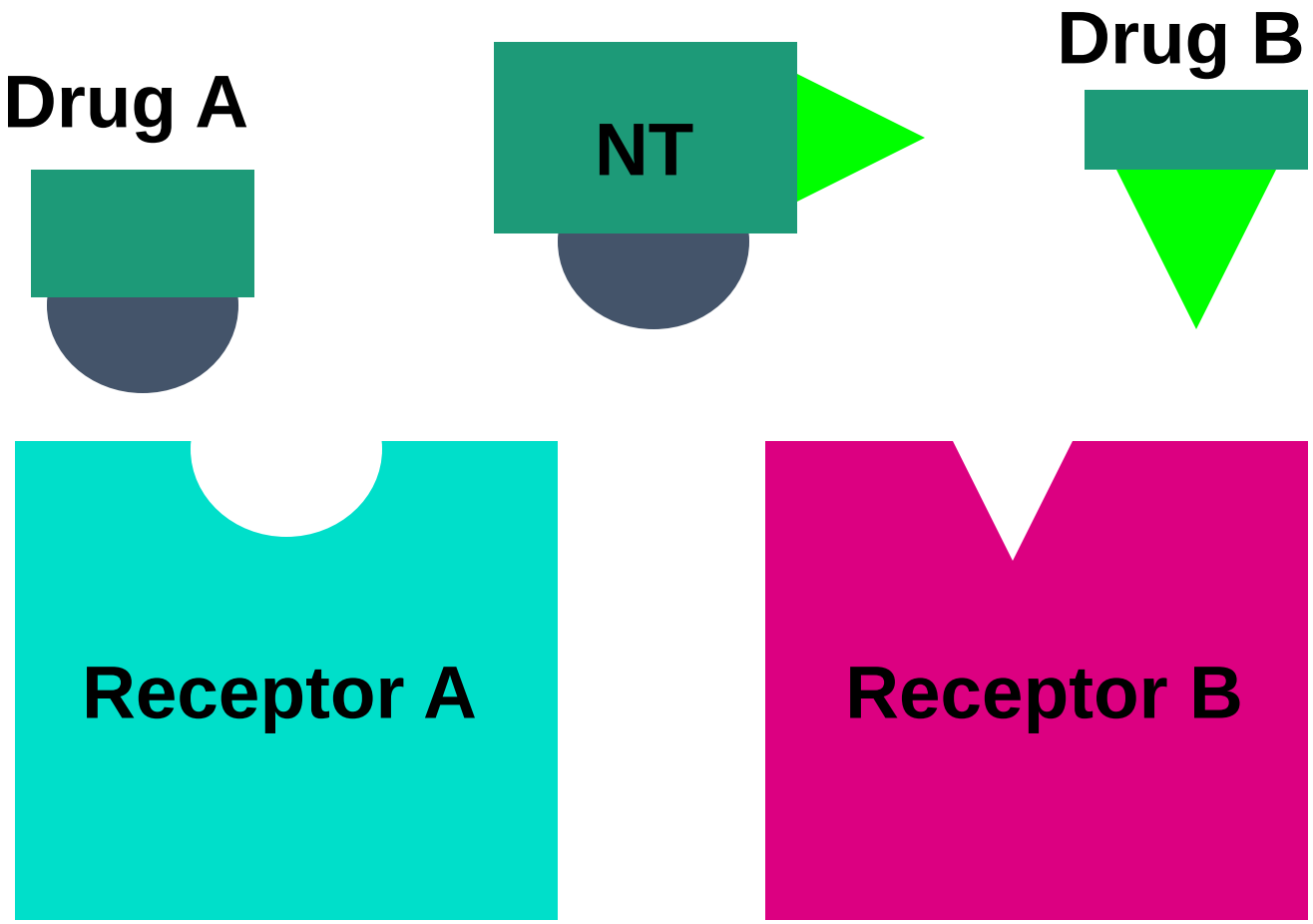
Drugs that bind to but **do not activate** neuroreceptors,

thereby blocking the actions of neurotransmitters or the neuroreceptor agonists.

