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

Functional Unit (Neuron)

- Axon hillock:
  has the largest number (greatest density) of voltage gated Na^+ channels.
  - That's why axon hillock has the lowest threshold for action potential
  - action potential occurs mainly in the axon hillock but can also occur in the soma, because it has voltage gated channels.

  However, it cannot occur in the dendrites because they lack voltage gated channels → very high threshold potential

- Axon types:
  1) myelinated
     - PNS: Schwann cells form myelin
     - CNS: oligodendrocytes

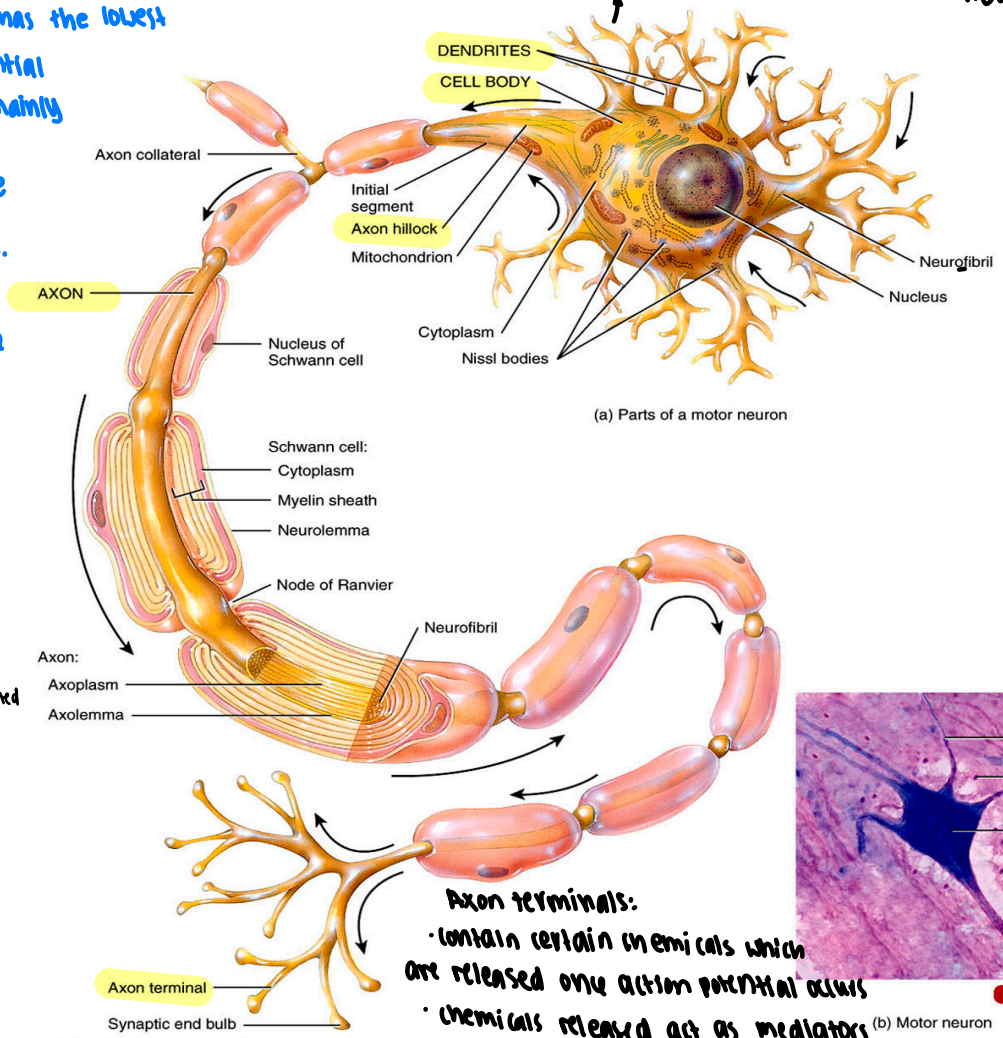
  interrupted by

  2) unmyelinated
     (Nodes of Ranvier)
- where action potential occurs in the myelinated neurons

like trees (branched)

- neurons consist of
  1) dendrites
  2) axon
  3) soma (cell body)
     - contains: nucleus, ER, Nissl's granules, mitochondria
       sites of protein synthesis
     - lacks centrioles because neurons don't divide, once they are damaged or if the cell dies it won't be regenerated.

