Neuron types and Neurotransmitters

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Objectives

- Understand synaptic transmission
- List types of sensory neurons
- Classify neurotransmitters
- Explain the mechanism of neurotransmission
- Judge the types of receptors for the neurotrasmitters

Transmission of Receptor Information to the Brain

- the larger the nerve fiber diameter the faster the rate of transmission of the signal
- velocity of transmission can be as fast as 120 m/sec or as slow as 0.5 m/sec
- nerve fiber classification
  - type A - myelinated fibers of varying sizes, generally fast transmission speed
    - subdivided into α, β, δ, γ
  - type C - unmyelinated fibers, small with slow transmission speed

Types of Nerve Fiber

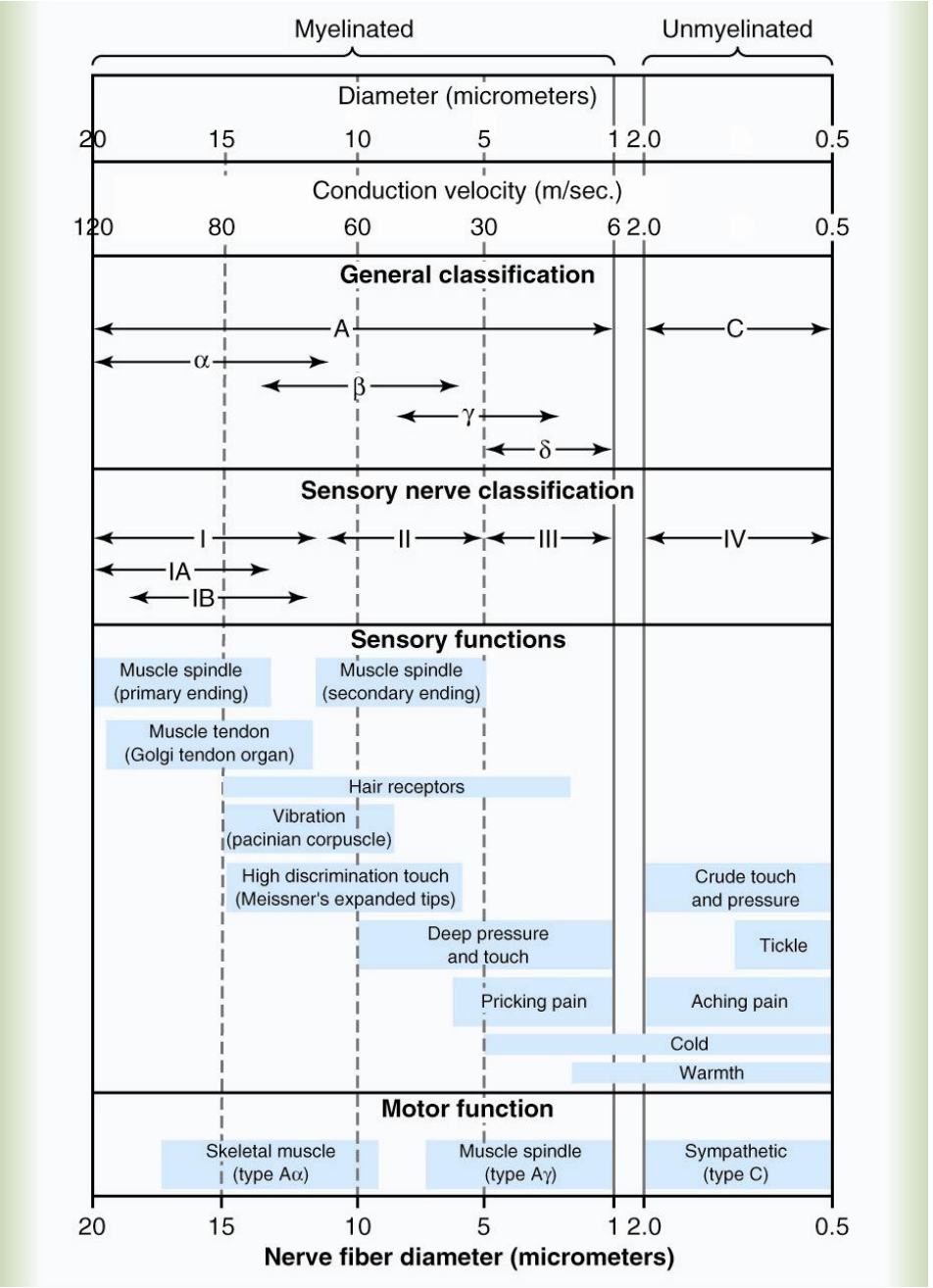
-Myelinated fibers –

Type A (types I, II and III)

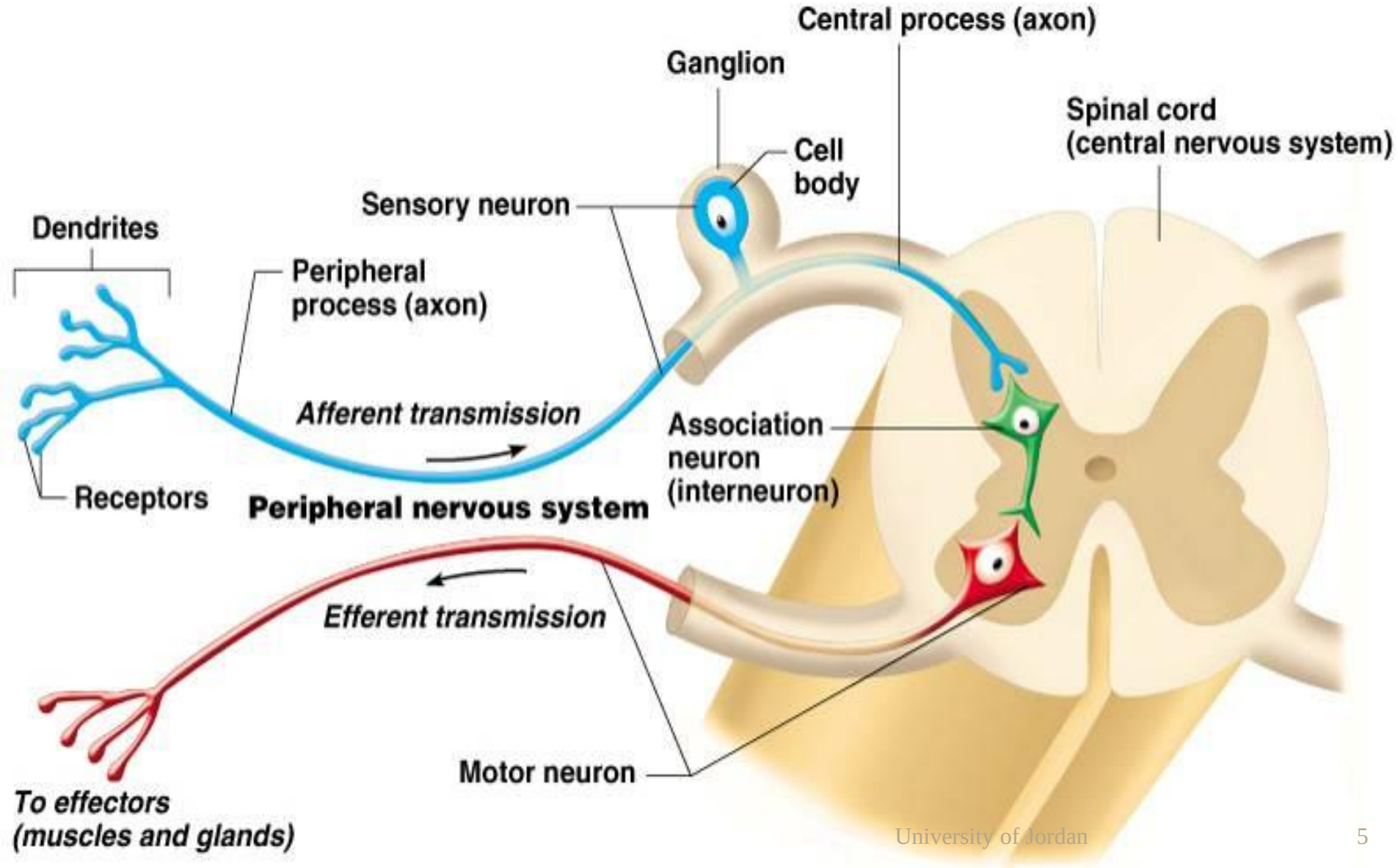
- A α
- A β
- A γ
- A δ

-Umyelinated Fibers-

Type C (type IV)



Neuron Classification



Structural Classification of Neurons

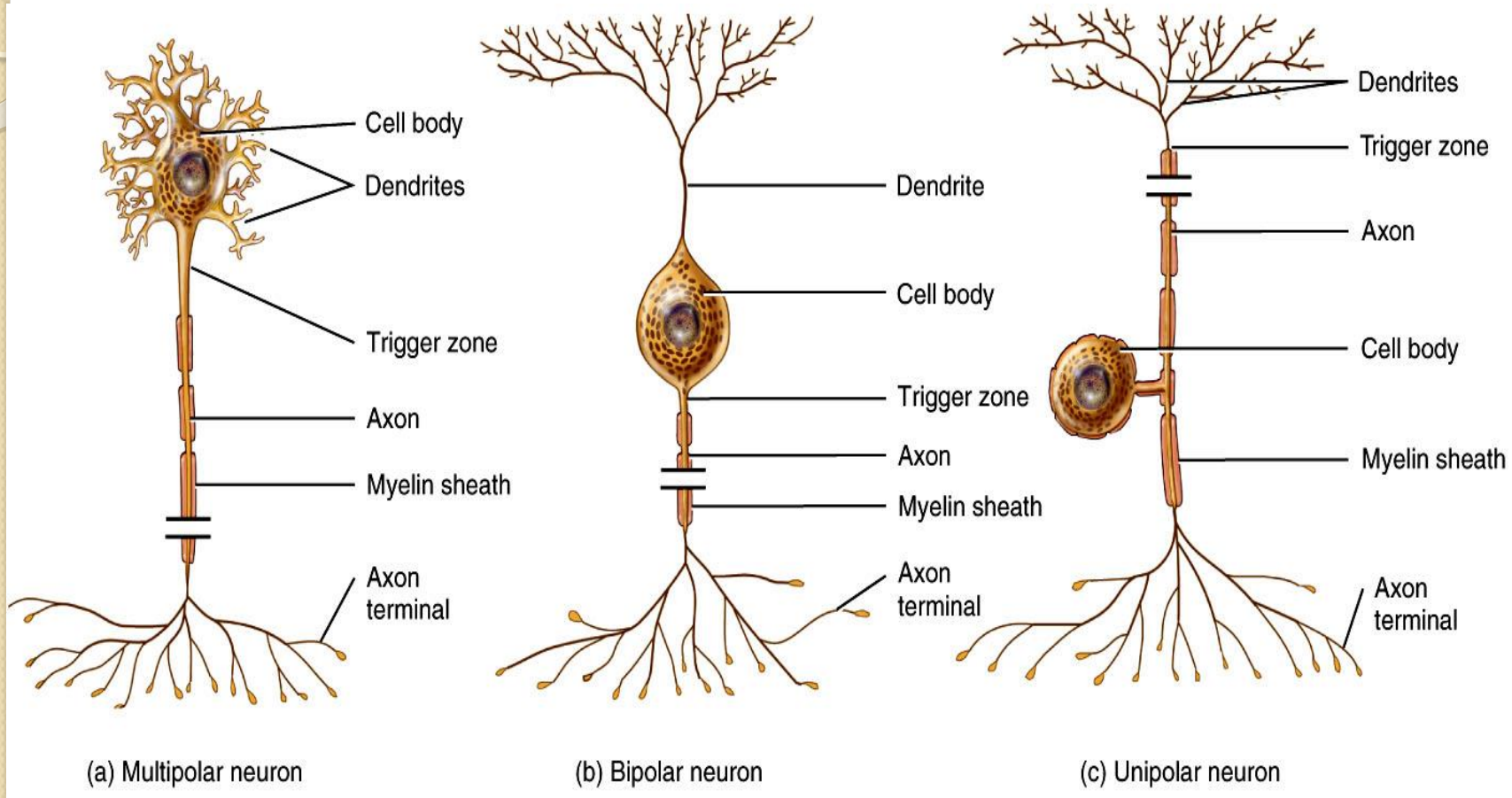


Figure 12.03 Tortora - PAP 12/e

Neurotransmitters

- Chemical substances that function as synaptic transmitters

1. Small molecules which act as rapidly acting transmitters
   - acetylcholine, norepinephrine, dopamine, serotonin, GABA, glycine, glutamate, NO
2. Neuropeptides
   - more potent than small molecule transmitters, cause more prolonged actions
   - endorphins, enkephalins, VIP, ect.
   - hypothalamic releasing hormones
   - TRH, LHRH, ect.
   - pituitary peptides
   - ACTH, prolactin, vasopressin, ect.