- Same NT can bind to different -R
- different part of NT ~

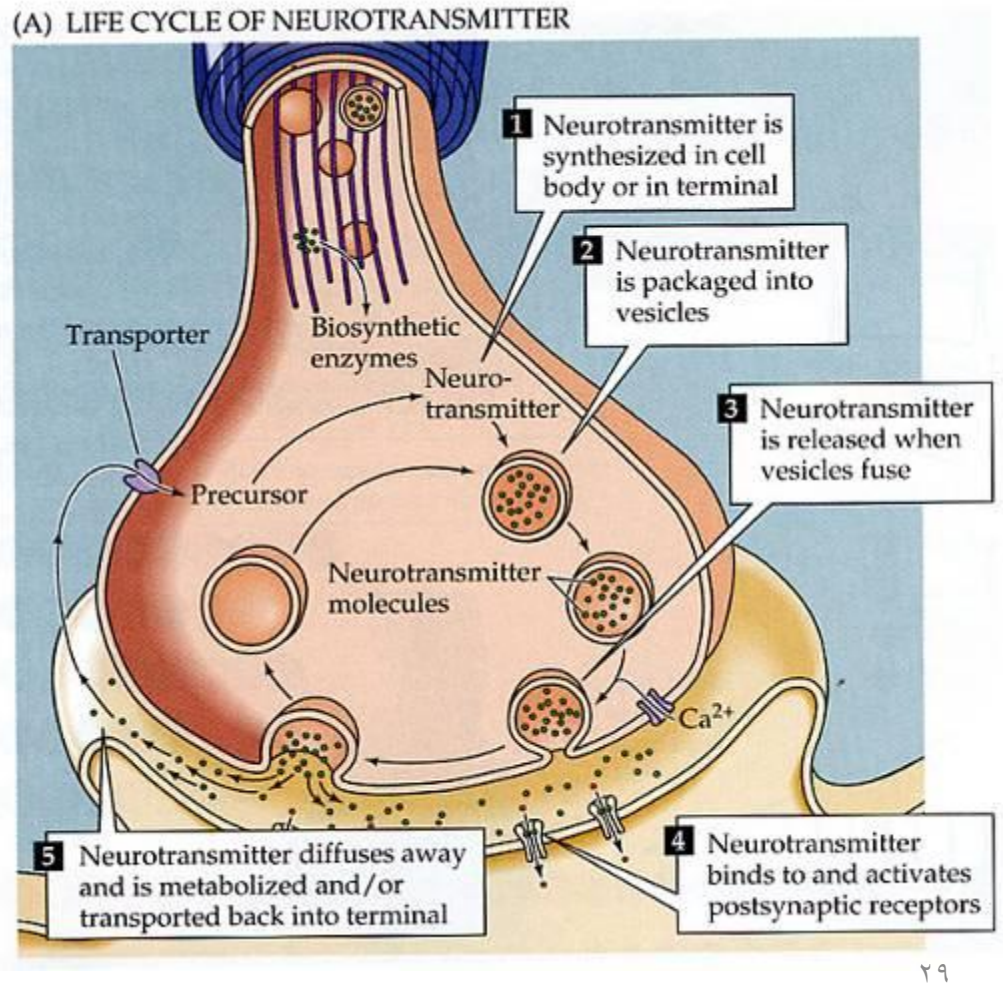


Specificity of drugs



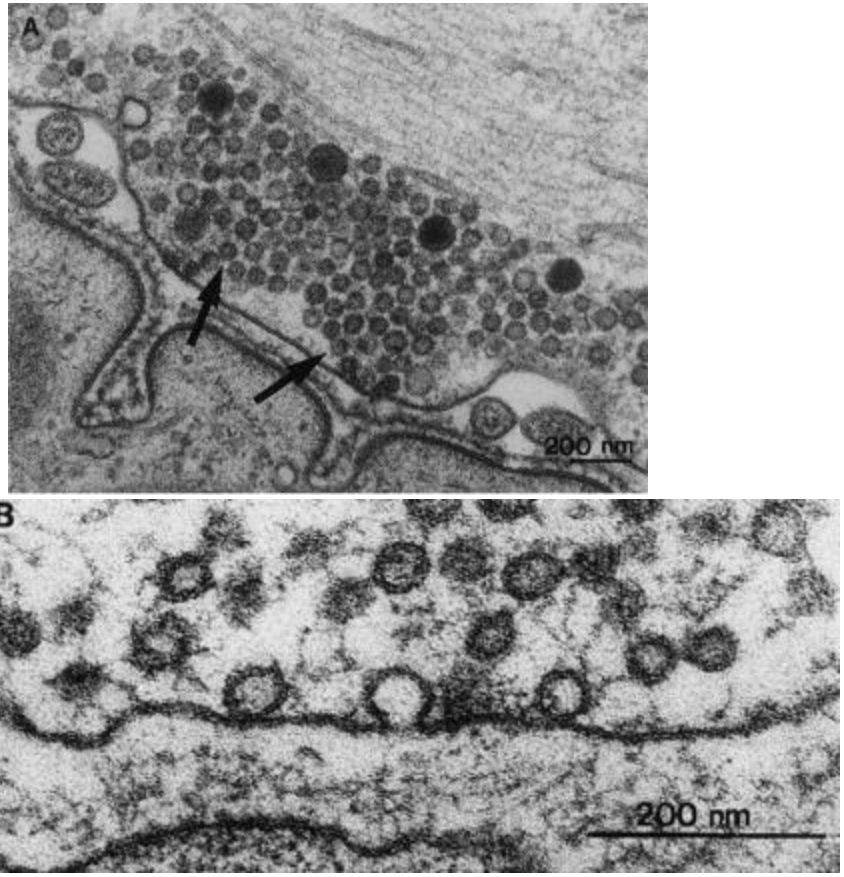
Five key steps in neurotransmission

- Synthesis
- Storage
- Release
- Receptor Binding
- Inactivation

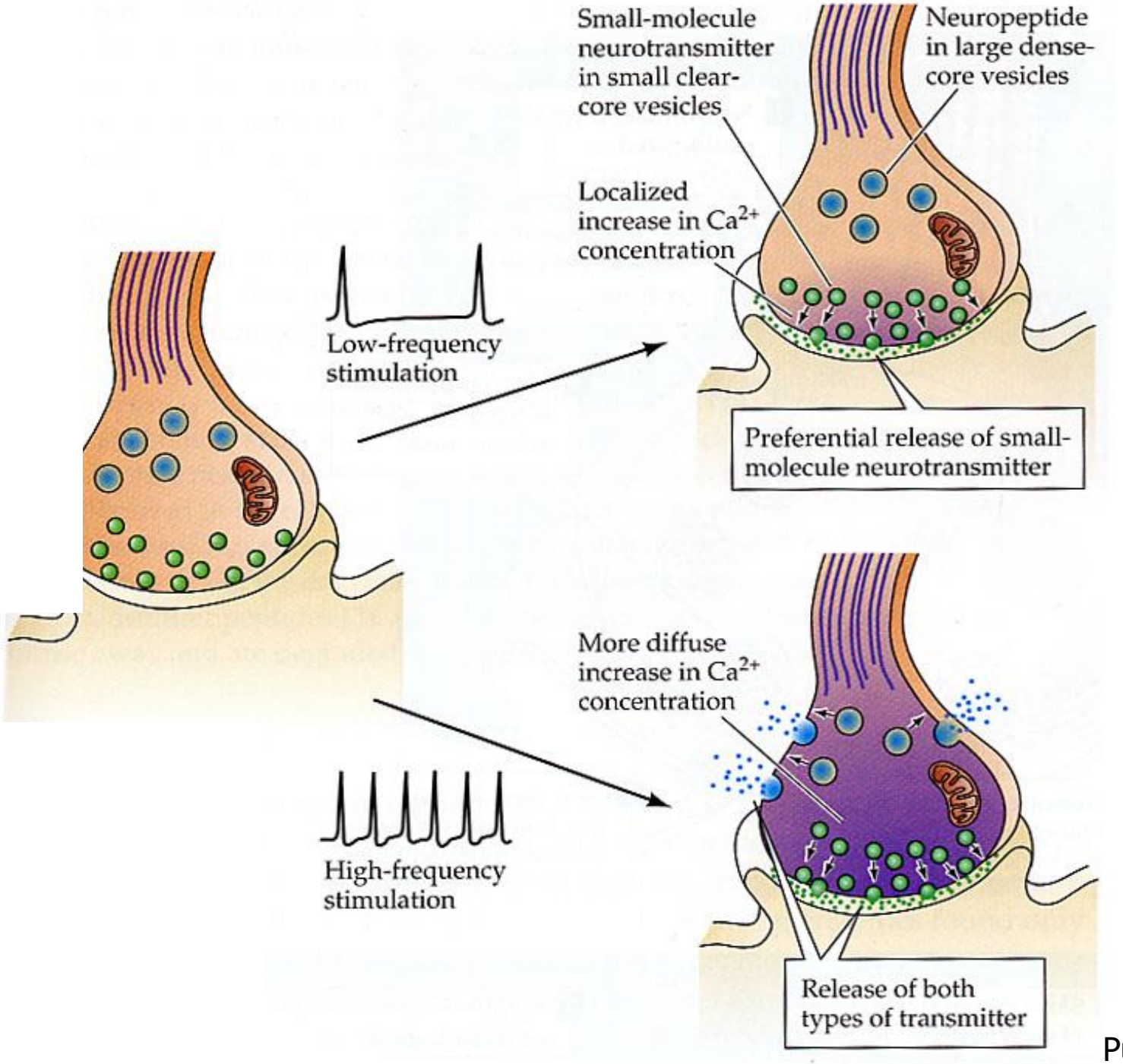


Purves, 2001

Synaptic vesicles



- Concentrate and protect transmitter
- Can be docked at active zone
- Differ for classical transmitters (small, clear-core) vs. neuropeptides (large, dense-core)


Small-molecule neurotransmitter in small clear-core vesicles
Neuropeptide in large dense-core vesicles
Localized increase in Ca^{2+} concentration
Low-frequency stimulation
Preferential release of small-molecule neurotransmitter
More diffuse increase in Ca^{2+} concentration
High-frequency stimulation
Release of both types of transmitter