Neurons are delicate cells, that's why the CNS is enclosed w/ bone. Brain is enclosed in skull. Spinal cord is enclosed in the vertebral column.



Axon terminals:
- contain certain chemicals which are released once action potential occurs
- chemicals released act as mediators between action potential that occurs in the 1st neuron (presynaptic) & the following neuron (postsynaptic)

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 (head to toe) or as slow as 0.5 m/sec → unmyelinated
- Nerve fiber classification
  - type A - myelinated fibers of varying sizes, generally fast transmission speed
    - subdivided into a (alpha), b (beta), g (gamma), d (delta) based on their diameter
  - type B- partially myelinated neurons (3-14m/sec speed) - found in ANS
  - type C - unmyelinated fibers, small with slow transmission speed

Types of Nerve Fiber

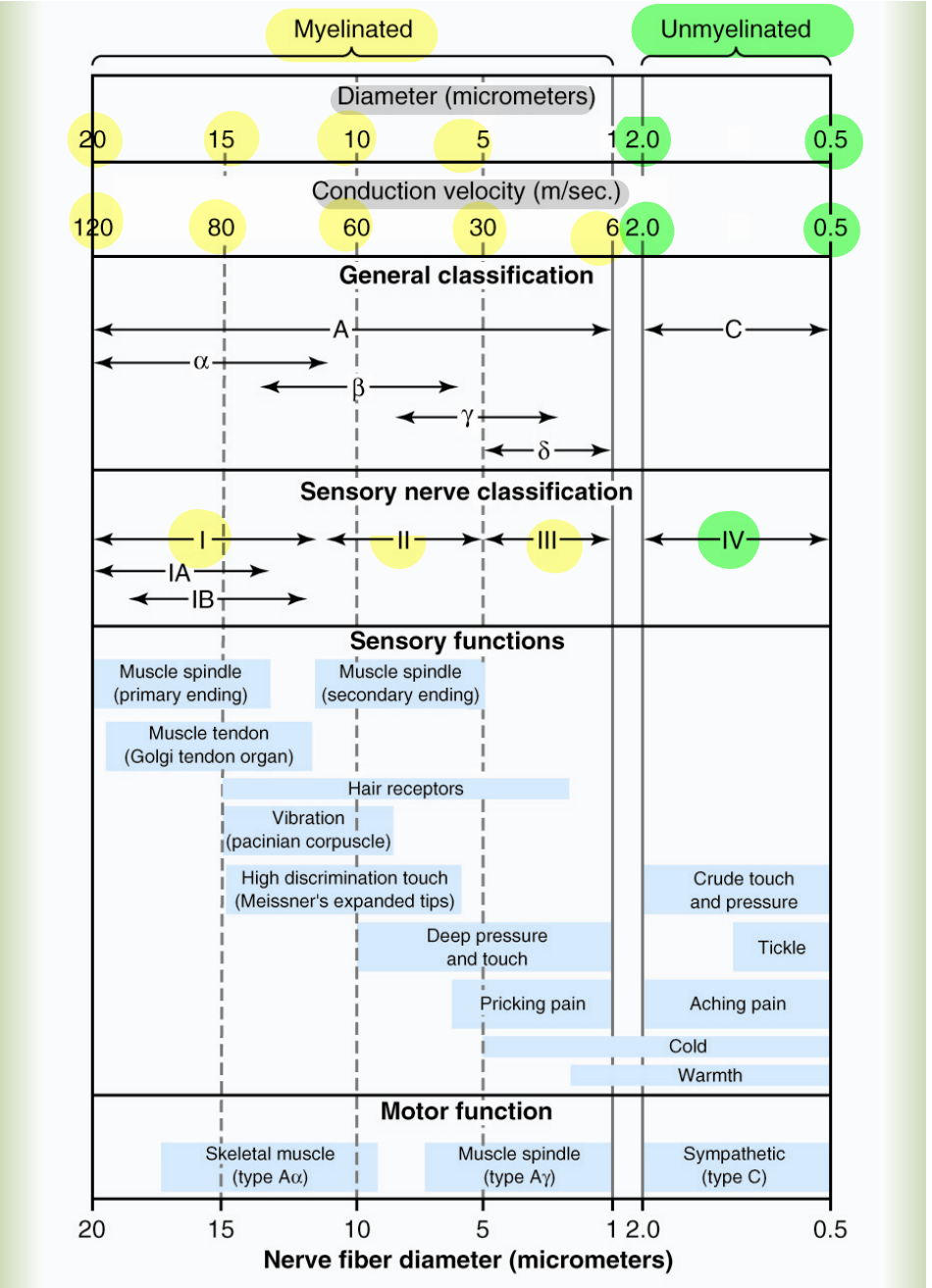
-Myelinated fibers – Type A (types I, II and III)