Neurotransmitters

Table 45–1

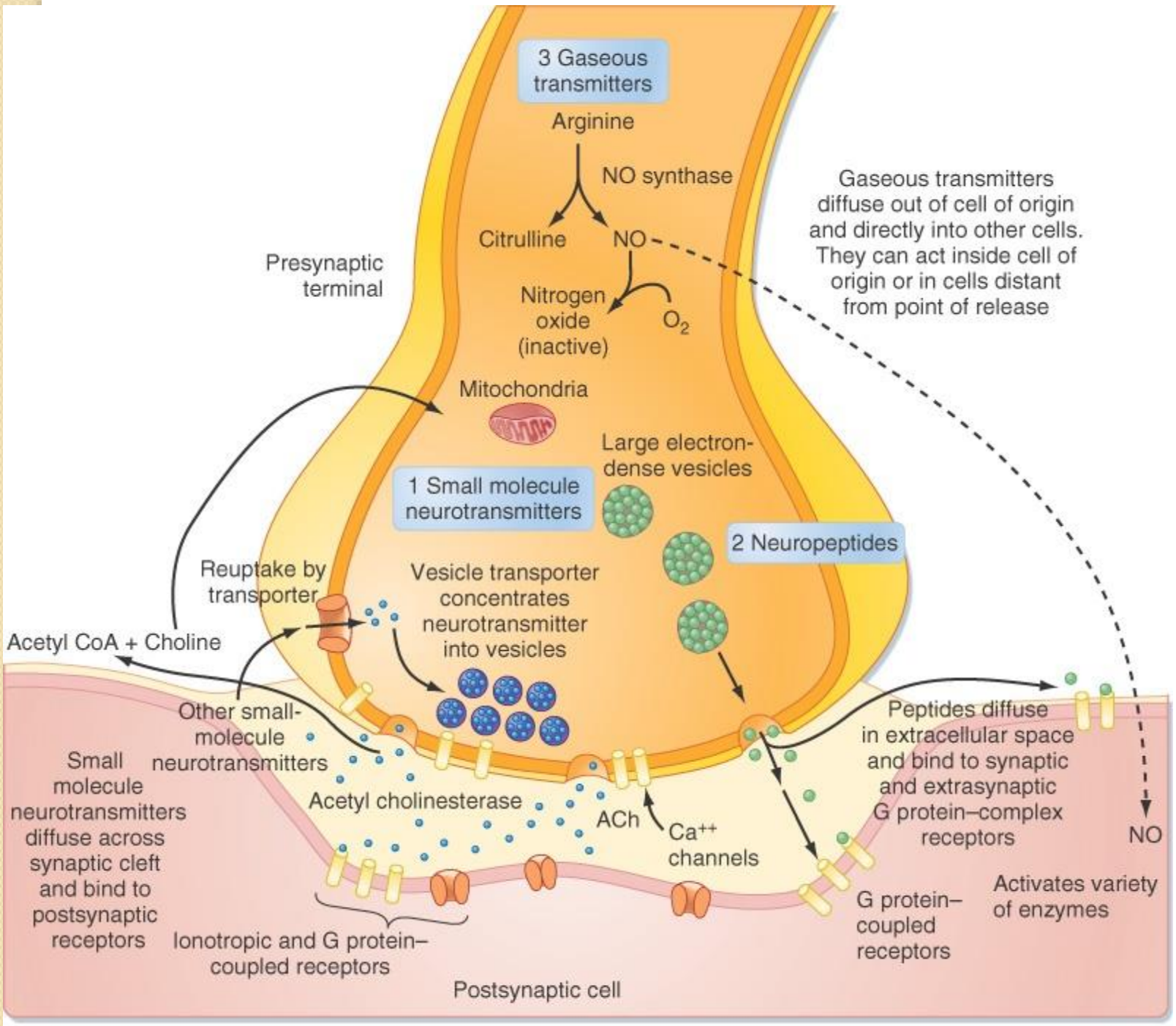
Small-Molecule, Rapidly Acting Transmitters

Class I
Acetylcholine
Class II: The Amines
Norepinephrine
Epinephrine
Dopamine
Serotonin
Histamine
Class III: Amino Acids
Gamma-aminobutyric acid (GABA)
Glycine
Glutamate
Aspartate
Class IV
Nitric oxide (NO)

Table 45–2

Neuropeptide, Slowly Acting Transmitters or Growth Factors

Hypothalamic-releasing hormones
Thyrotropin-releasing hormone
Luteinizing hormone–releasing hormone
Somatostatin (growth hormone inhibitory factor)
Pituitary peptides
Adrenocorticotropic hormone (ACTH)
β-Endorphin
α-Melanocyte-stimulating hormone
Prolactin
Luteinizing hormone
Thyrotropin
Growth hormone
Vasopressin
Oxytocin
Peptides that act on gut and brain
Leucine enkephalin
Methionine enkephalin
Substance P
Gastrin
Cholecystokinin
Vasoactive intestinal polypeptide (VIP)
Nerve growth factor
Brain-derived neurotropic factor
Neurotensin
Insulin
Glucagon
From other tissues
Angiotensin II
Bradykinin
Carnosine
Sleep peptides
Calcitonin



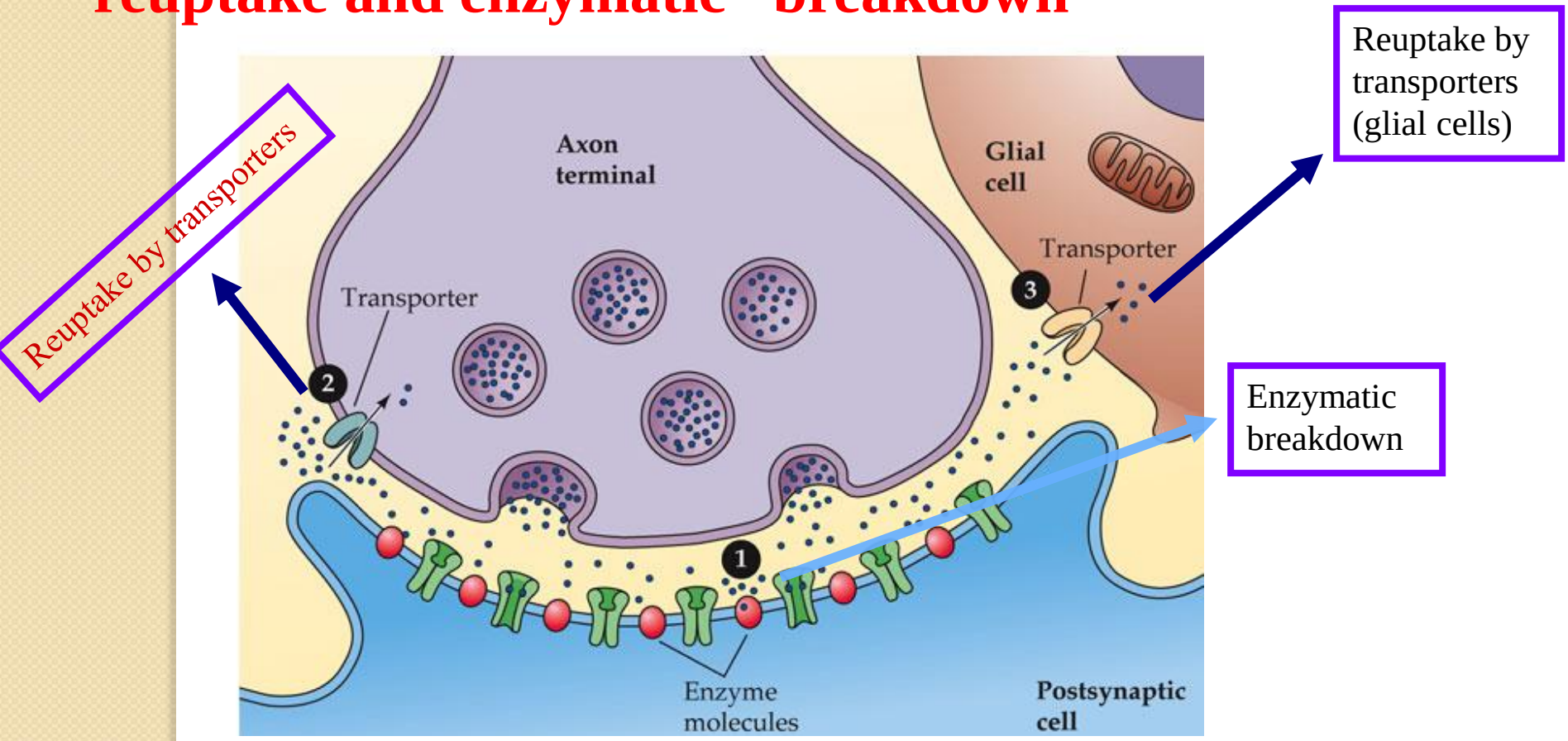
Comparison between Small Molecules and Neuropeptides Neurotramsmitters (NT)

- Small molecules NT are rapidly acting as compared to slowly acting neuropepides
- Neuron has only one NT but may have one or more NP
- Small molecules NT are have short lived action compared to prolonged time of action for neuropeptides
- Small molecules NT are excreted in larger amounts compared to smaller quantities of neuropeptide
- Small molecules NT vesicles are recycled but neuropeptide ones are not
- Neuropeptides are co-secreted with small molecules NT
- Neuropeptides are synthesized at the soma while small molecules could be formed at the presynaptic terminals

Removal of Neurotransmitter

- Diffusion
  - move down concentration gradient
- Enzymatic degradation
  - Acetylcholinesterase for (Ach), peptidases for neuropeptides
- Uptake by neurons or glia cells
  - neurotransmitter transporters
  - Prozac = serotonin reuptake inhibitor

- **Transmitter Inactivation: reuptake and enzymatic breakdown**



Neurotransmitter can be recycled in presynaptic terminal or can be broken down by enzymes within the cell

II Neurotransmitters and receptors

Basic Concepts of NT and receptor

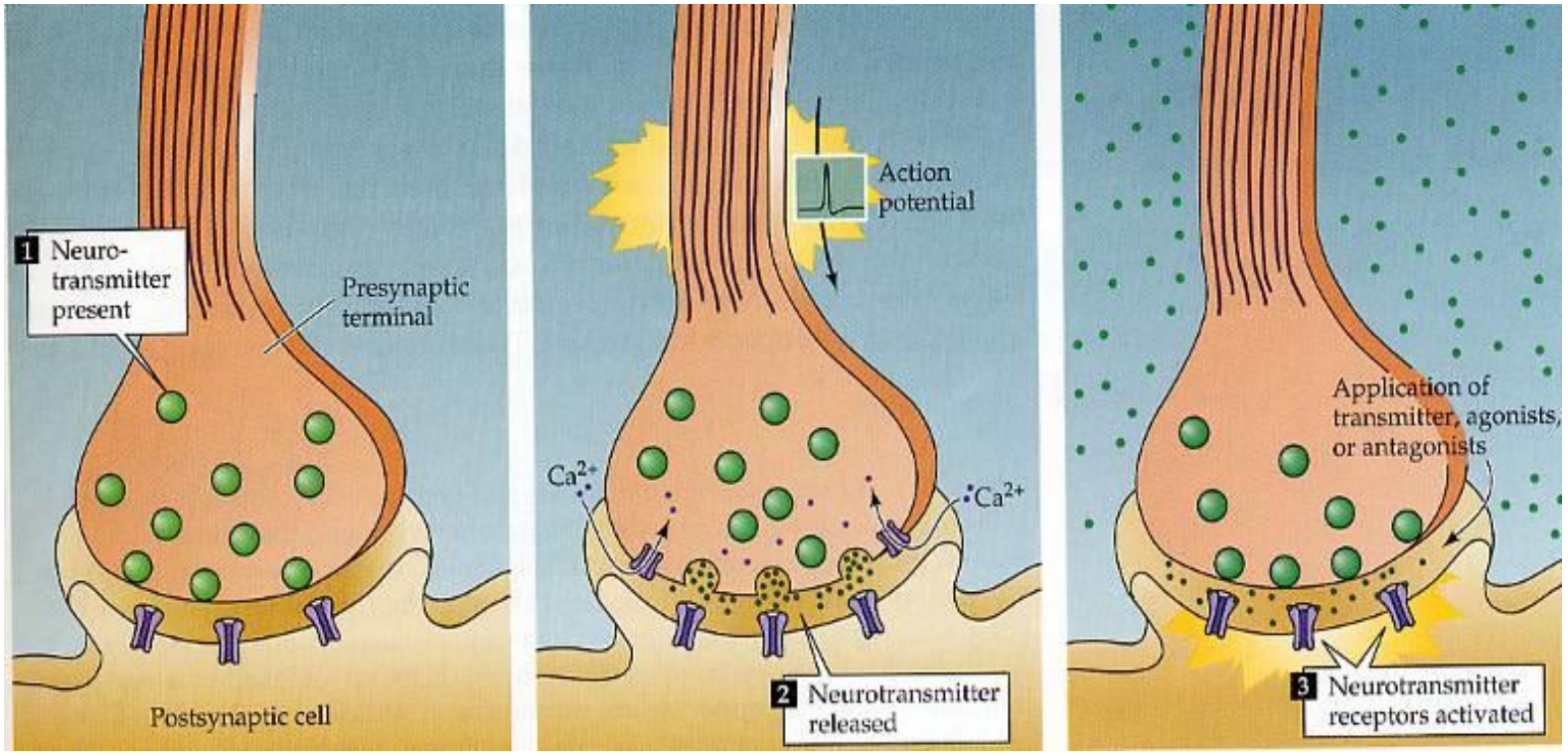
Neurotransmitter: Endogenous signaling molecules that alter the behaviour of neurons or effector cells.

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

- Vast array of 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



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.

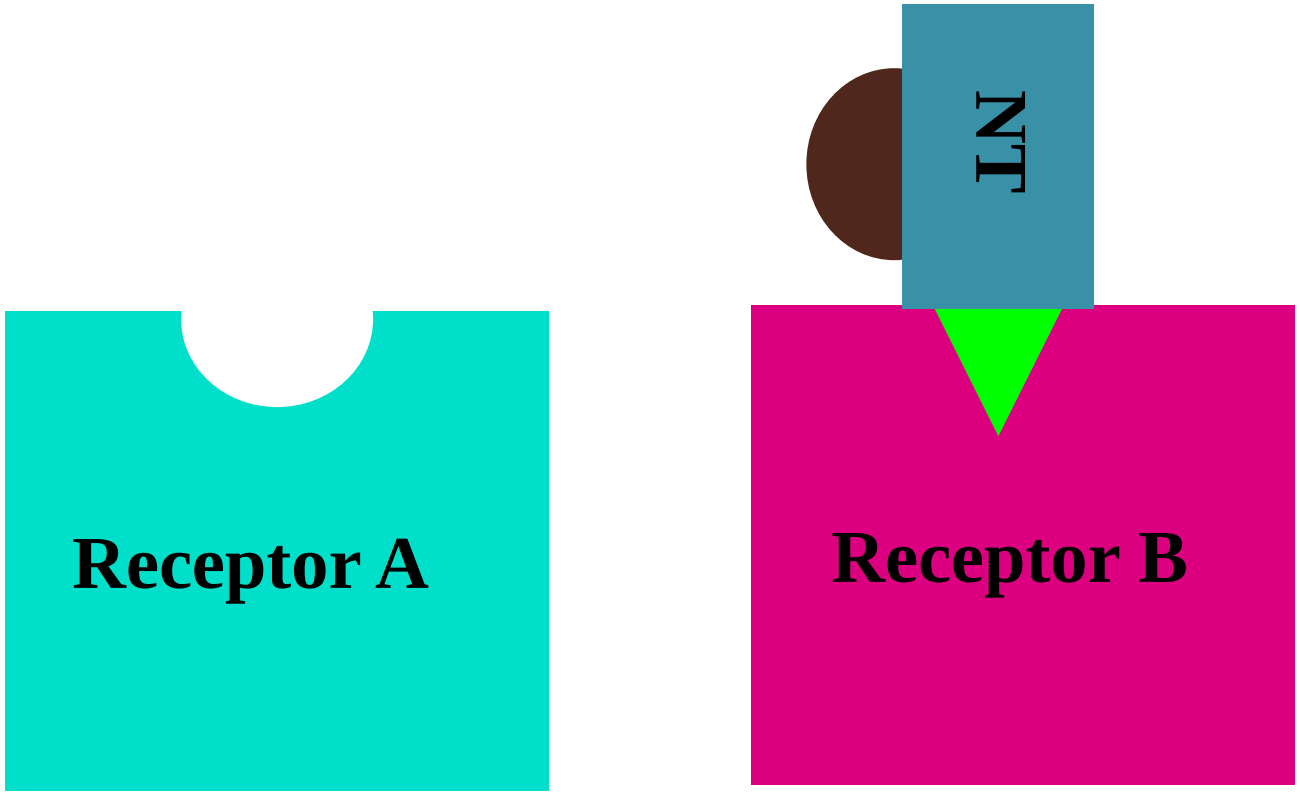
Drugs are often designed as receptor agonists to treat a variety of diseases and disorders when the original chemical substance is missing or depleted.