Purves, 2001

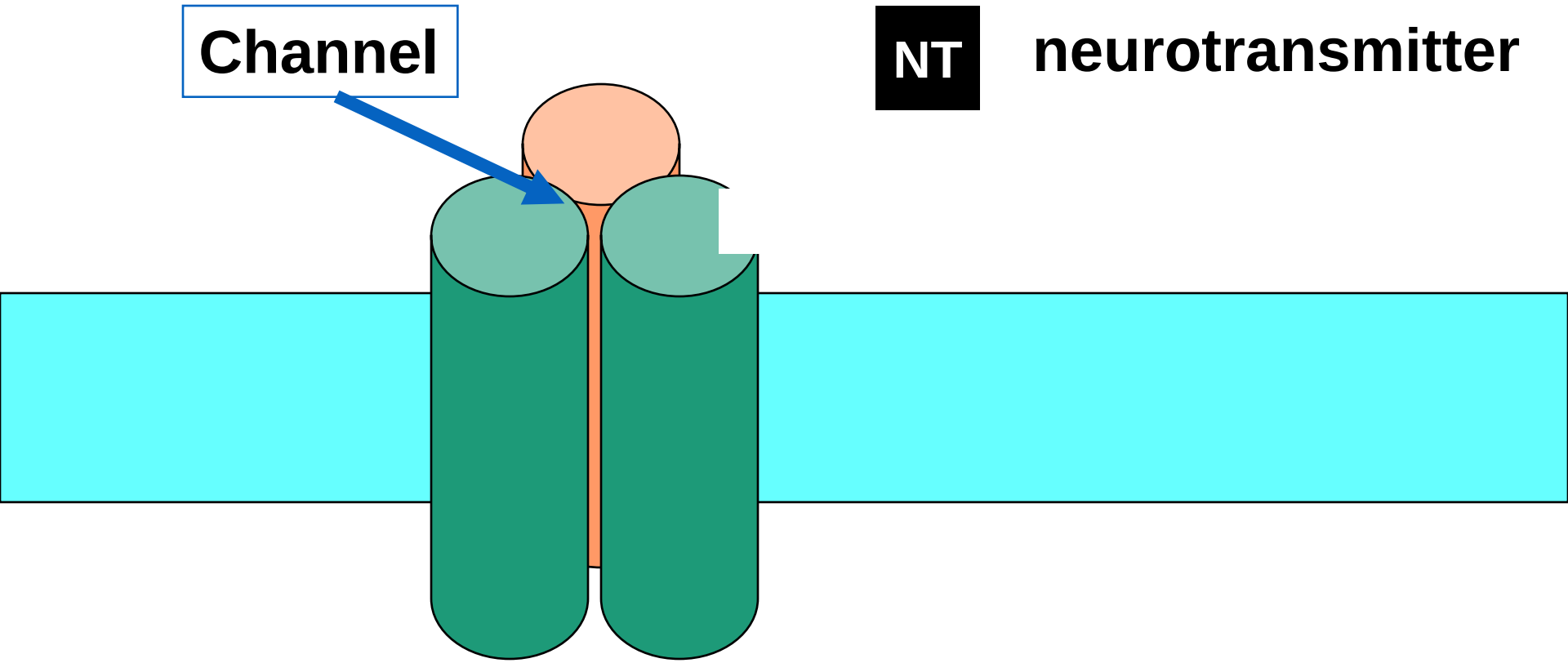
Receptors determine whether:???

- Synapse is excitatory or inhibitory
  - NE is excitatory at some synapses, inhibitory at others
- Transmitter binding activates ion channel directly or indirectly.
  - **Directly**
    - ionotropic receptors
    - **fast**
  - **Indirectly**
    - metabotropic receptors
    - G-protein coupled
    - **slow**

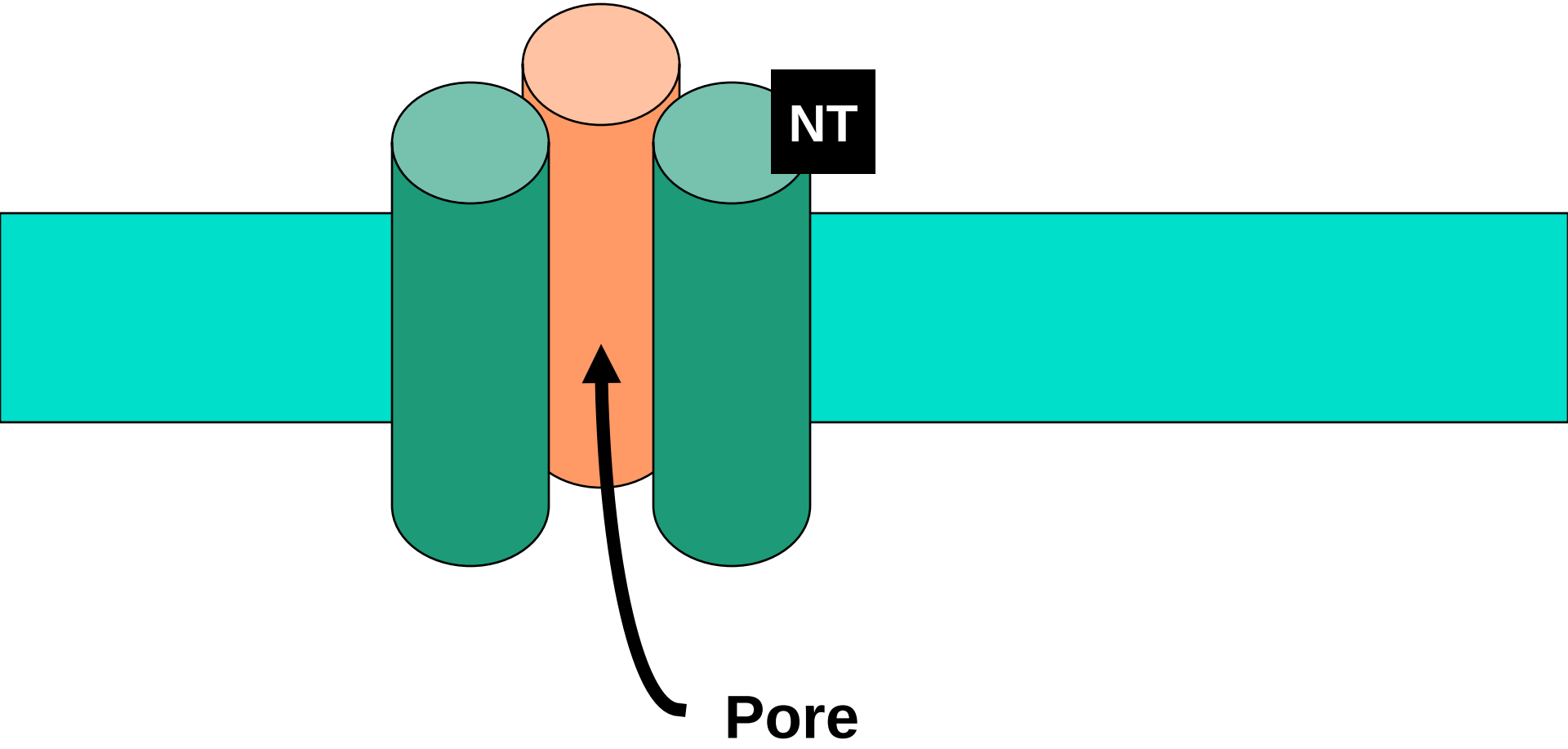
Receptor Activation

- **Ionotropic channel**
  - directly controls channel
  - fast
- **Metabotropic channel**
  - second messenger systems
  - receptor indirectly controls channel ~