diameter- 1 µm - 20 µm
speed- 6 m/sec - 120 m/sec

- A α - largest myelinated fiber
- A β
- A γ
- A δ - smallest

(decrease in diameter)

-Umyelinated Fibers- Type C (type IV)

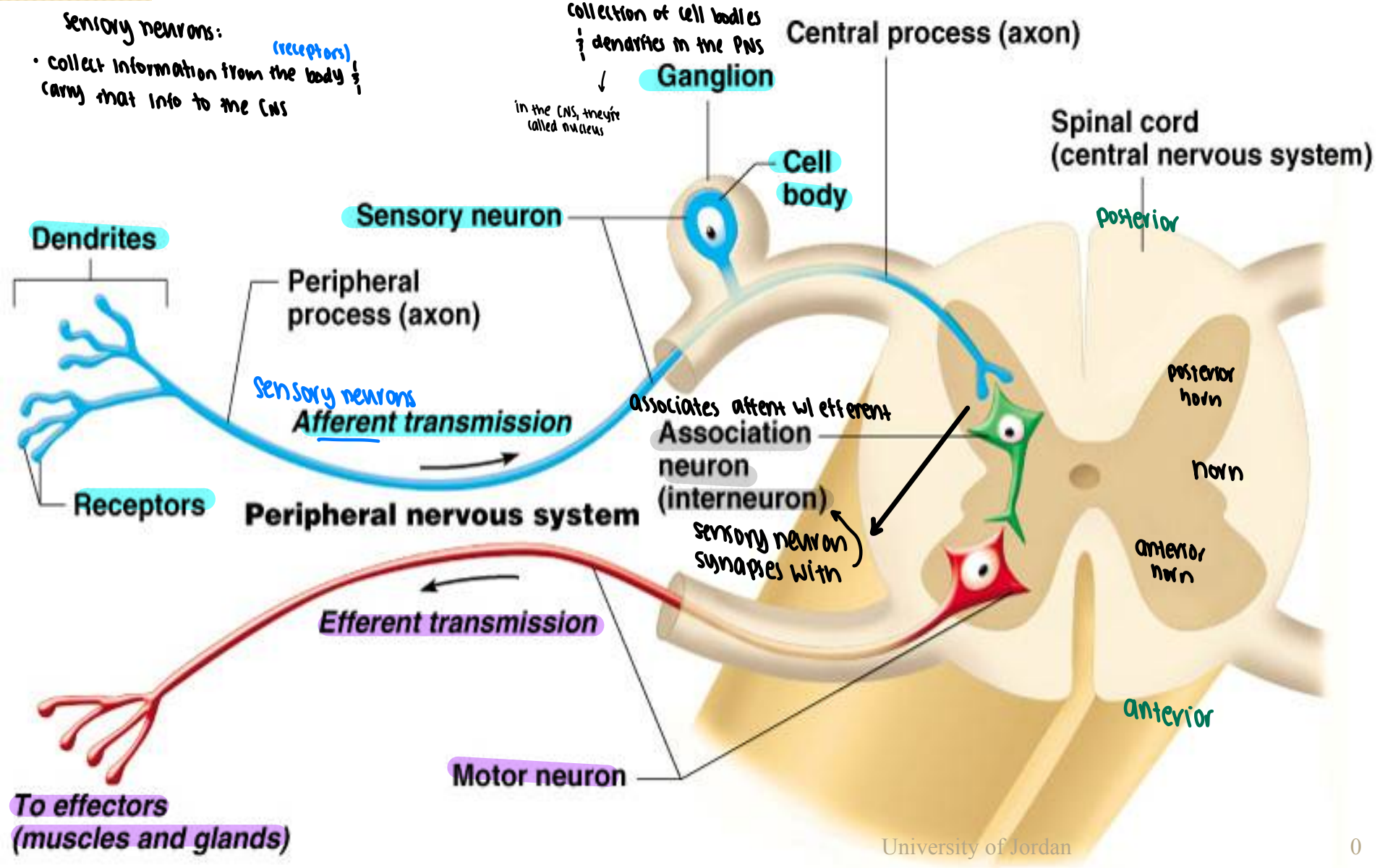


Neuron Classification

(according to function)
- afferent — arrives at the brain
- efferent — exit the brain

Sensory neurons:
- Collect information from the body (receptors) & carry that info to the CNS

Collection of cell bodies & dendrites in the PNS → in the CNS, they're called nucleus