Antagonist

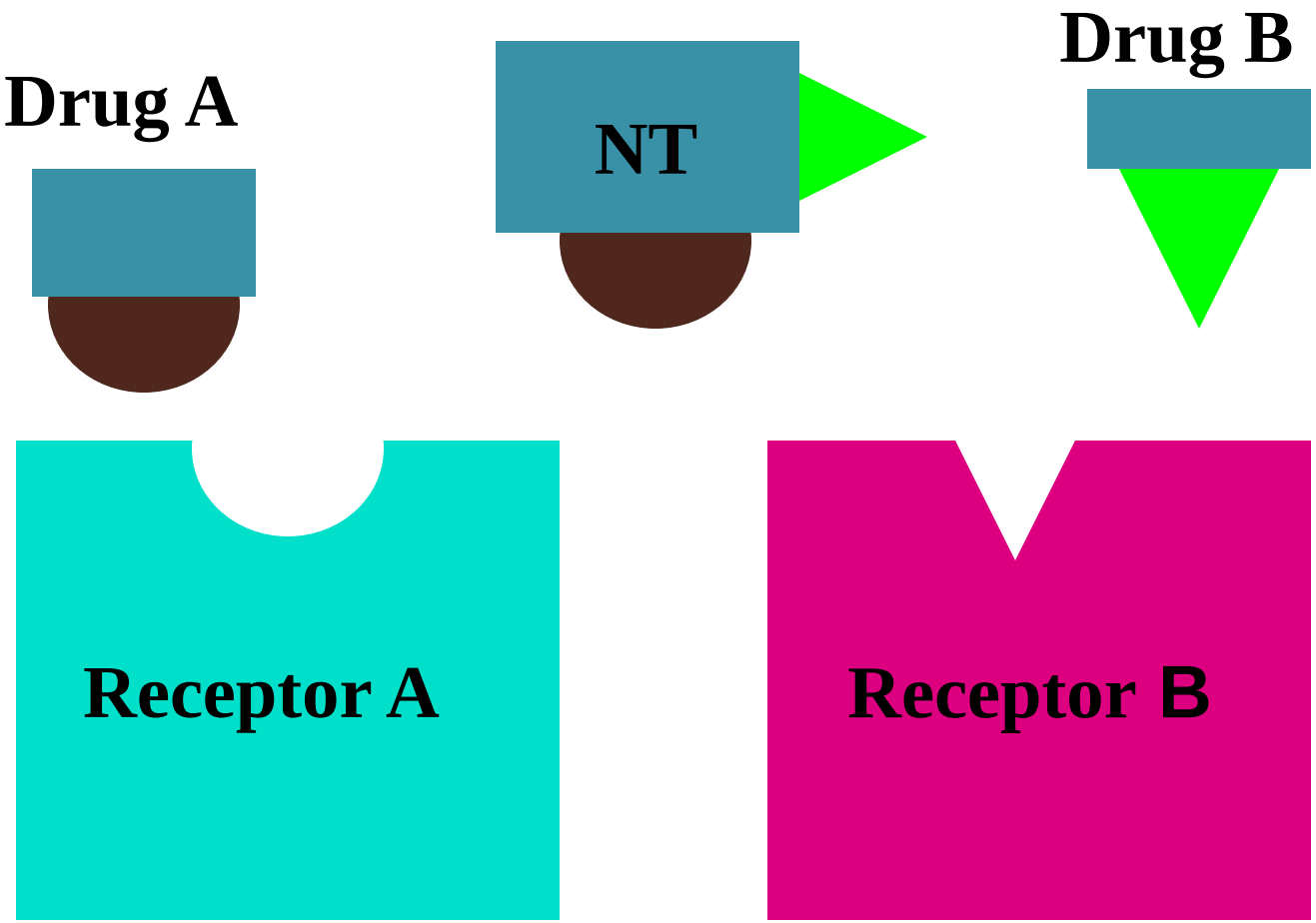
Drugs that bind to but do not activate neuroreceptors,

thereby blocking the actions of neurotransmitters or the neuroreceptor agonists.

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

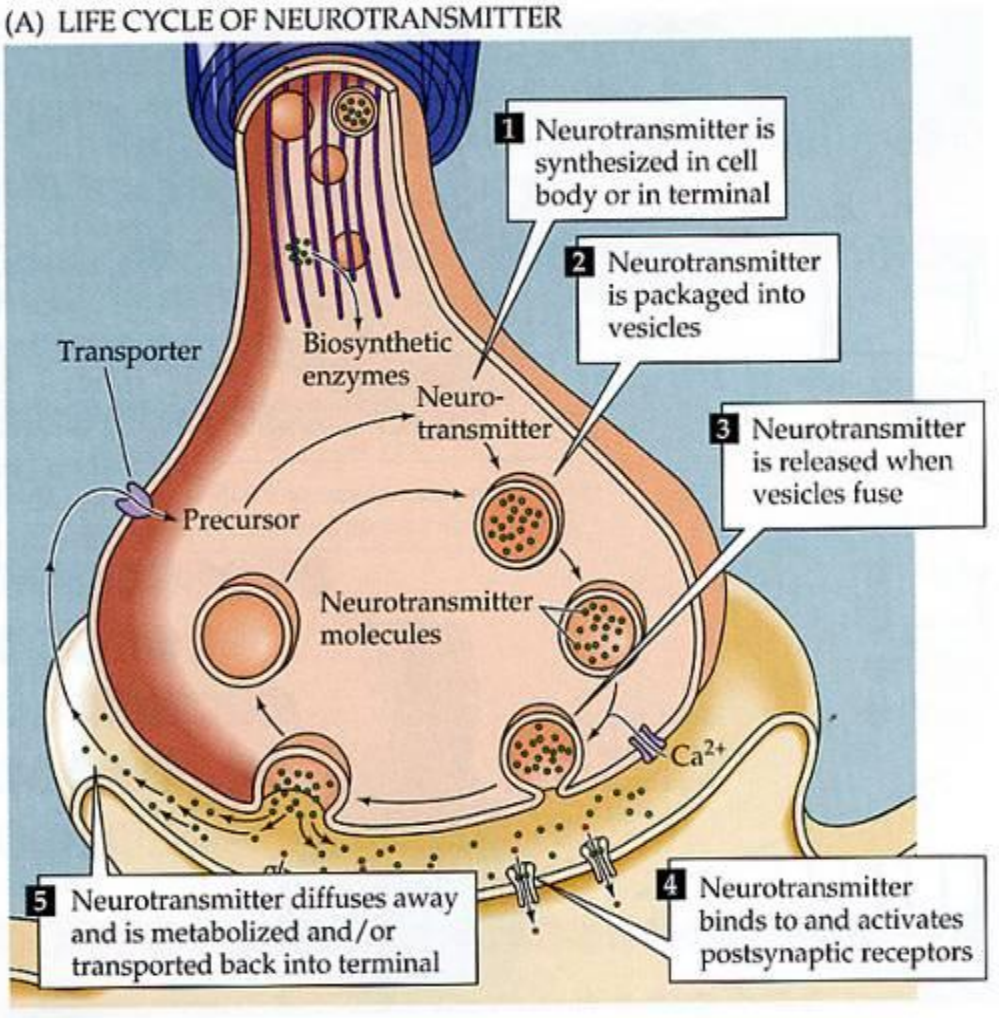


Specificity of drugs

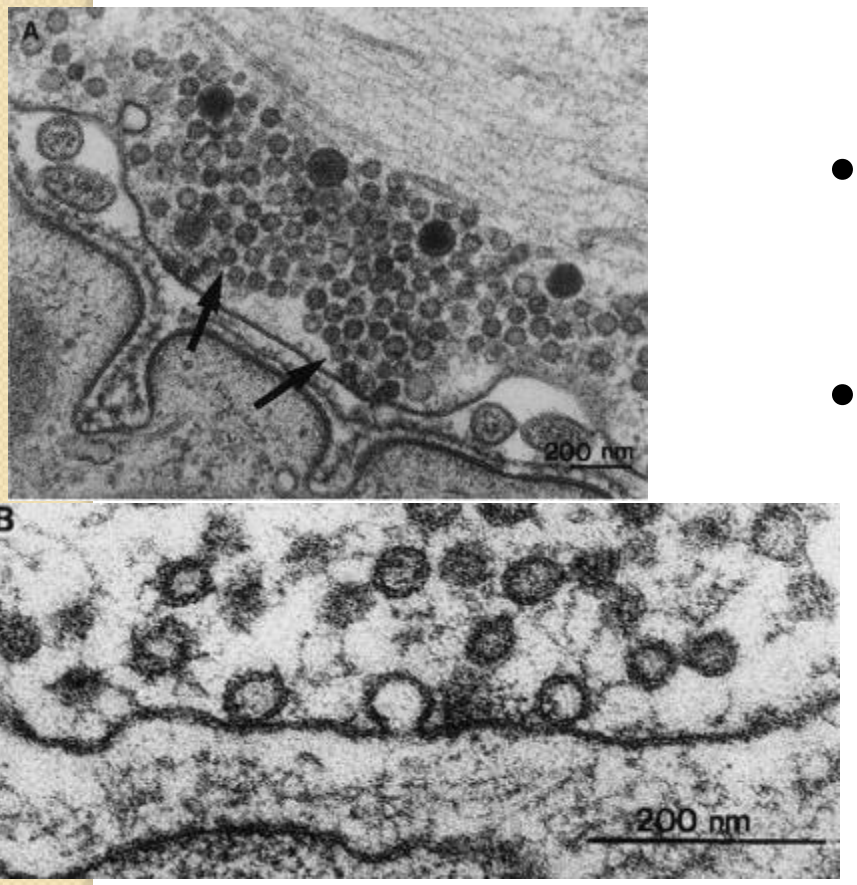


Five key steps in neurotransmission

- Synthesis
- Storage
- Release
- Receptor Binding
- Inactivation



Synaptic vesicles



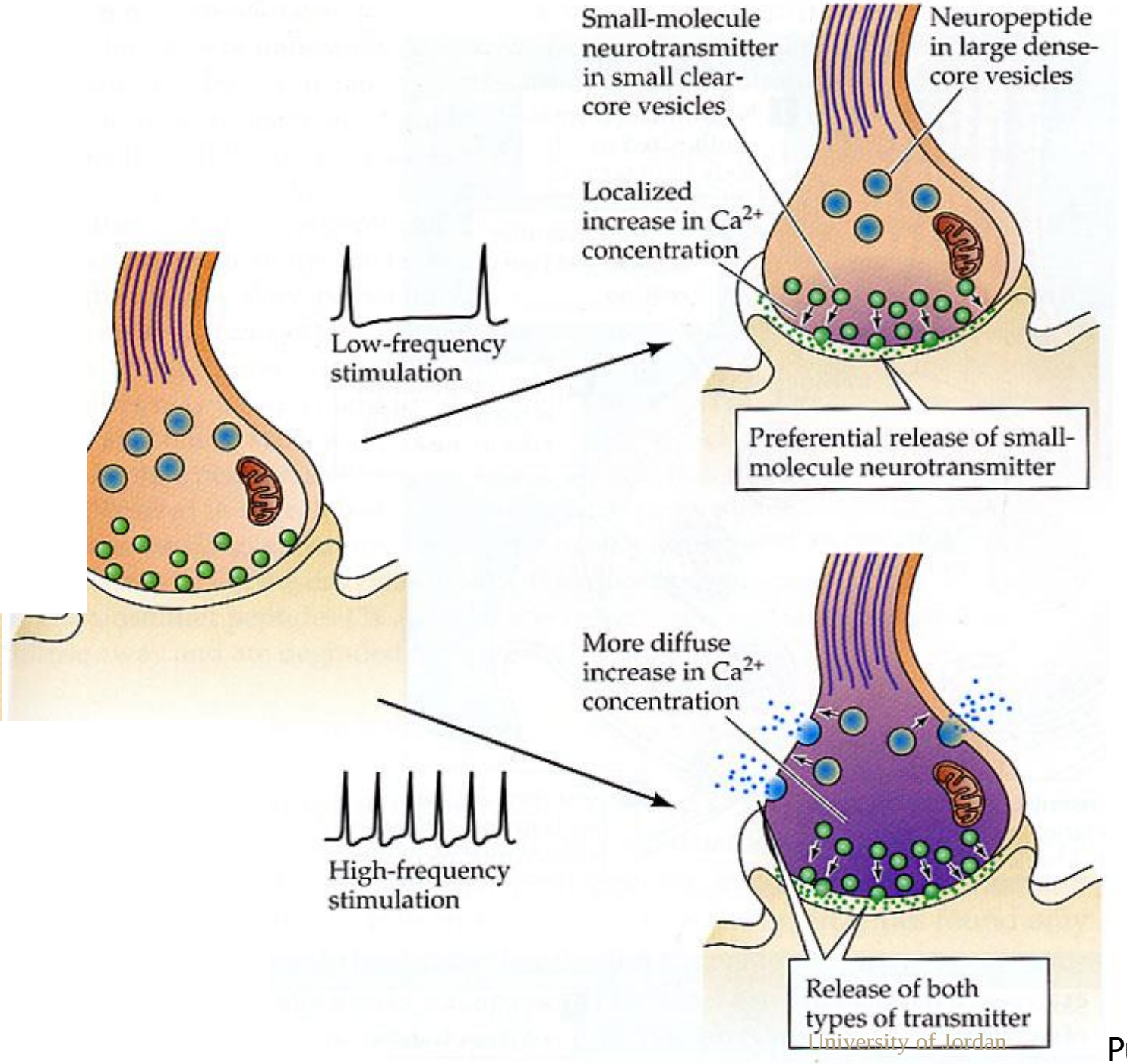
- Concentrate and protect transmitter
- Can be docked at active zone
- Differ for classical transmitters (small, clear-core) vs. neuropeptides (large, dense-core)

Neurotransmitter Co-existence (Dale principle)

Some neurons in both the PNS and CNS produce both a classical neurotransmitter (ACh or a catecholamine) and a polypeptide neurotransmitter.