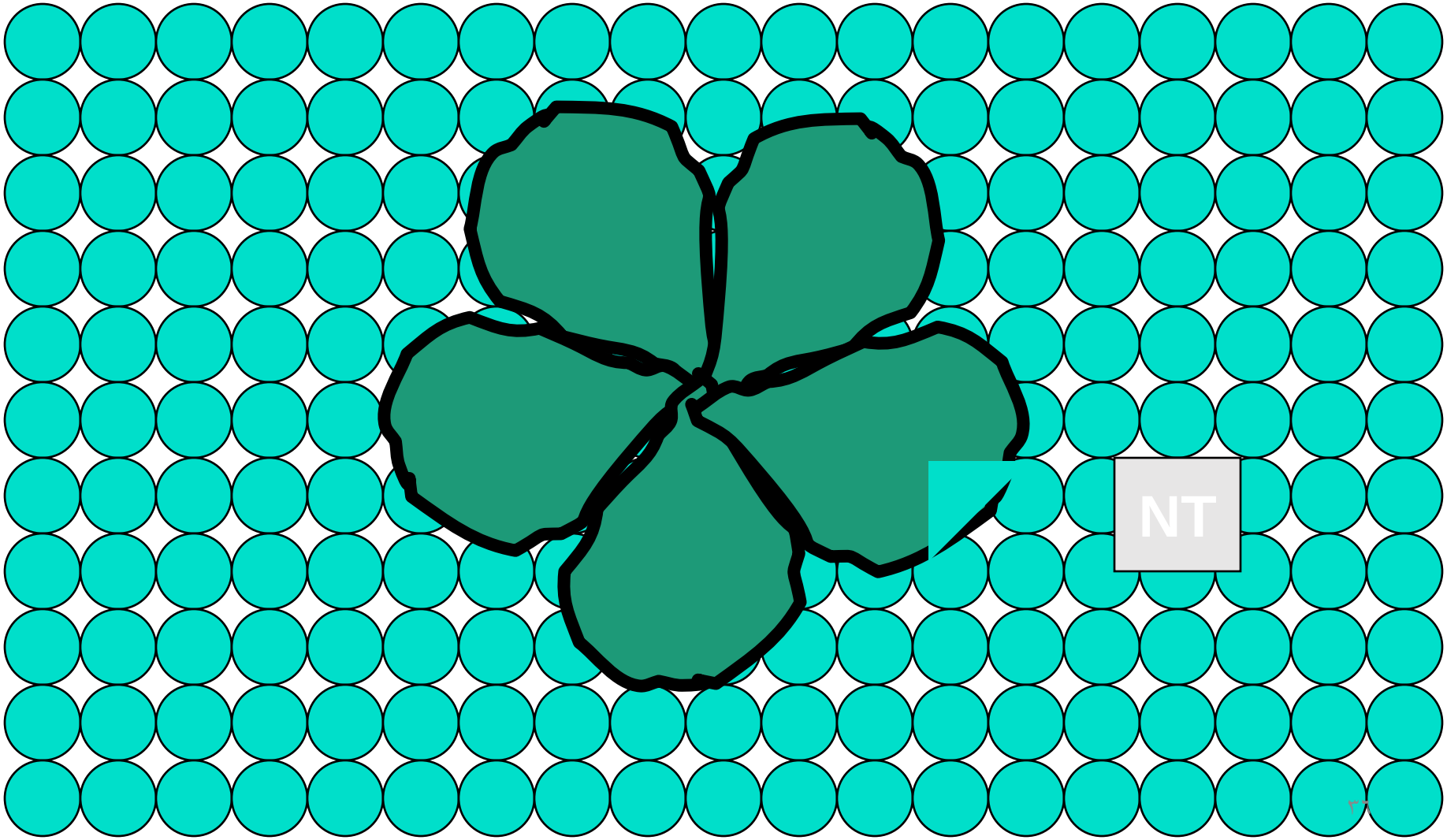
(1) Ionotropic Channels



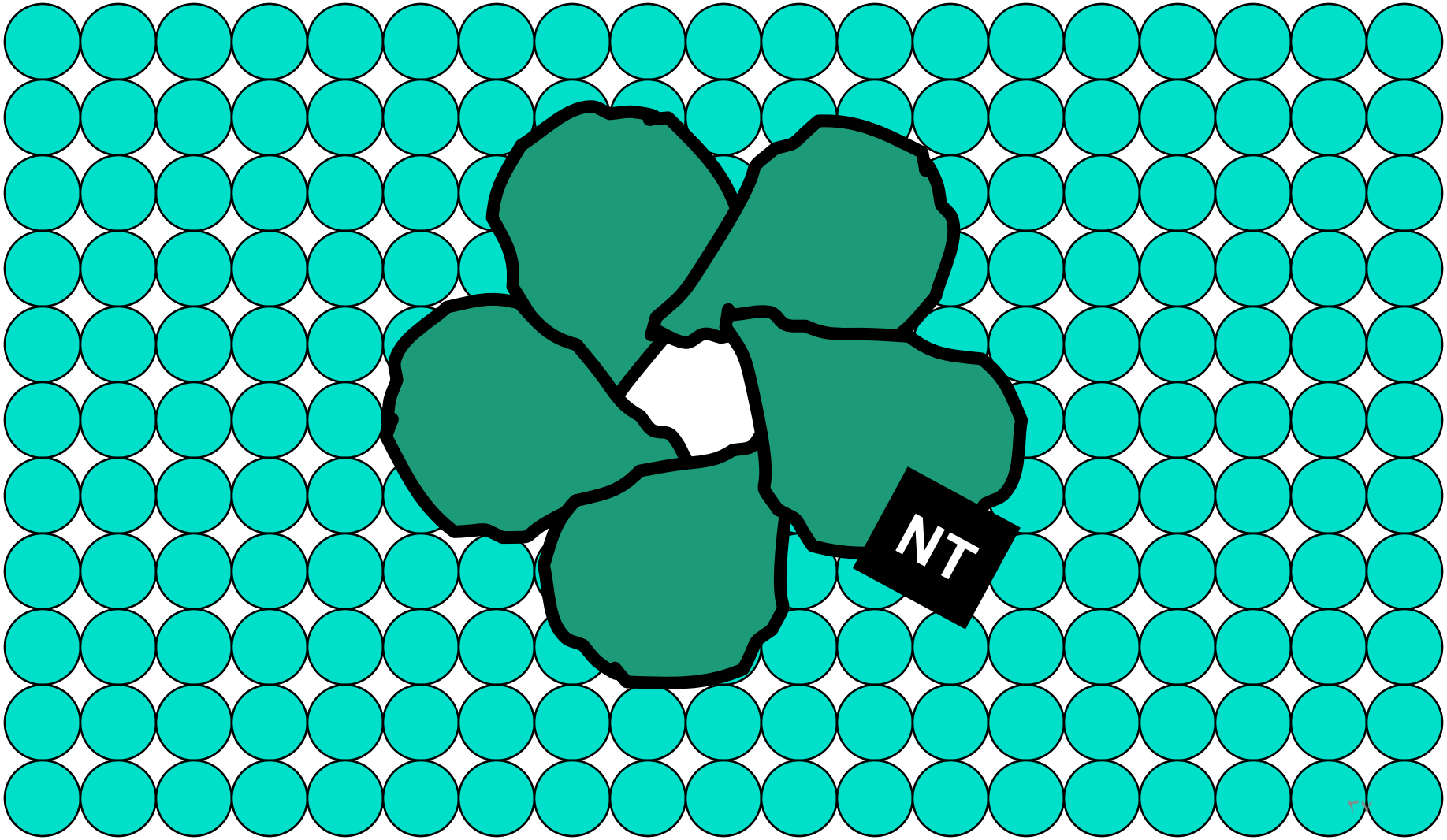
Ionotropic Channels



Ionotropic Channels



Ionotropic Channels



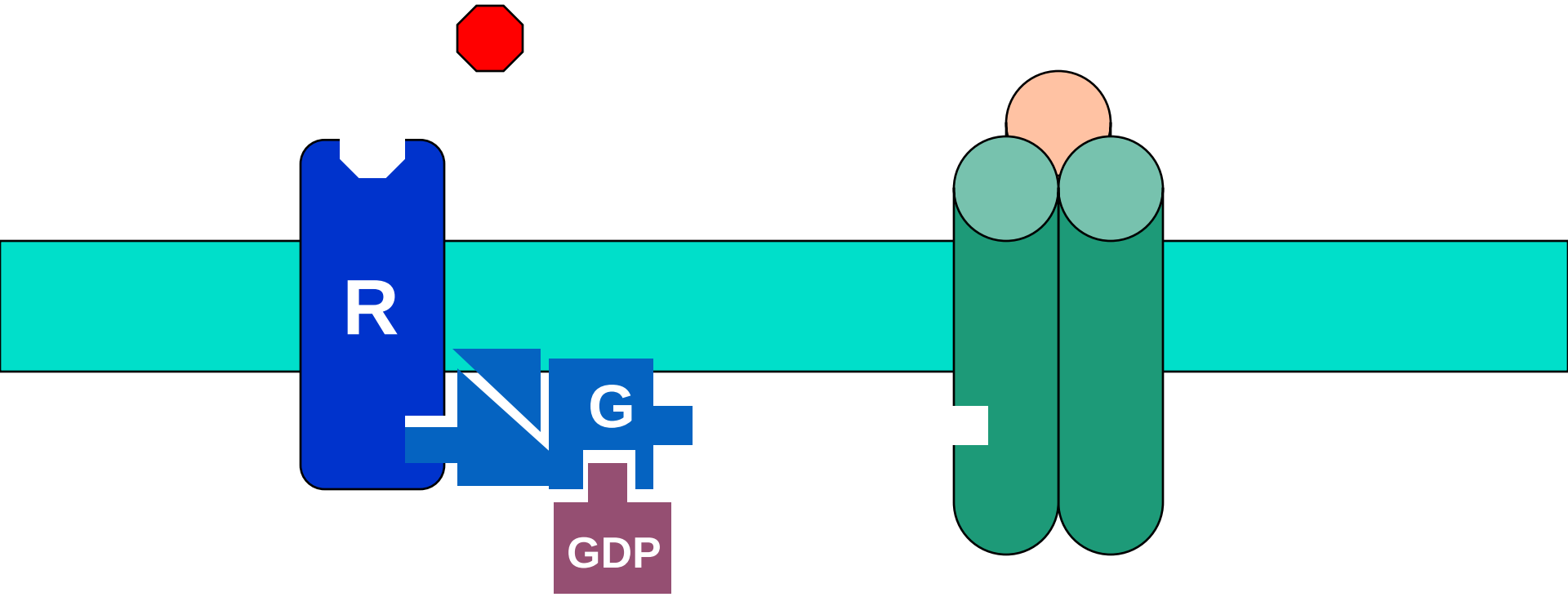
(2) **Metabotropic Channels**

- Receptor separate from channel
- G proteins
- 2d messenger system
  - cAMP
  - other types
- Effects
  - Control channel
  - Alter properties of receptors
  - regulation of gene expression ~