Structural Classification of Neurons

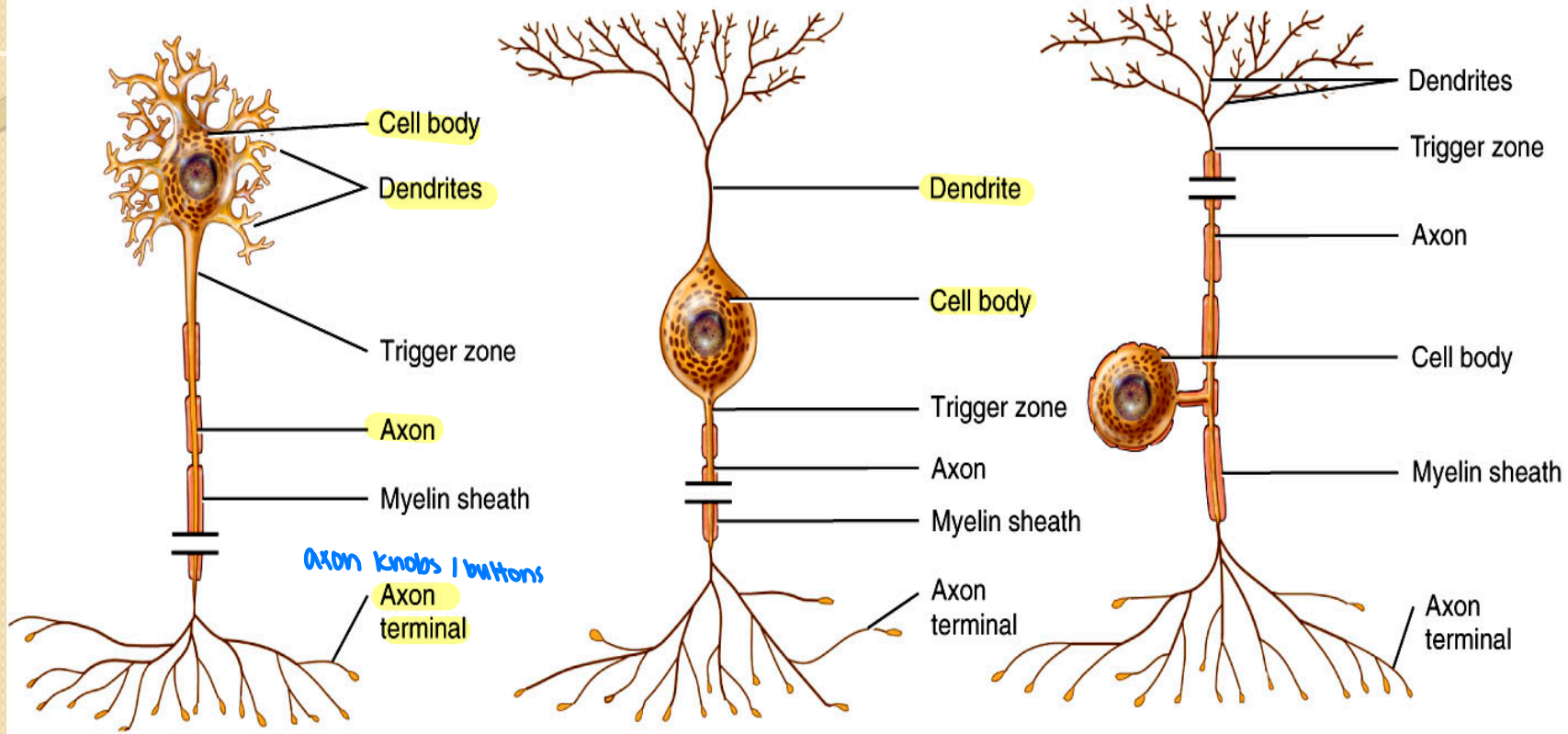


Figure 12.03 Tortora - PAP 12/e

- divided into 2 parts (up & down)
- found in the visual system

- found in the olfactory system (smell)

Neurotransmitters

chemicals that act as mediators between action potential in pre & postsynaptic neurons around the synapse

- Chemical substances that function as synaptic transmitters

1. Small molecules which act as rapidly acting transmitters

   acetylcholine, norepinephrine, dopamine, serotonin, GABA, glycine, glutamate, NO, & CO

2. Neuropeptides (Neuromodulators)

   more potent than small molecule transmitters, cause more prolonged actions

vasoactive intestinal peptide

all peptides

- endorphins, enkephalins, VIP, ect.
- hypothalamic releasing hormones
- TRH, LHRH, ect. GnRH ≈ 10 amino acids
  3 amino acids
- pituitary peptides
- ACTH, prolactin, vasopressin, ect. ADH

39 amino acids

stimulates breast milk formation

Neurotransmitters

Table 45–1

Small-Molecule, Rapidly Acting Transmitters

- **Class I**
  - Acetylcholine
- **Class II: The Amines** → derived from tyrosine
  - Norepinephrine
  - Epinephrine-CH_3 } → difference is methyl group
  - Dopamine
  - Serotonin
  - Histamine
- **Class III: Amino Acids**: rapidly acting small molecule neurotransmitter
  - Gamma-aminobutyric acid (GABA)
  - Glycine ← inhibitory
  - Glutamate ← excitatory
  - Aspartate ← excitatory
- **Class IV**
  - Nitric oxide (NO), CO