They are contained in different synaptic vesicles that can be distinguished using the electron microscope.

The neuron can thus release either the classical neurotransmitter or the polypeptide neurotransmitter under different conditions.


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

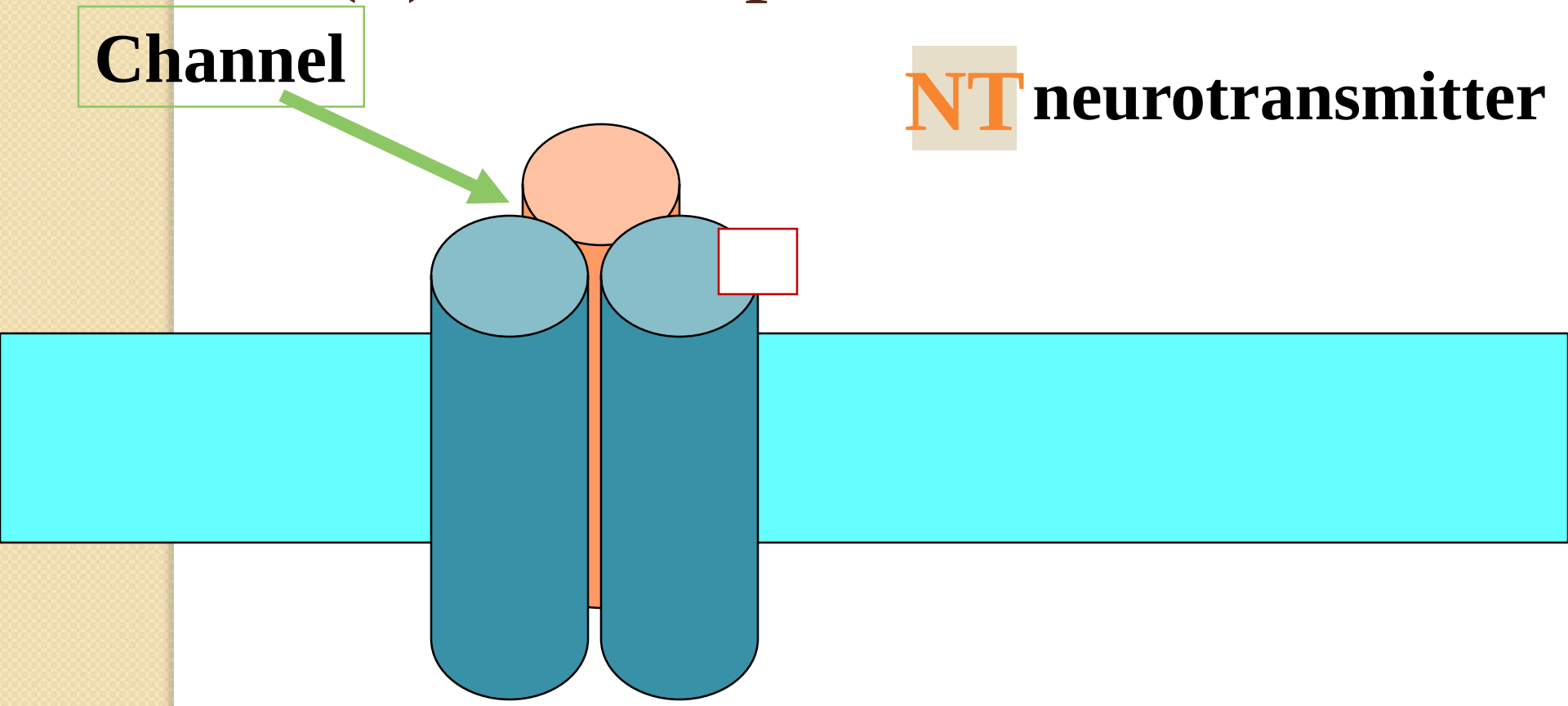
Receptors determine whether:

- 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

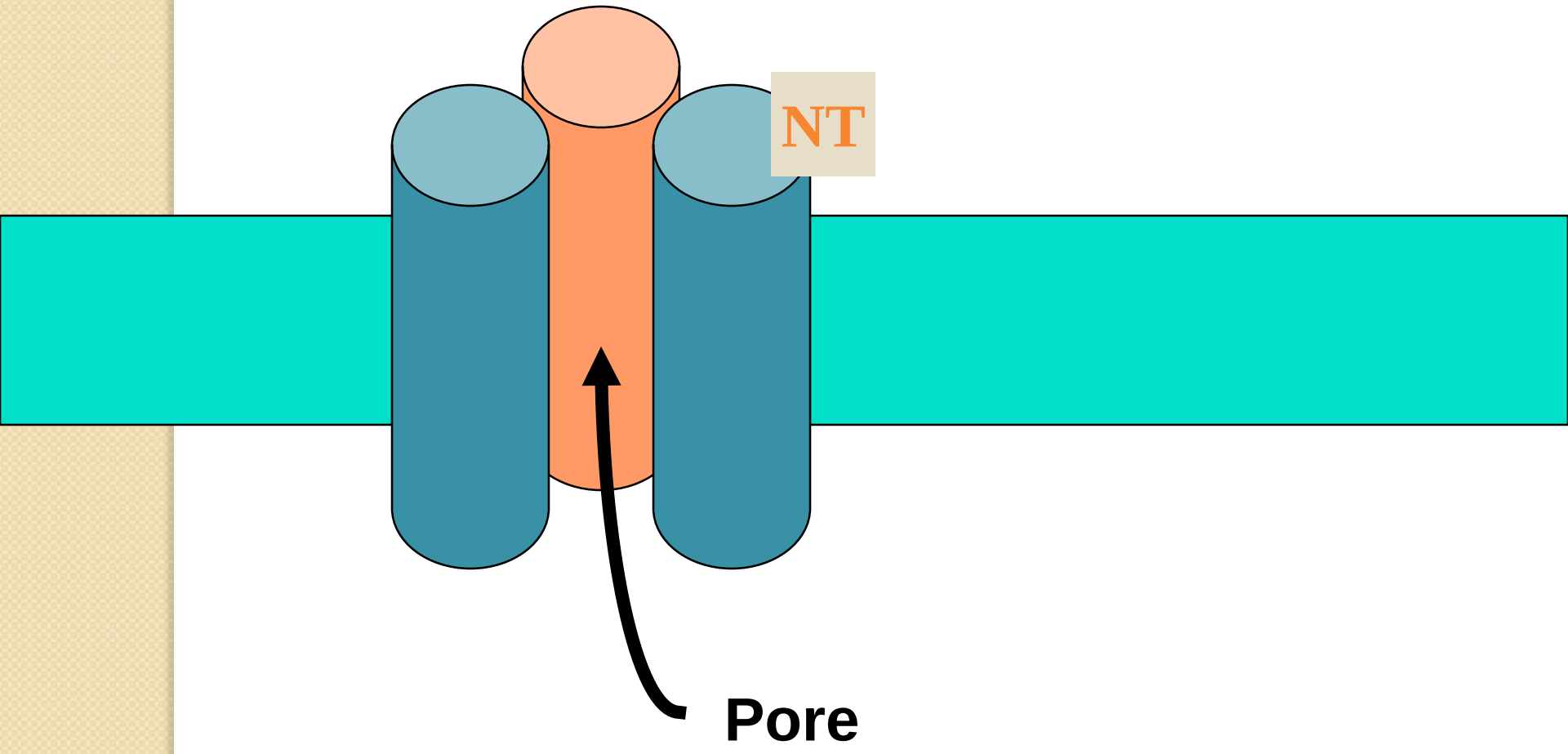
Receptor Activation

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

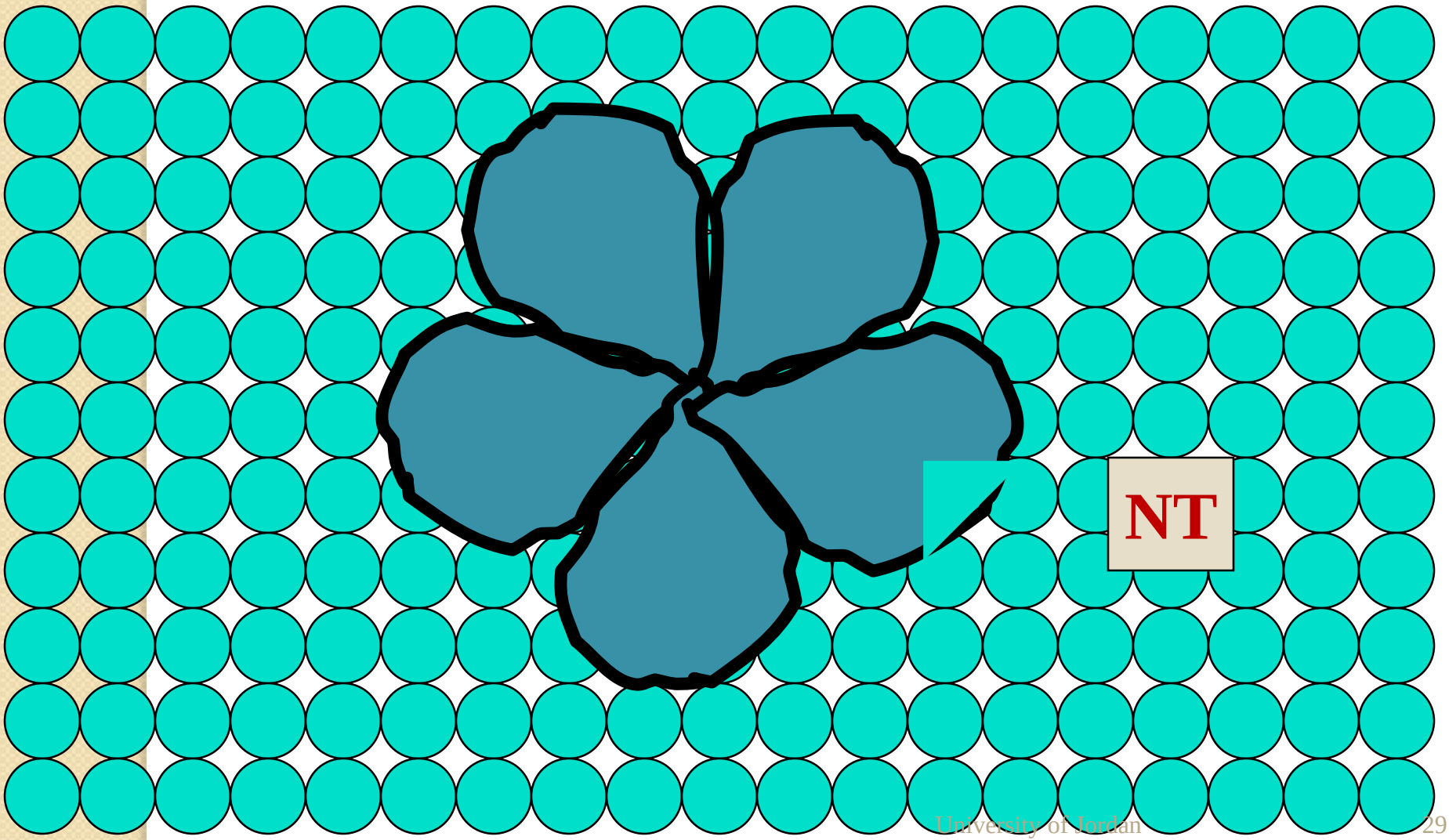
(1) Ionotropic Channels



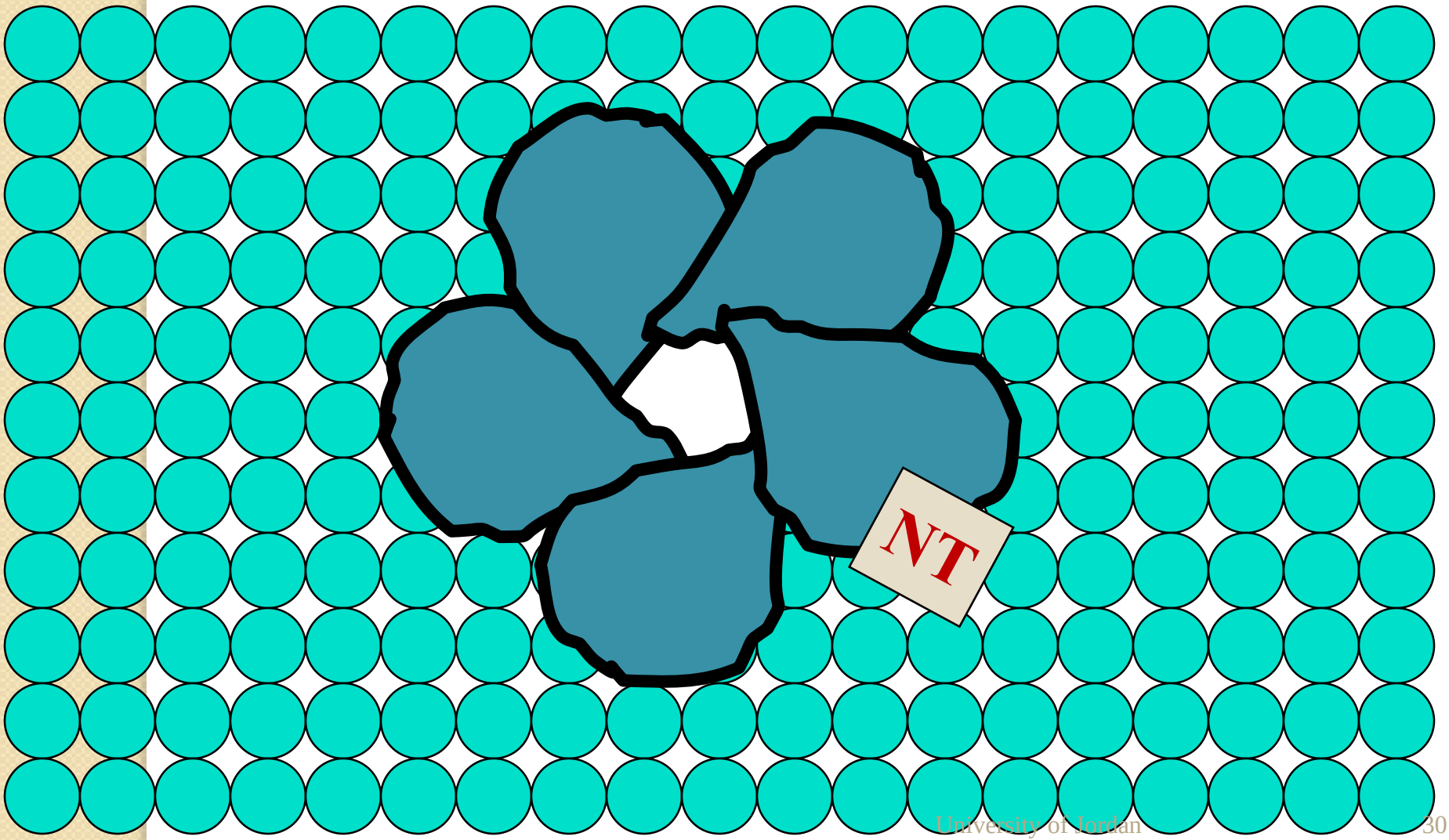
Ionotropic Channels



Ionotropic Channels



Ionotropic Channels



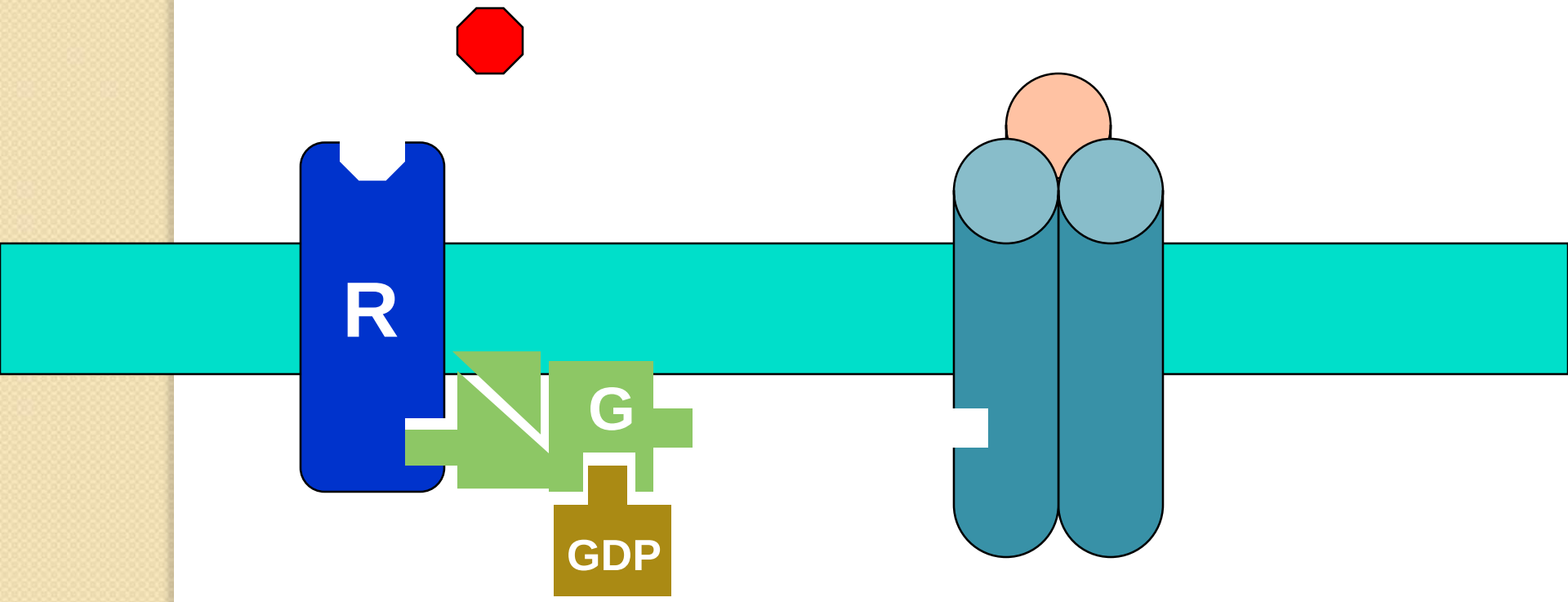
Metabotropic Channels

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

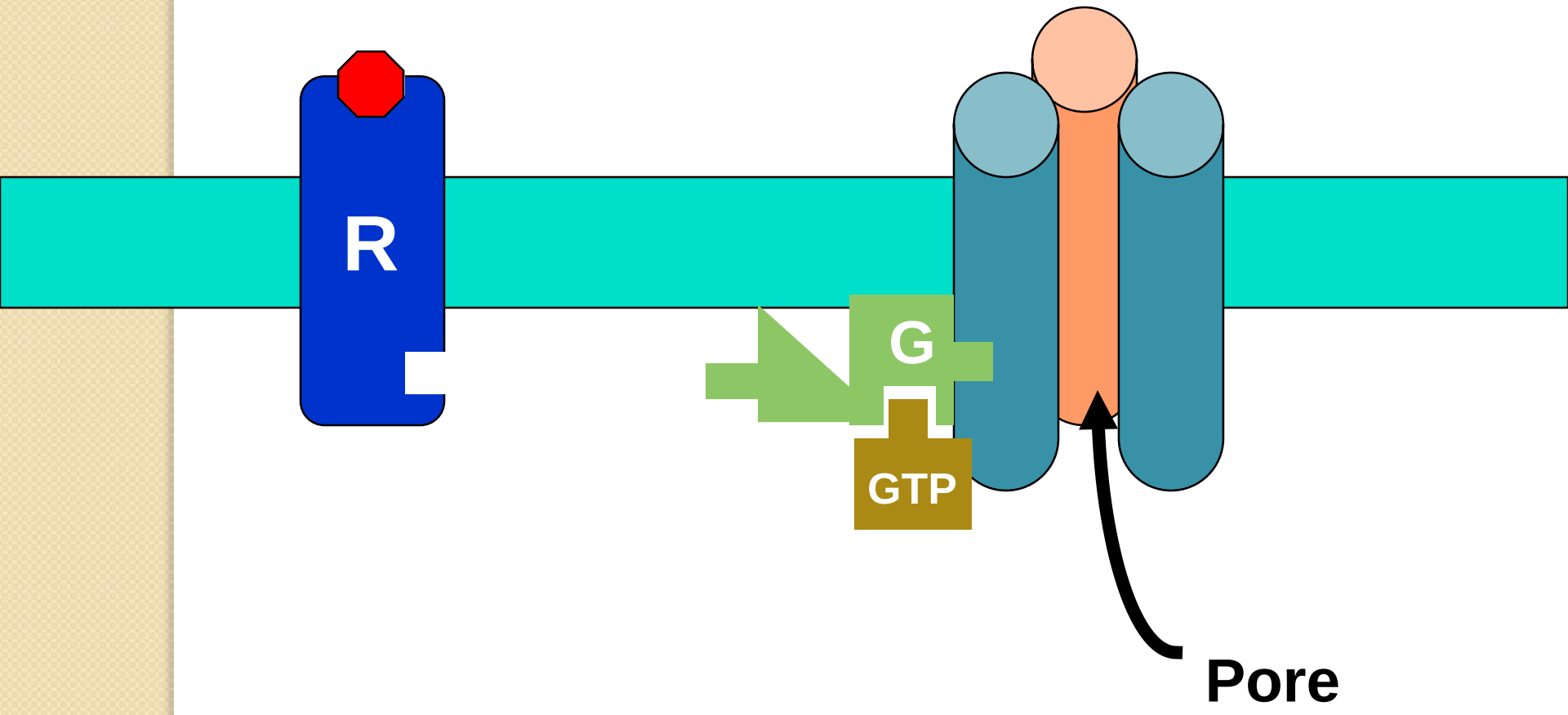
G protein: direct control

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

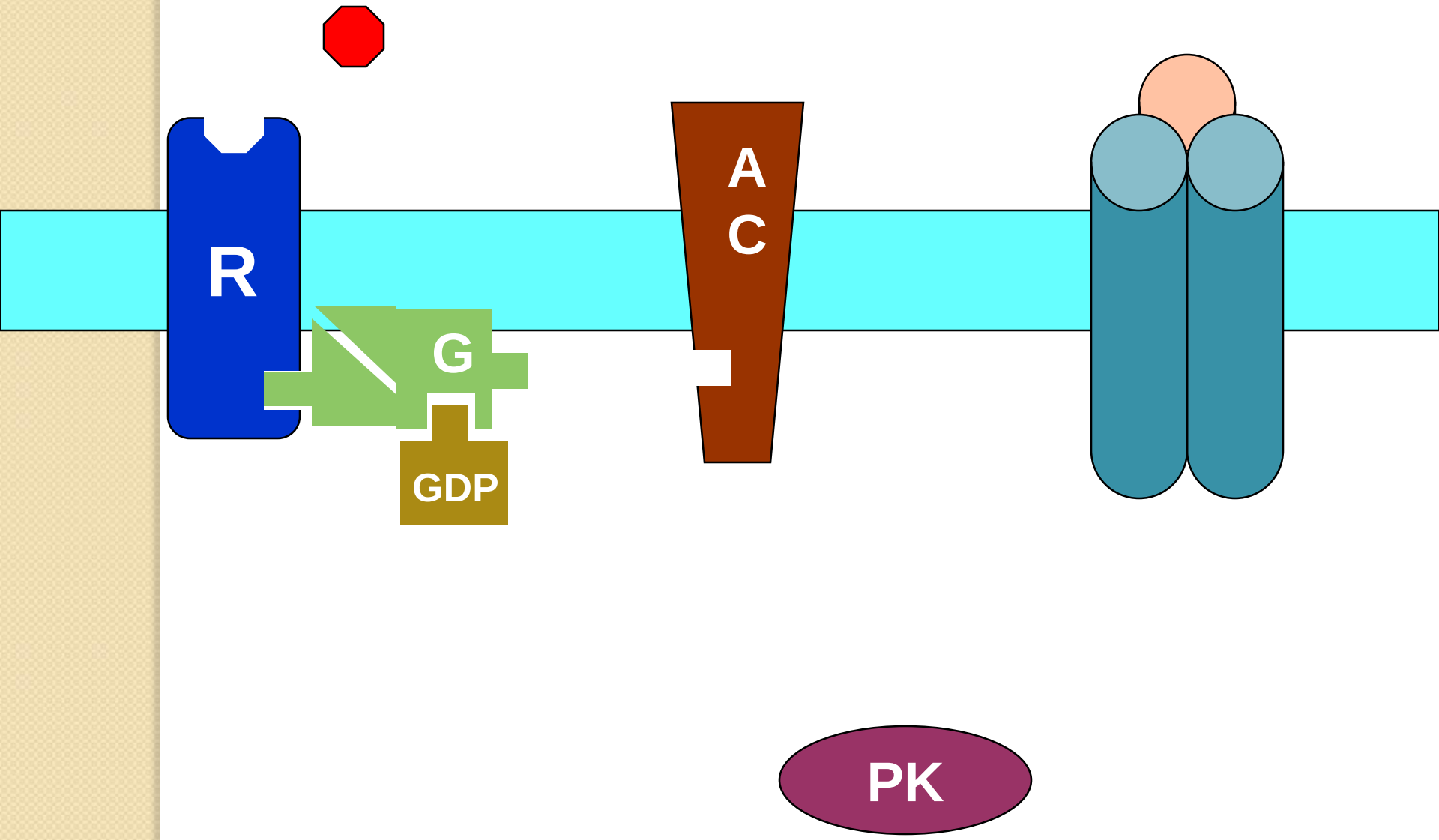
G protein: direct control



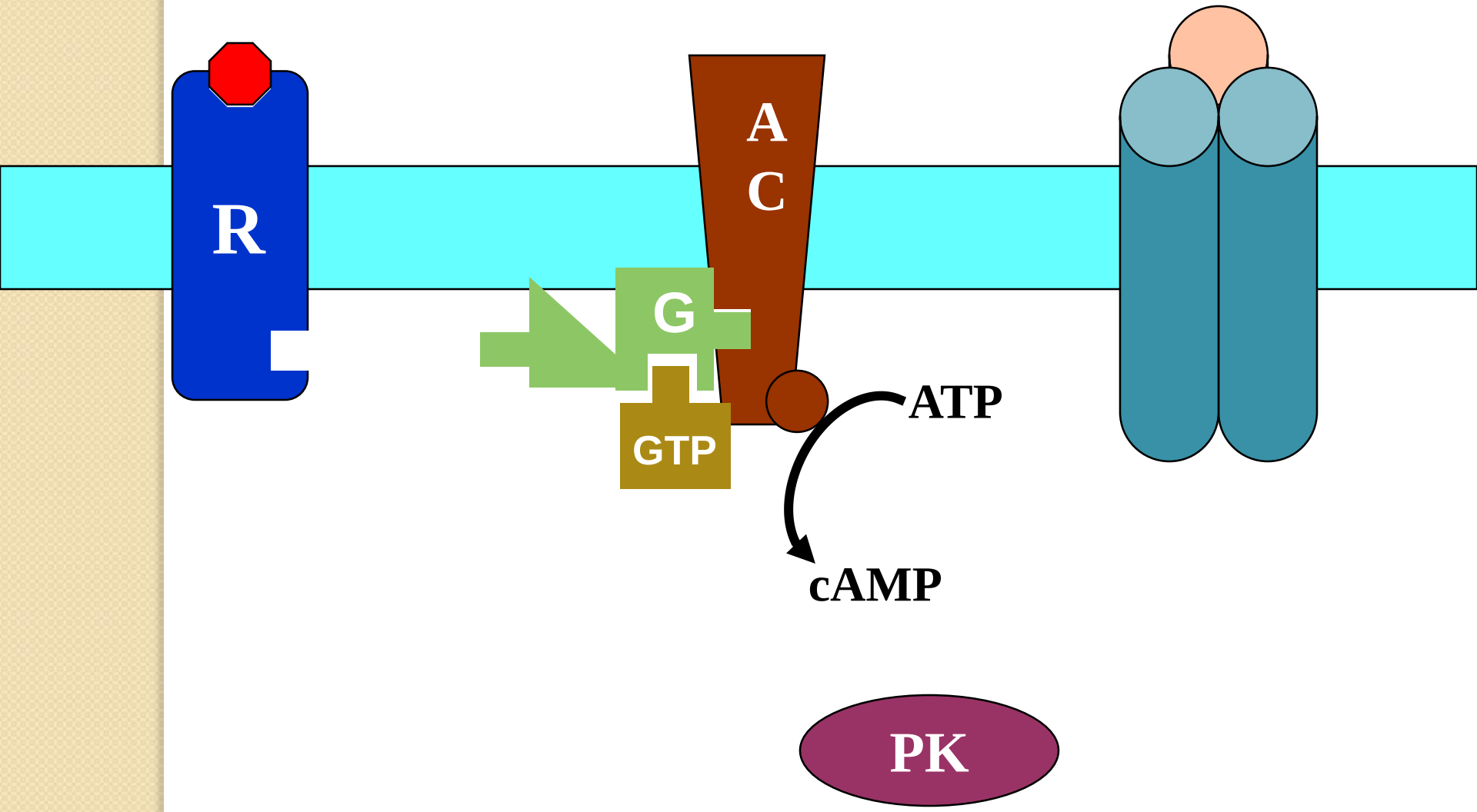
G protein: direct control