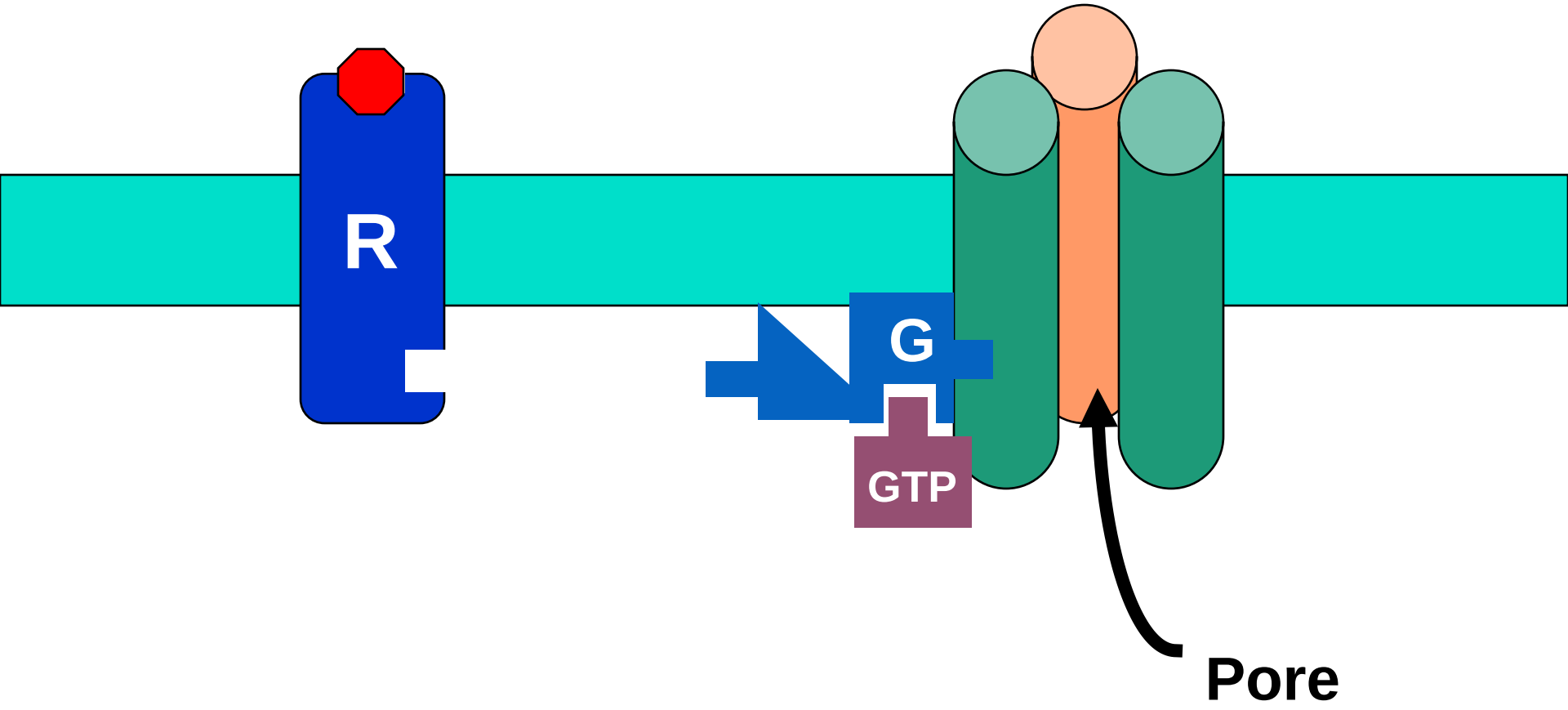
G protein: direct control

- NT is 1st messenger
- G protein binds to channel
  - opens or closes
  - relatively fast ~