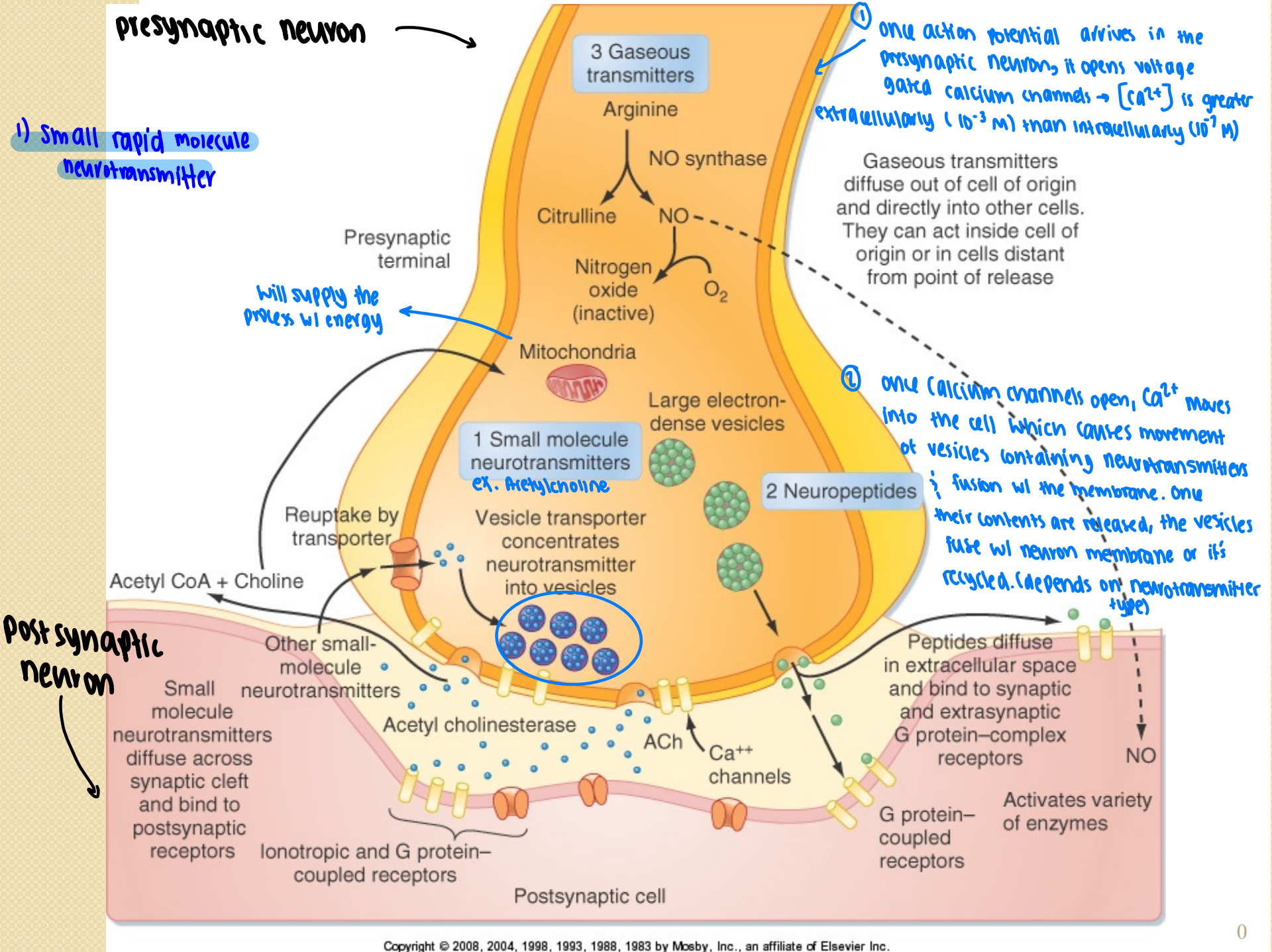
- released in greater quantities
- rapidly broken by enzymes
- short-lived action – because

Table 45–2

Neuropeptide, Slowly Acting Transmitters or Growth Factors → modulate rapidly acting neurotransmitter action
↳ are all peptides or proteins