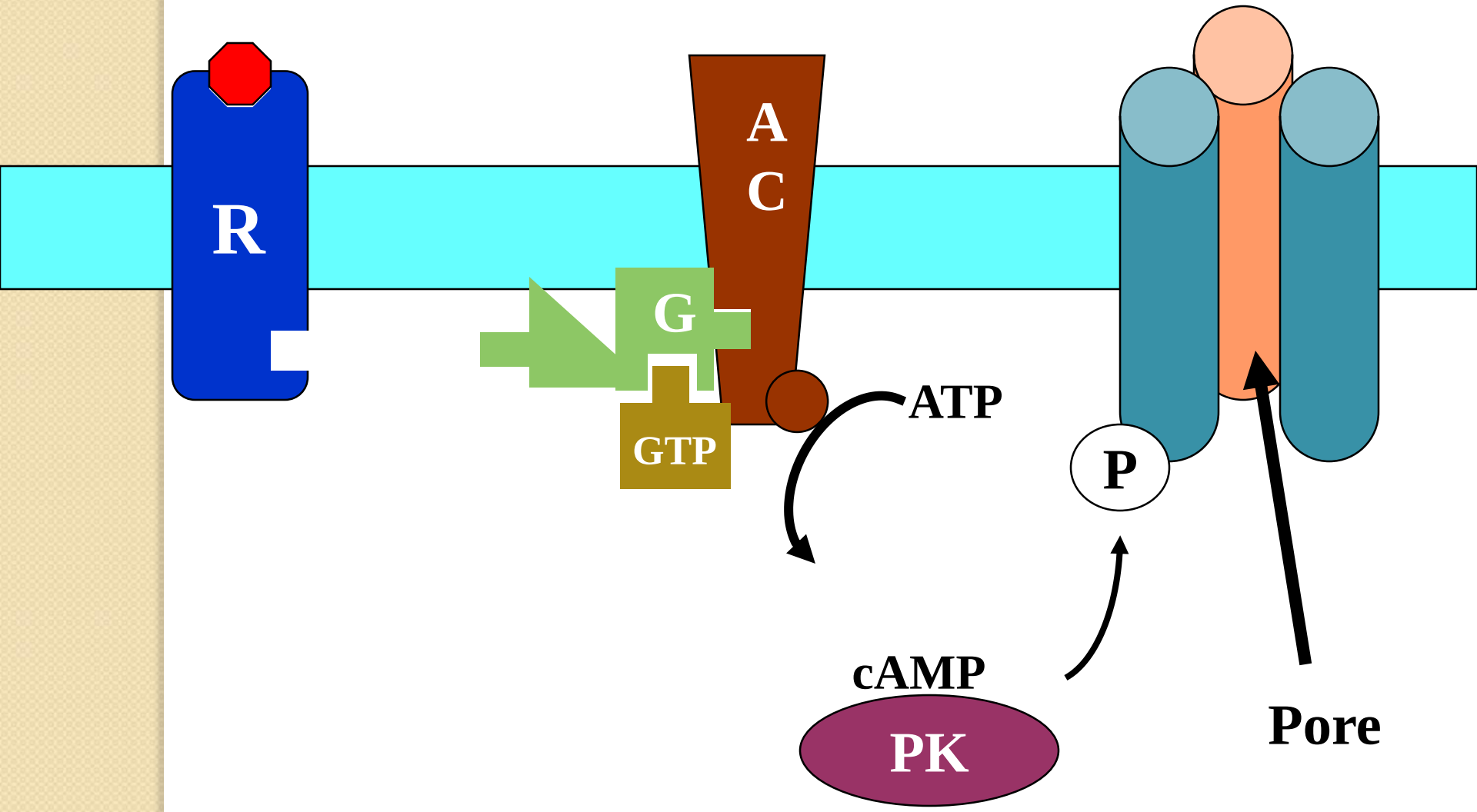
G protein: Protein Phosphorylation



G protein: Protein Phosphorylation



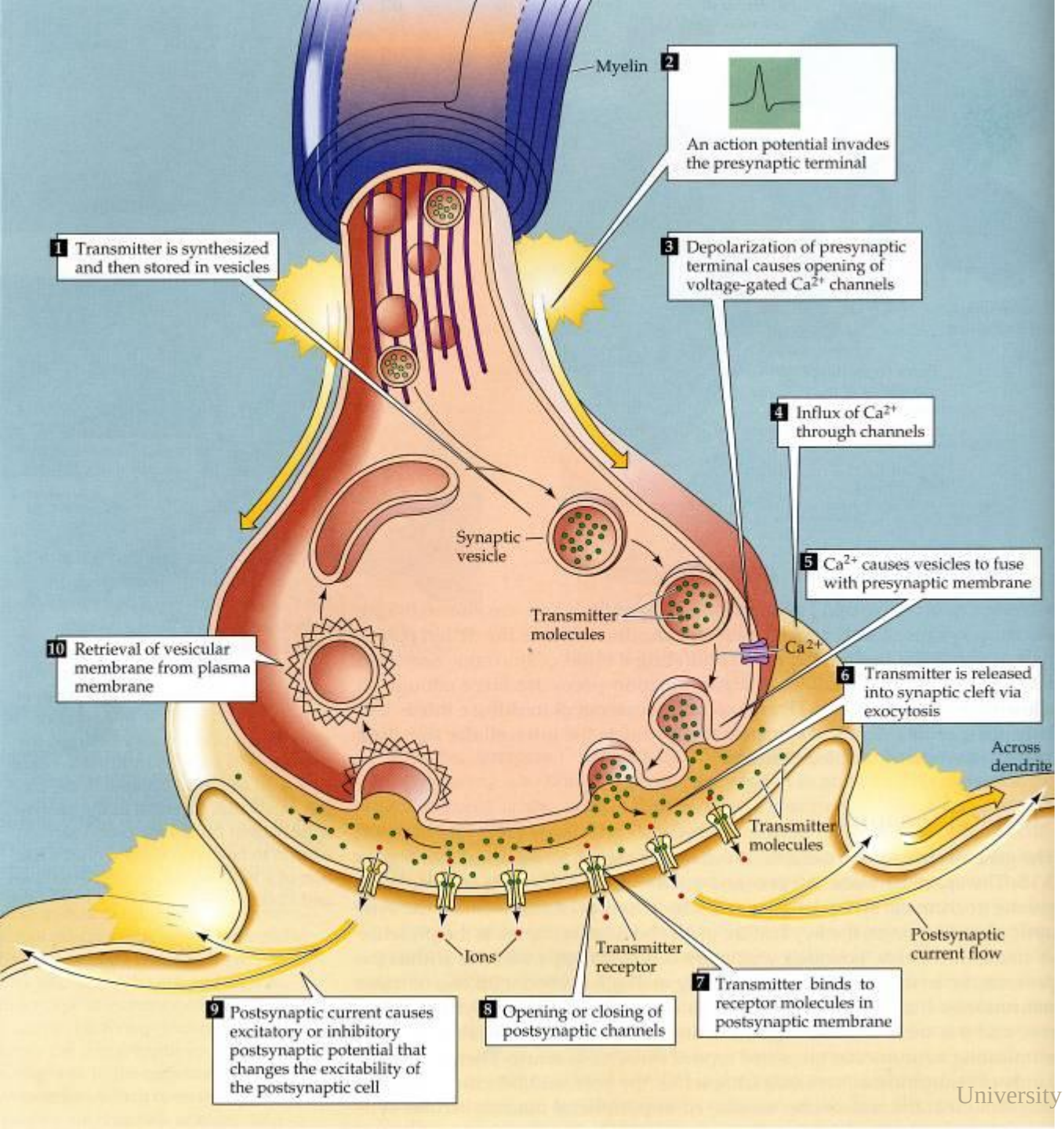
G protein: Protein Phosphorylation



Transmitter Inactivation

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

Summary of Synaptic Transmission

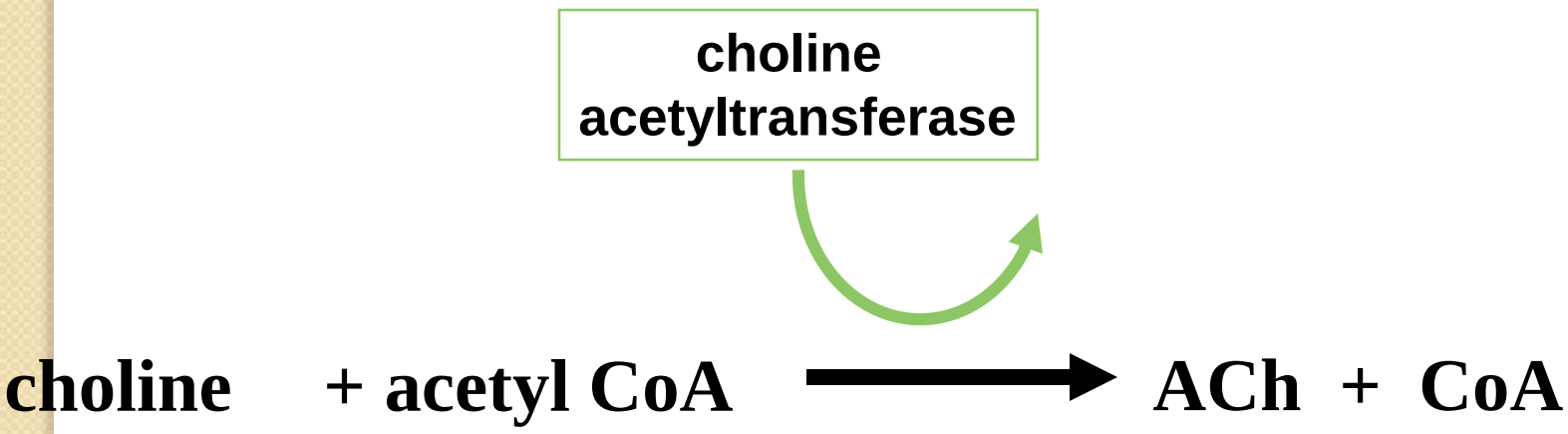


Purves,2001

Some Important Transmitters

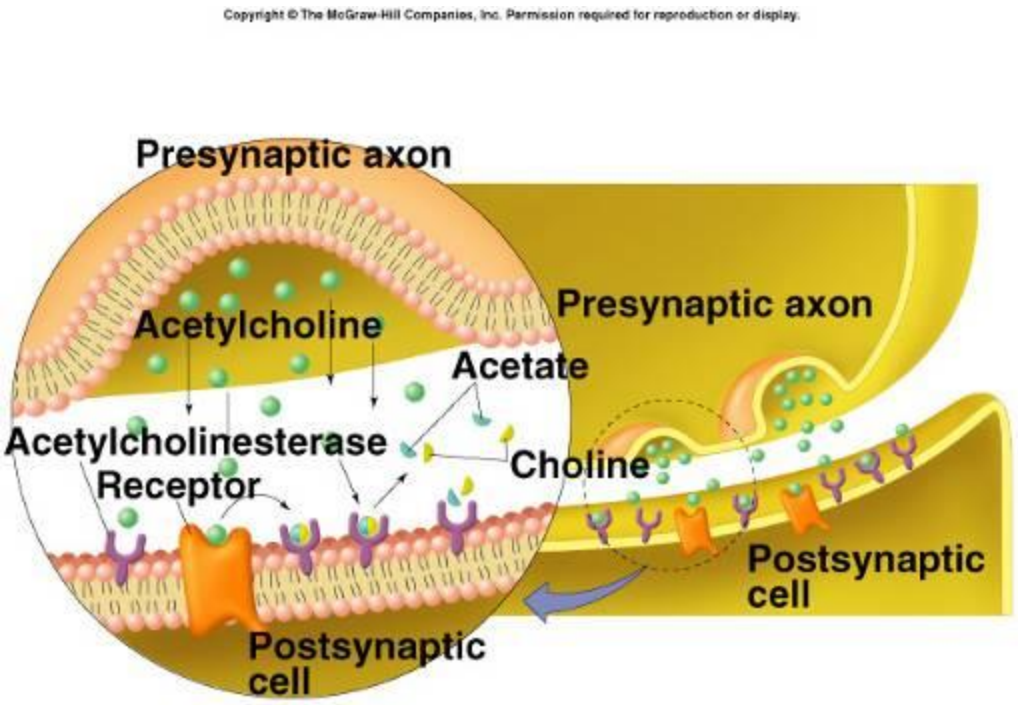
(1) Acetylcholine (ACh) as NT

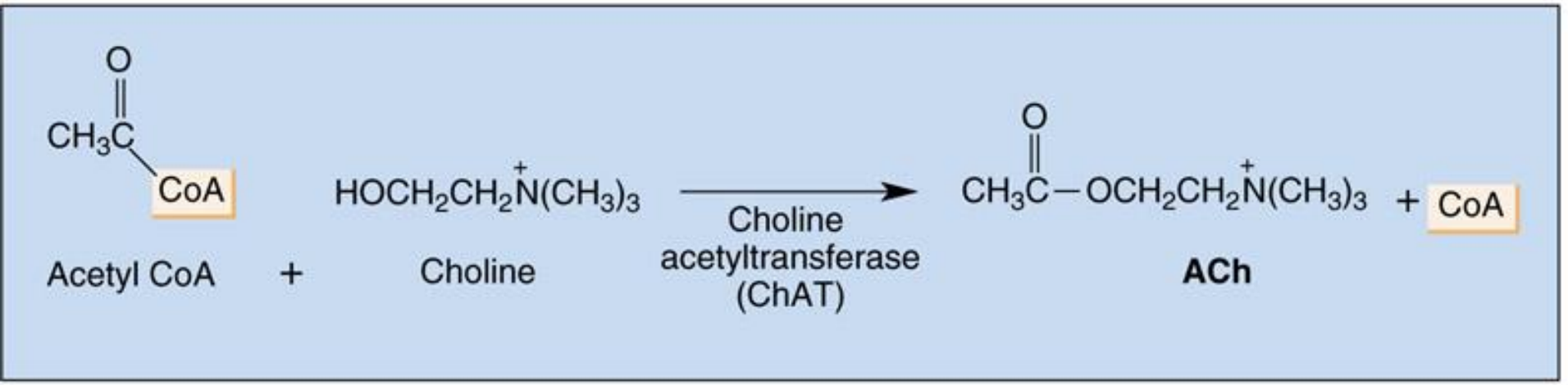
Acetylcholine Synthesis



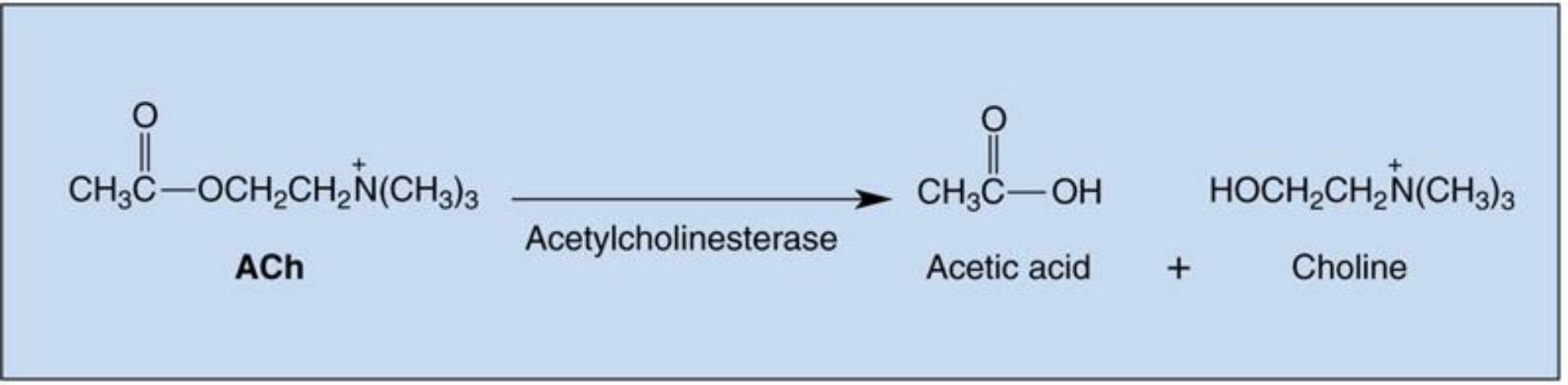
Acetylcholinesterase (AChE)

- Enzyme that inactivates ACh.
  - Present on postsynaptic membrane or immediately outside the membrane.
- Prevents continued stimulation.