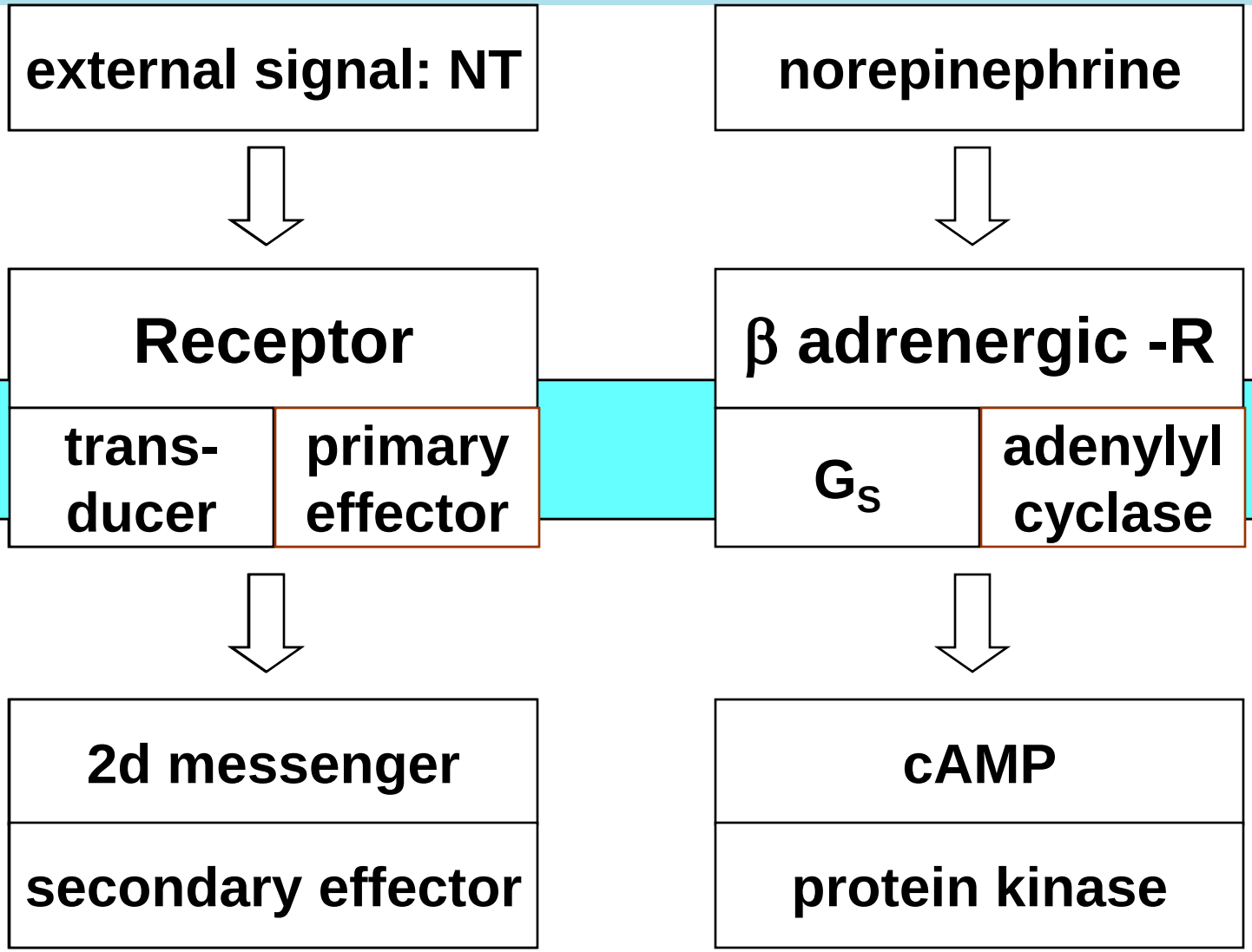
G protein: direct control



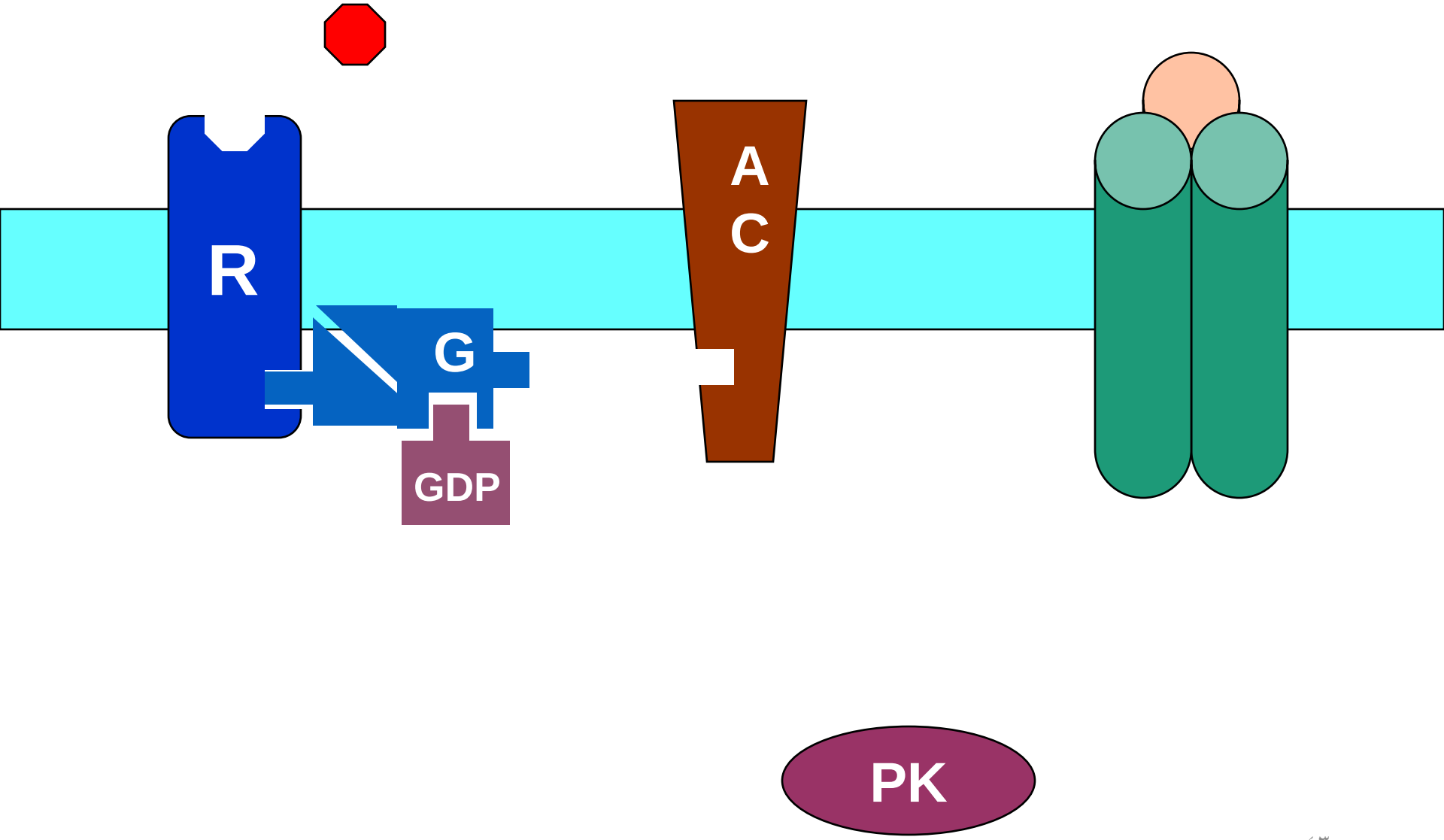
G protein: direct control



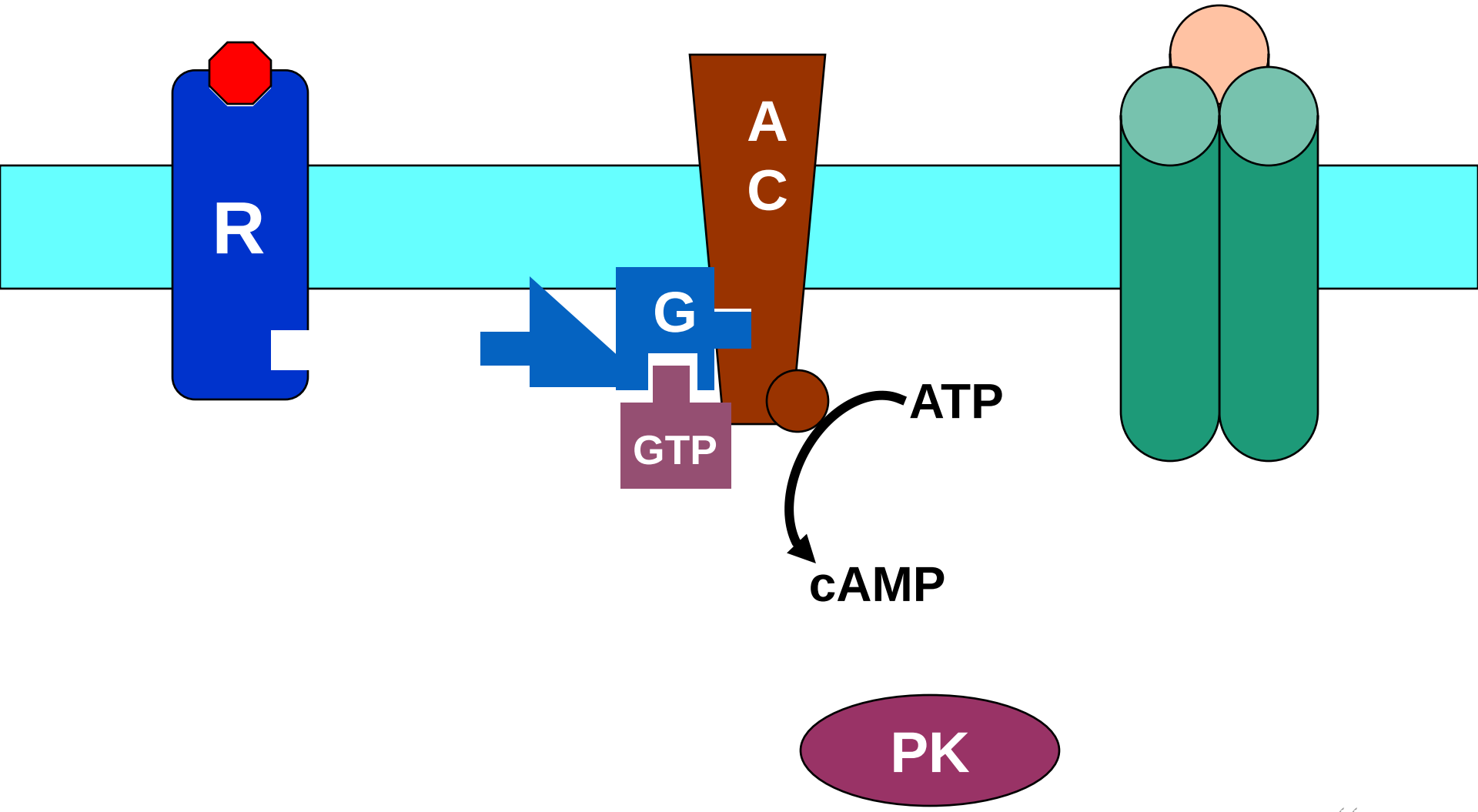
G protein: Protein Phosphorylation



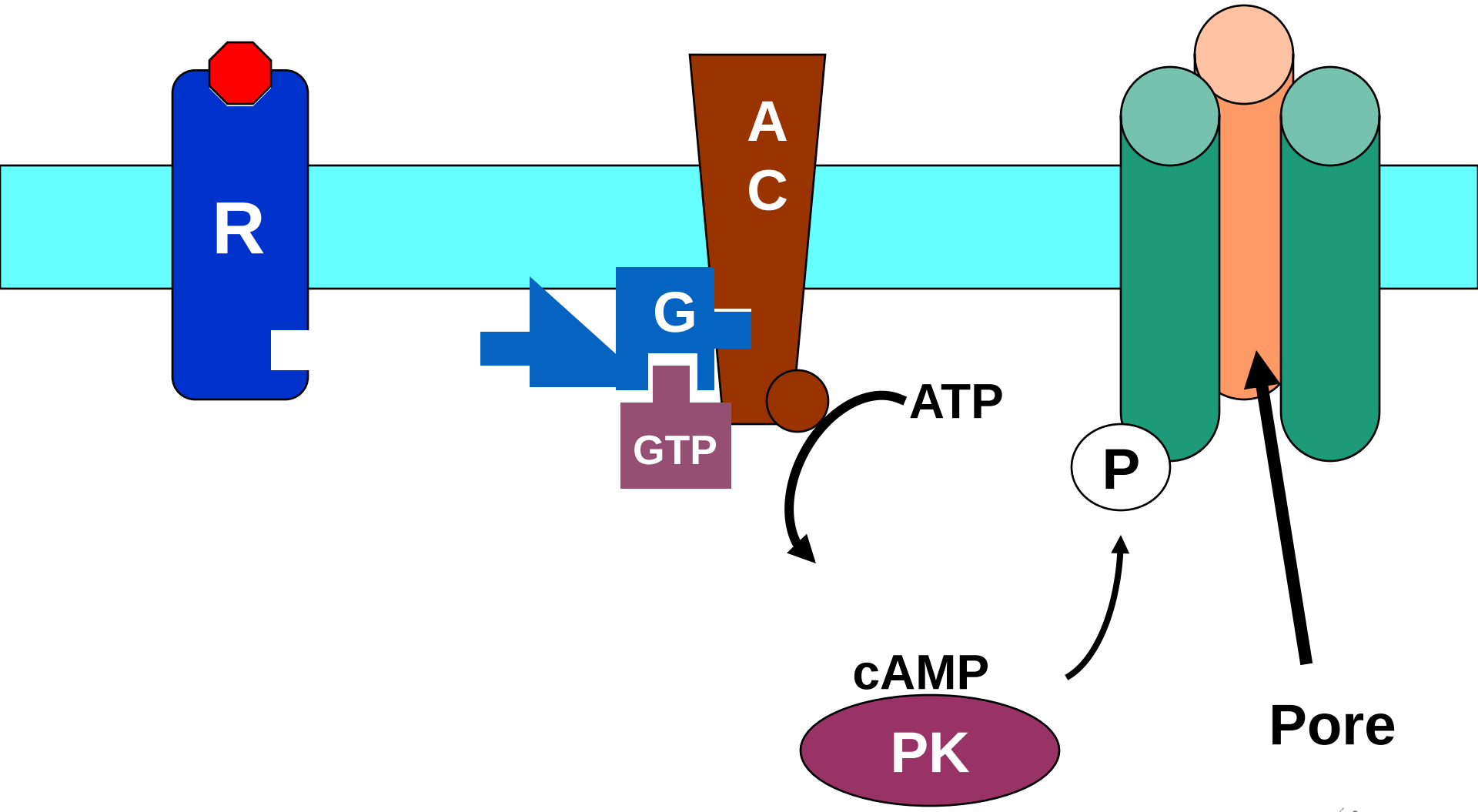
G protein: Protein Phosphorylation



G protein: Protein Phosphorylation