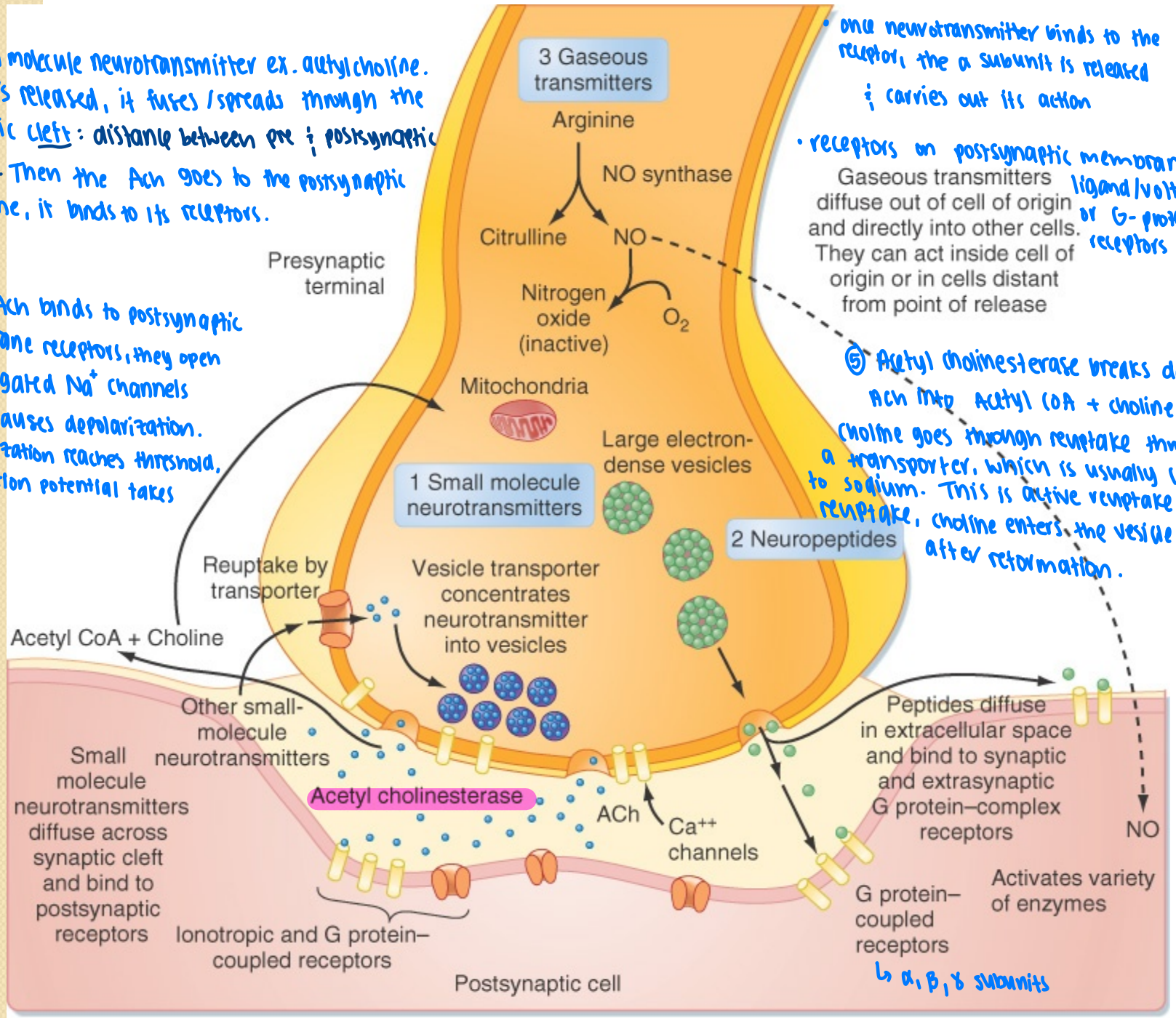
- **Hypothalamic-releasing hormones**
  - Thyrotropin-releasing hormone
  - Luteinizing hormone–releasing hormone
  - Somatostatin (growth hormone inhibitory factor)
- **Pituitary peptides**
  - Adrenocorticotropic hormone (ACTH)
  - β-Endorphin
  - α-Melanocyte-stimulating hormone
  - Prolactin
  - Luteinizing hormone
  - Thyrotropin
  - Growth hormone
  - Vasopressin
  - Oxytocin
- **Peptides that act on gut and brain**
  - Leucine enkephalin } → endogenous opiates (made in our body; similar to morphine)
  - Methionine enkephalin
  - Substance P - pain
  - Gastrin - stomach
  - 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

- Do not memorize this list :)



③ Small molecule neurotransmitter ex. acetylcholine. once it's released, it fuses / spreads through the synaptic cleft : distance between pre & postsynaptic neurons. Then the Ach goes to the postsynaptic membrane, it binds to its receptors.

④ once Ach binds to postsynaptic membrane receptors, they open ligand-gated Na^+ channels which causes depolarization. If depolarization reaches threshold, then action potential takes place.