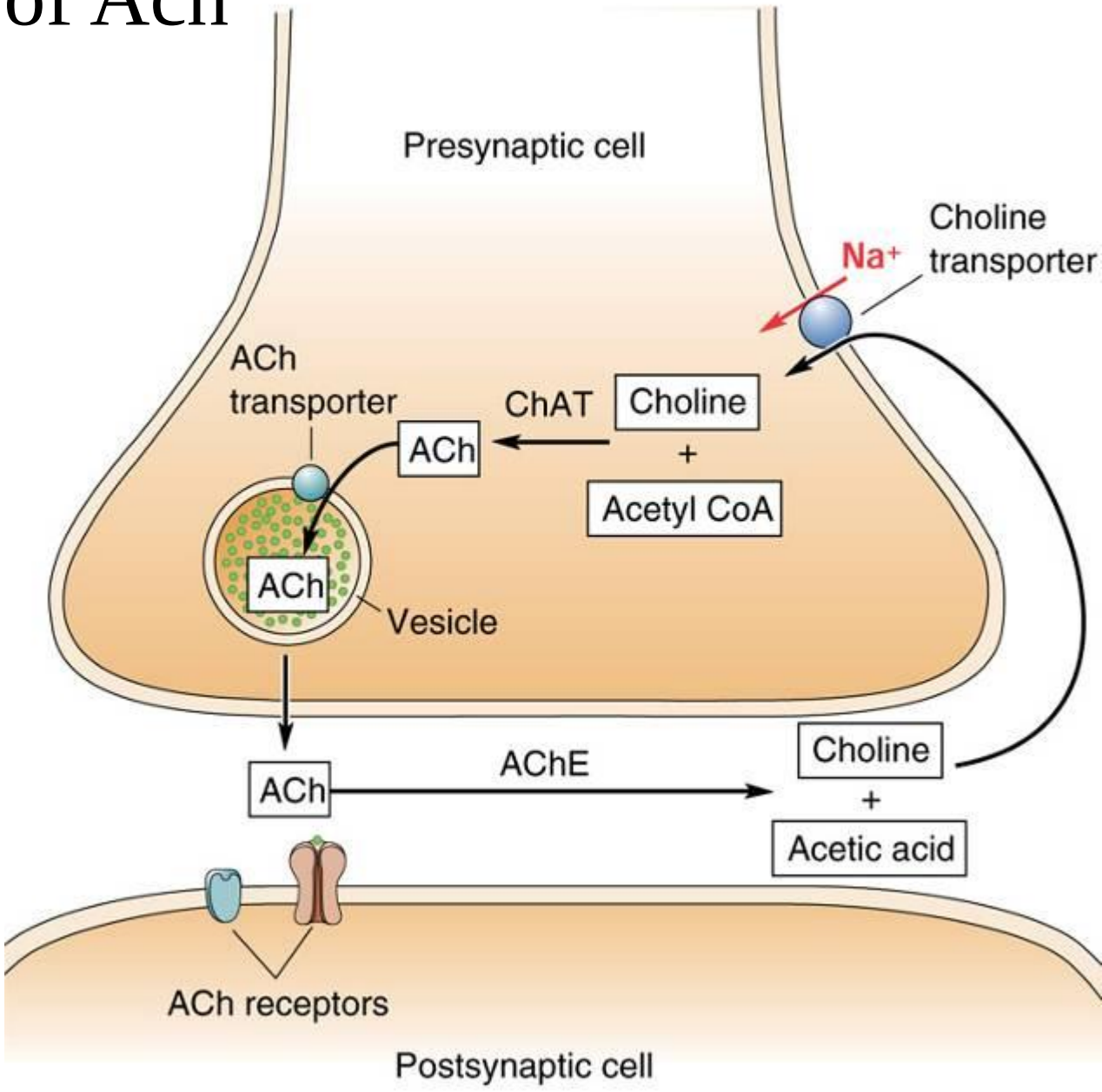

O
CH3C
CoA
Acetyl CoA
+
HOCH2CH2N+(CH3)3
Choline
Choline acetyltransferase (ChAT)
O
CH3C—OCH2CH2N+(CH3)3
ACh
+ CoA

(a)


O
CH3C—OCH2CH2N+(CH3)3
ACh
Acetylcholinesterase
O
CH3C—OH
Acetic acid
+
HOCH2CH2N+(CH3)3
Choline

(b)

The Life Cycle of Ach



Ach - Distribution

- **Peripheral N.S.**
  - Excites somatic skeletal muscle (neuro-muscular junction)
  - Autonomic NS

    Ganglia

    Parasympathetic NS--- Neuroeffector junction

    Few sympathetic NS – Neuroeffector junction
- Central N.S. - widespread

  Hippocampus

  Hypothalamus ~

Ach Receptors

- ACh is both an excitatory and inhibitory NT, depending on organ involved.
  - –Causes the opening of chemical gated ion channels.
- Nicotinic ACh receptors:
  - –Found in autonomic ganglia (N_1) and skeletal muscle fibers (N_2).
- Muscarinic ACh receptors:
  - –Found in the plasma membrane of smooth and cardiac muscle cells, and in cells of particular glands .

Acetylcholine Neurotransmission

- "Nicotinic" subtype Receptor:
  - Membrane Channel for Na^+ and K^+
  - Opens on ligand binding
  - Depolarization of target (neuron, muscle)
  - Stimulated by Nicotine, etc.
  - Blocked by Curare, etc.
  - Motor endplate (somatic) (N_2),
  - all autonomic ganglia, hormone producing cells of adrenal medulla (N_1)

Acetylcholine Neurotransmission

- "Muscarinic" subtype Receptor: M_1
  - Use of signal transduction system
    - Phospholipase C, IP_3, DAG, cytosolic Ca^{++}
  - Effect on target: cell specific (heart ↓, smooth muscle intestine ↑)
  - Blocked by Atropine, etc.
  - All parasympathetic target organs
  - Some *sympathetic* targets (endocrine sweat glands, skeletal muscle blood vessels - dilation)

Acetylcholine Neurotransmission

- "Muscarinic" subtype: M_2
  - Use of signal transduction system
    - via G-proteins, opens K^+ channels, decrease in cAMP levels
  - Effect on target: cell specific
  - CNS
  - Stimulated by ?
  - Blocked by Atropine, etc.

Cholinergic Agonists

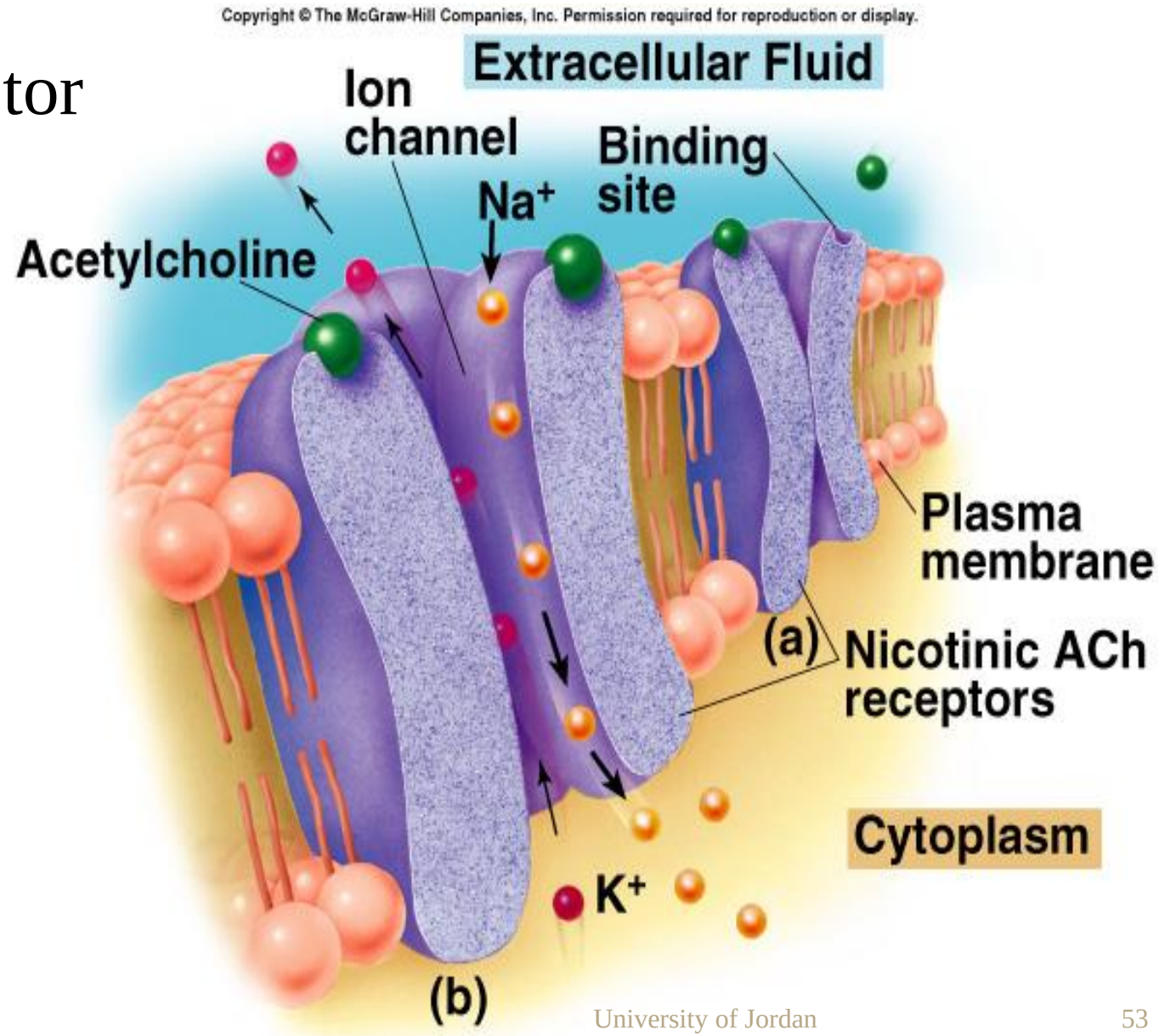
- Direct
  - Muscarine
  - Nicotine
- Indirect
  - AChE Inhibitors ~