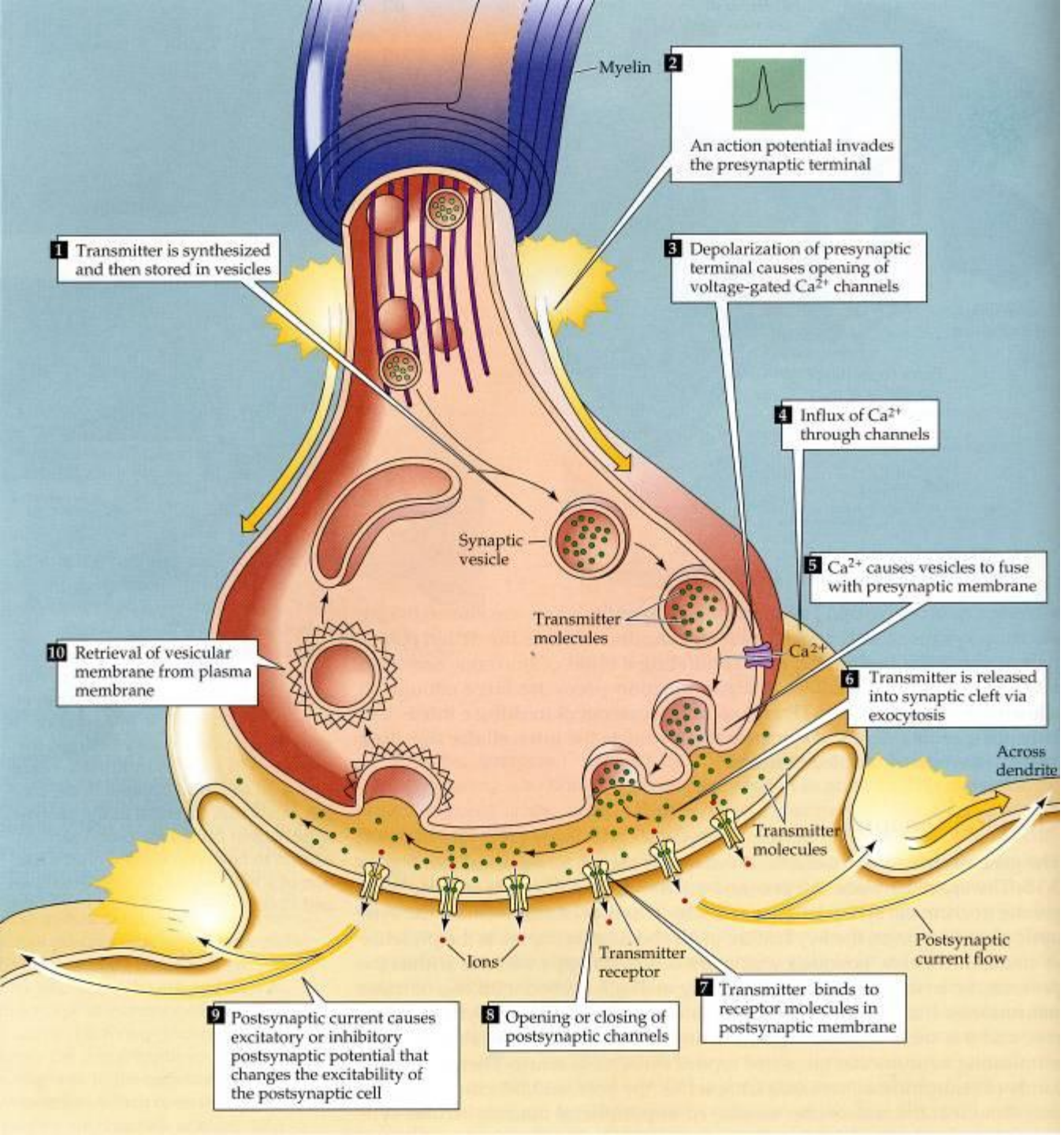


G protein: Protein Phosphorylation



(3) **Transmitter Inactivation**

- Reuptake by presynaptic terminal
- Uptake by glial cells
- Enzymatic degradation
- Presynaptic receptor
- Diffusion
- Combination of above



Summary of Synaptic Transmission

Purves,2001

Fatigue of synaptic transmission

❖ due to exhaustion of the stores of the transmitter substance in the synaptic terminal.

❖Effect of acidosis and alkalosis on synaptic transmission

❖ **Effect of drugs on synaptic transmission**:

- ↓O2 and anesthetics **↓ excitability**
- **Caffeine (coffee), theophylline (tea) and theobromine** (cocoa) **↑ excitability**

Thank you!