Cholinergic Antagonists

- Direct
  - Nicotinic - Curare
  - Muscarinic - Atropine

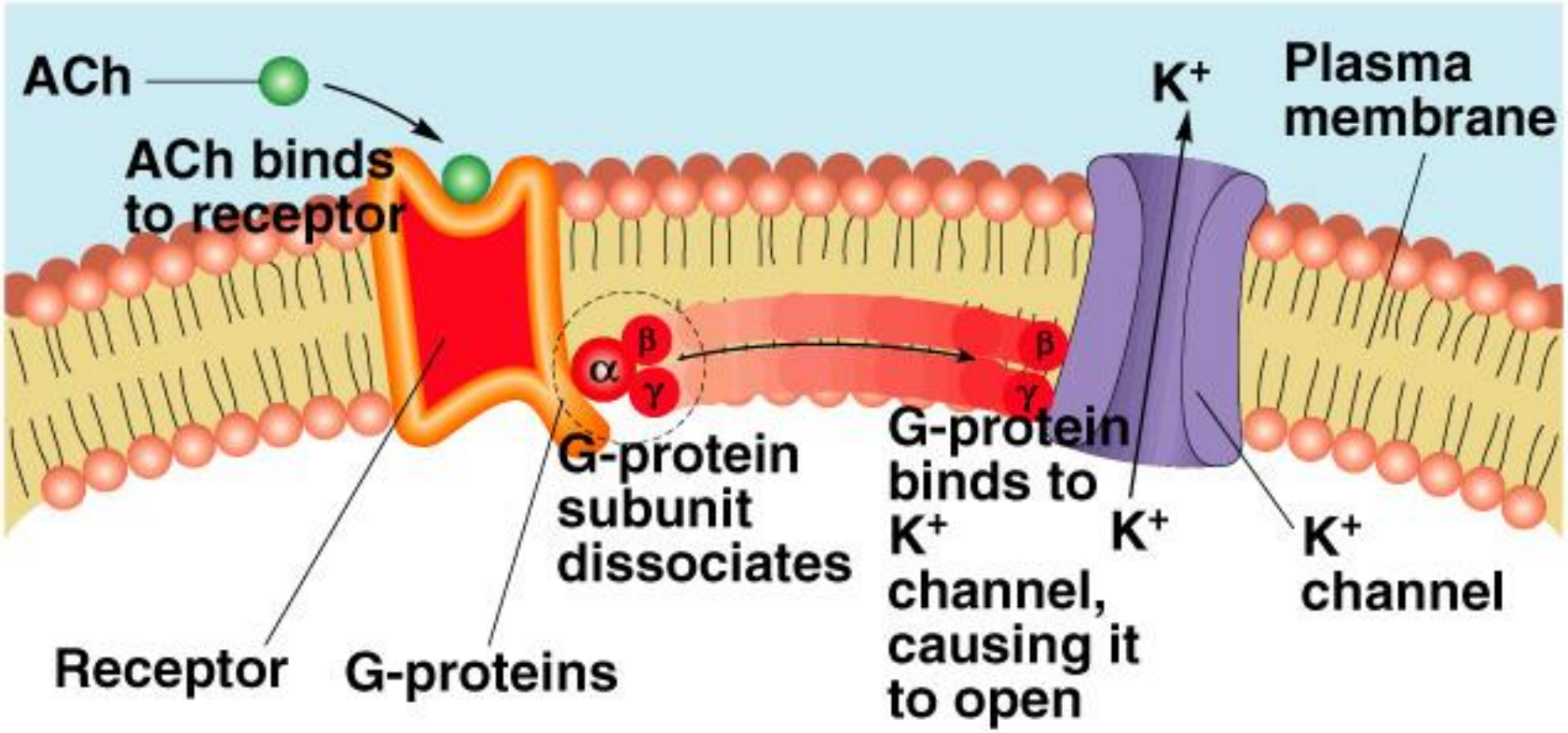
Ligand-Operated ACh Channels

N Receptor



G Protein-Operated ACh Channel

M receptor



(2) Monoamines as NT

Monoamines

- Catecholamines –

  Dopamine - DA

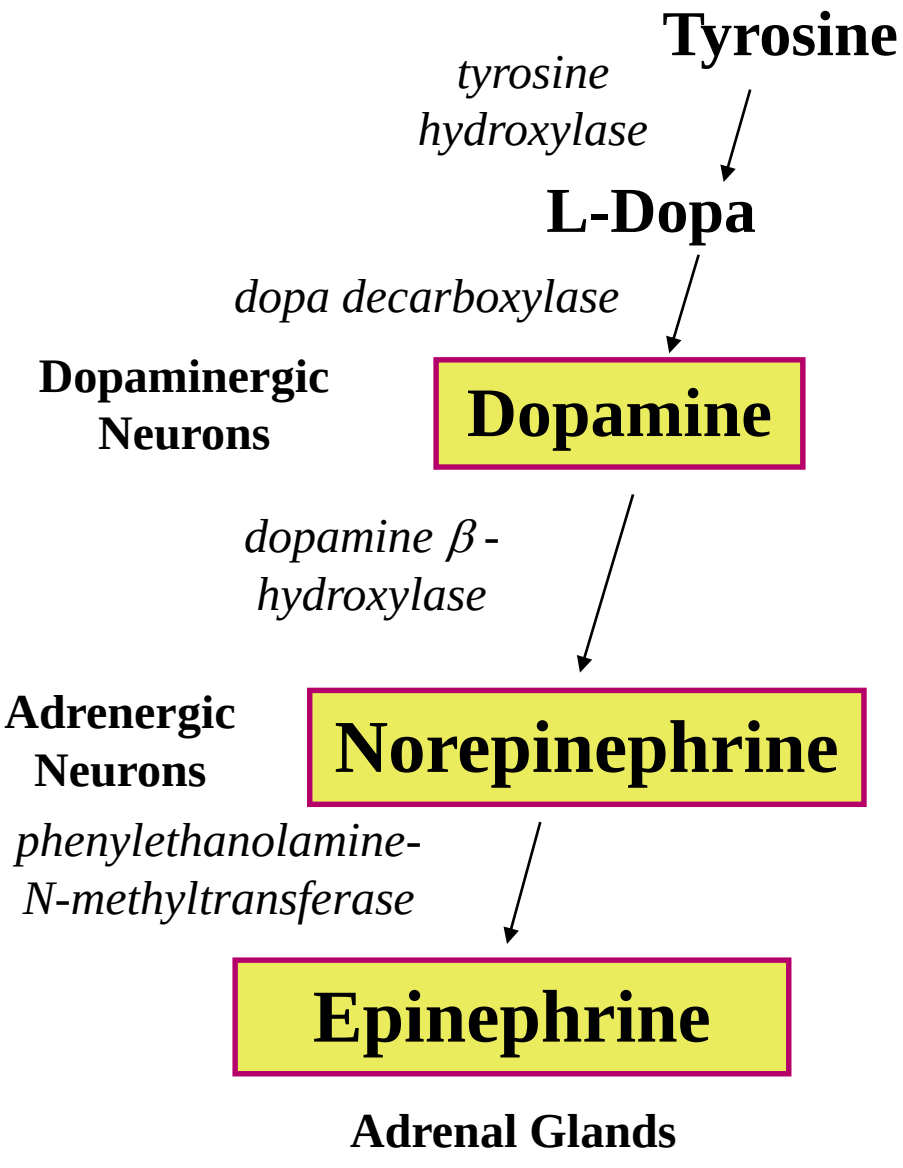
  Norepinephrine - NE

  Epinephrine - E

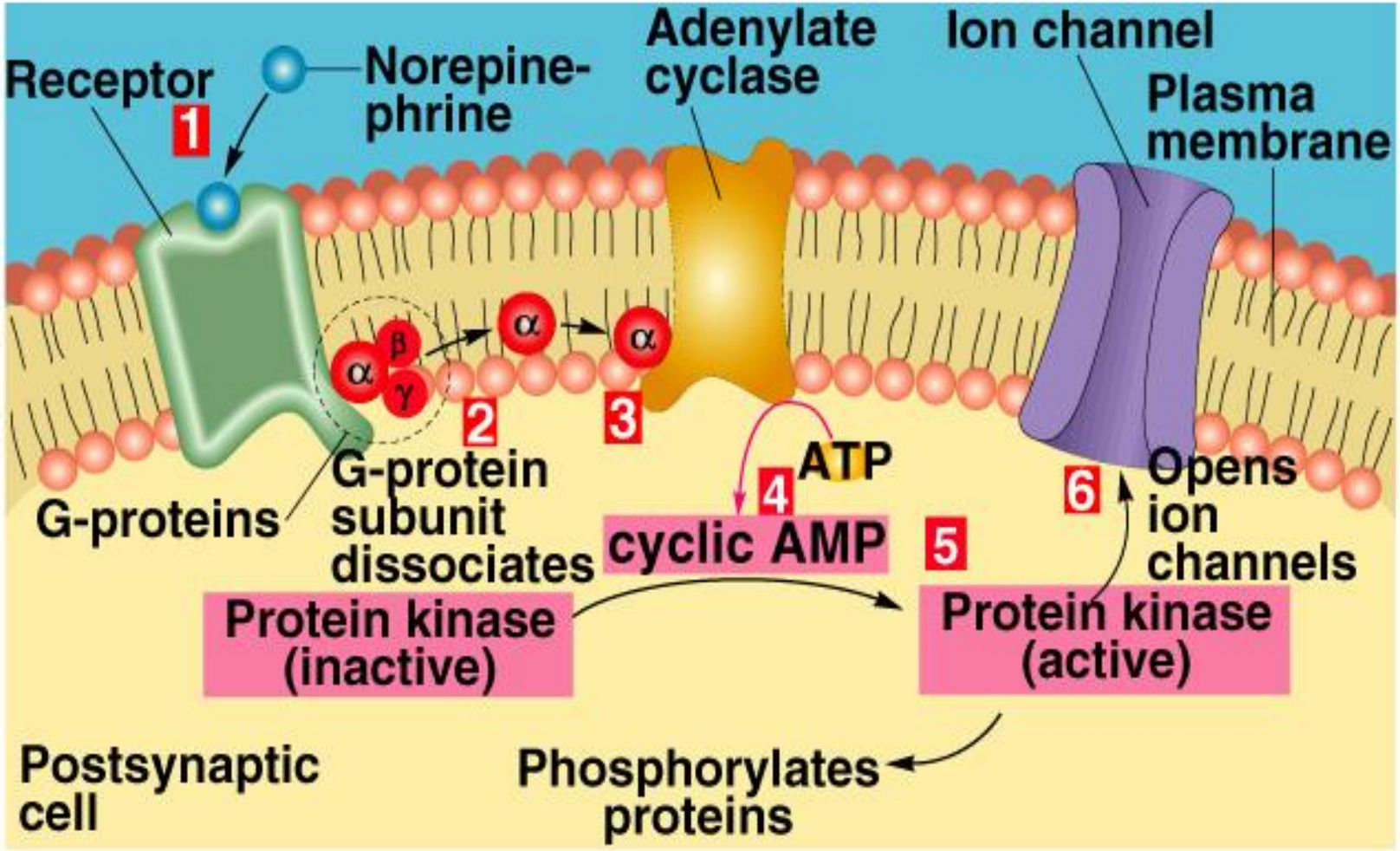
- Indolamines -

  Serotonin - 5-HT

Synthesis of Monoamine NT



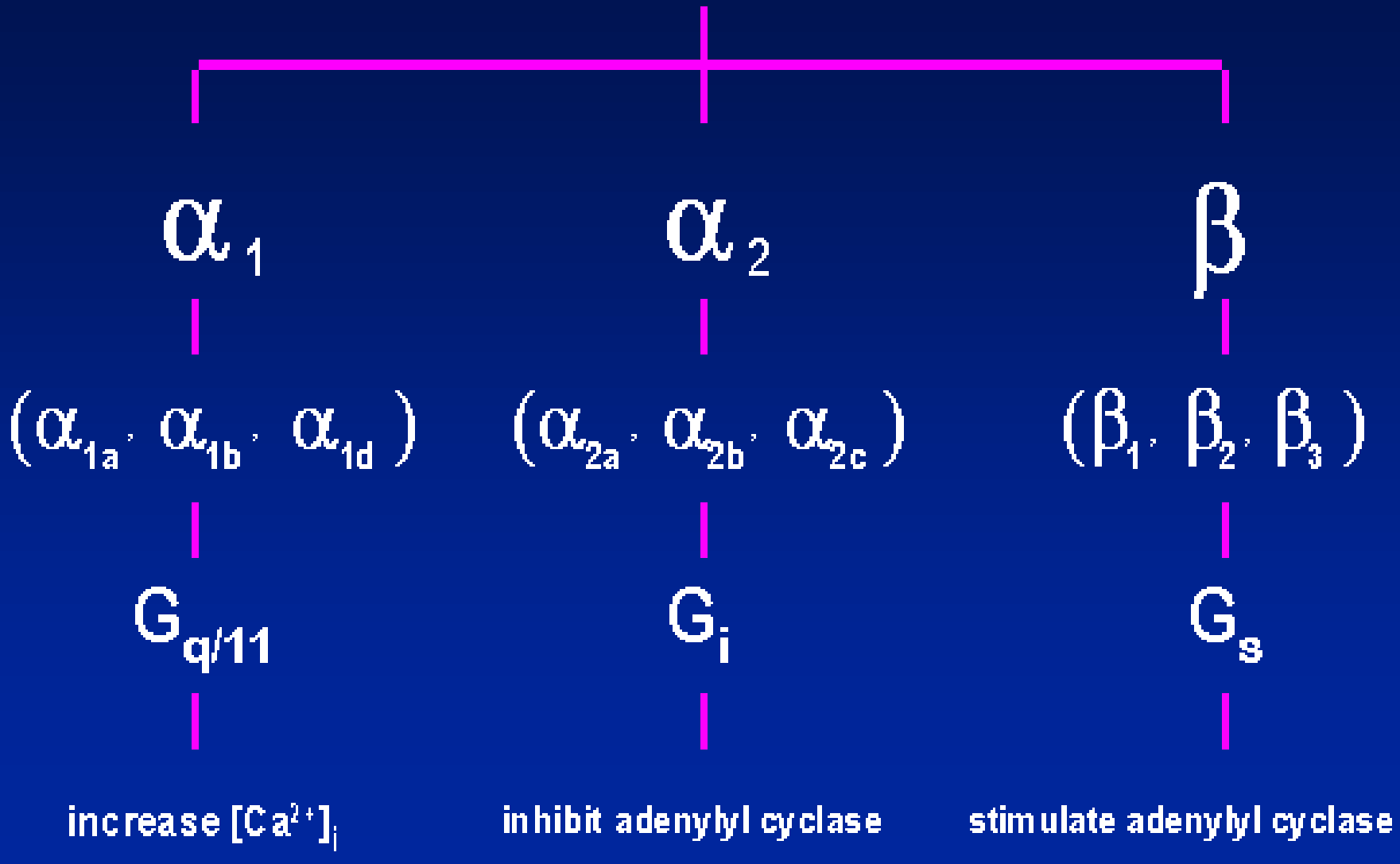
Mechanism of Action (β receptor)



Norepinephrine (NE) as NT

- NT in both PNS and CNS.
- PNS:
  - Smooth muscles, cardiac muscle and glands.
    - Increase in blood pressure, constriction of arteries.
- CNS:
  - General behavior.

Adrenergic Receptors



Adrenergic Neurotransmission

- α_1 Receptor
  - Stimulated by NE, E,
  - blood vessels of skin, mucosa, abdominal viscera, kidneys, salivary glands
  - vasoconstriction, sphincter constriction, pupil dilation

Adrenergic Neurotransmission

- α_2 Receptor
  - stimulated by, NE, E, ...
  - Membrane of adrenergic axon terminals (pre-synaptic receptors), platelets
  - inhibition of NE release (autoreceptor),
  - promotes blood clotting, pancreas decreased insulin secretion

Adrenergic Neurotransmission

- β_1 receptor
  - stimulated by E, ….
  - Mainly heart muscle cells,
  - increased heart rate and strength

Adrenergic Neurotransmission

- β_2 receptor
  - stimulated by E ..
  - Lungs, most other sympathetic organs, blood vessels serving the heart (coronary vessels),
  - dilation of bronchioles & blood vessels (coronary vessels), relaxation of smooth muscle in GI tract and pregnant uterus

Adrenergic Neurotransmission

- β_3 receptor
  - stimulated by E, ….
  - Adipose tissue,
  - stimulation of lipolysis

(3) Amino Acids as NT

- Glutamate acid and aspartate acid:
  - Excitatory Amino Acid (EAA)
- Gamma-amino-butyric acid (GABA) and glycine:
  - Inhibitory AA

(4) Polypeptides as NT

- CCK:
  - Promote satiety following meals.
- Substance P:
  - Major NT in sensations of pain.

(5) Monoxide Gas: NO and CO

- Nitric Oxide (NO)
  - Exerts its effects by stimulation of cGMP.
  - Involved in memory and learning.
  - Smooth muscle relaxation.
- Carbon monoxide (CO):
  - Stimulate production of cGMP within neurons.
  - Promotes odor adaptation in olfactory neurons.
  - May be involved in neuroendocrine regulation in hypothalamus.


THANK YOU