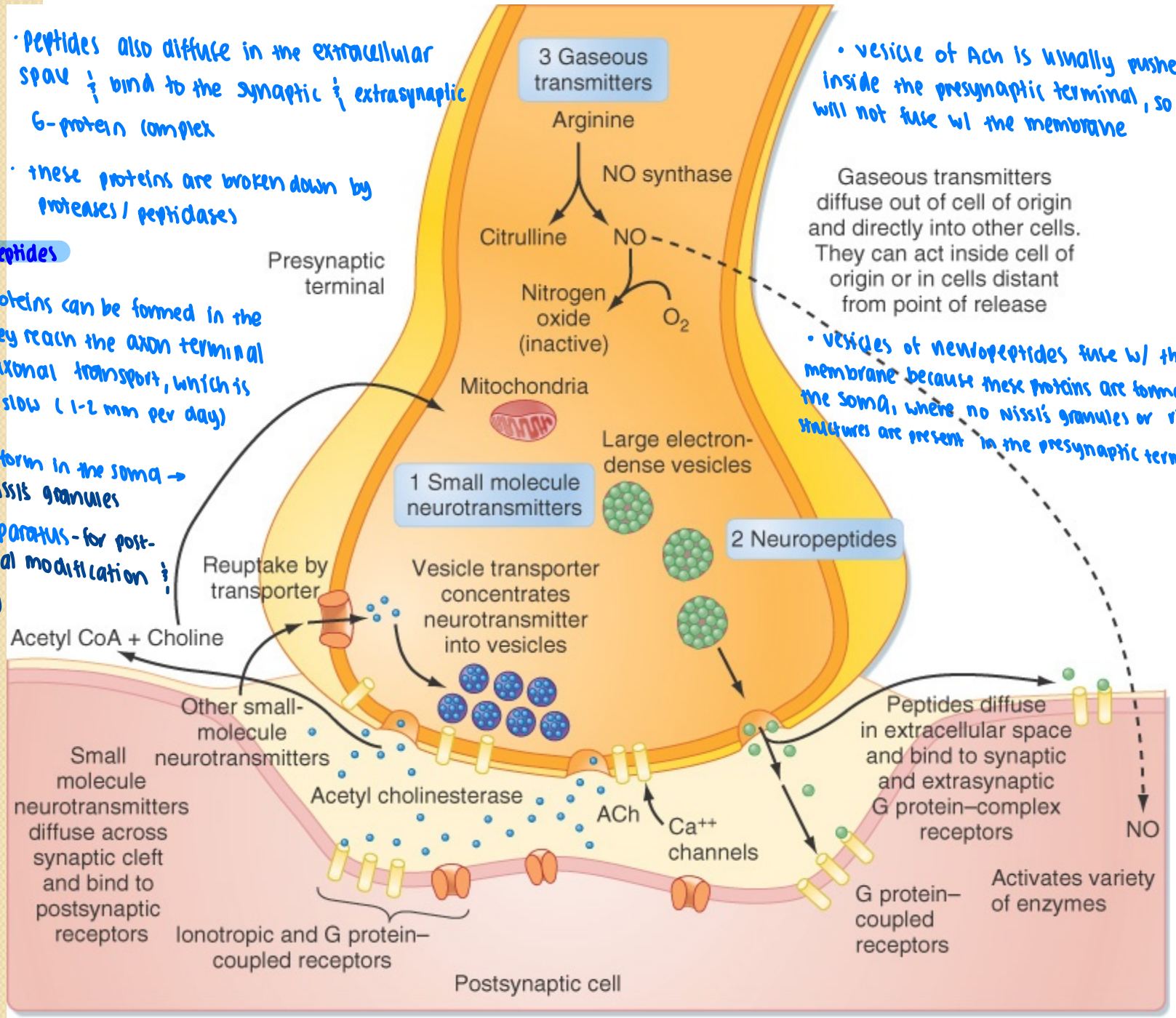
• once neurotransmitter binds to the receptor, the α subunit is released & carries out its action

• receptors on postsynaptic membranes can be ligand/voltage-gated, or G-protein coupled receptors

Gaseous transmitters diffuse out of cell of origin and directly into other cells. They can act inside cell of origin or in cells distant from point of release

⑤ Acetyl cholinesterase breaks down Ach into Acetyl CoA + choline. Choline goes through reuptake through a transporter, which is usually coupled to sodium. This is active reuptake. After reuptake, choline enters the vesicle again after reformation.

↳ α, β, γ subunits



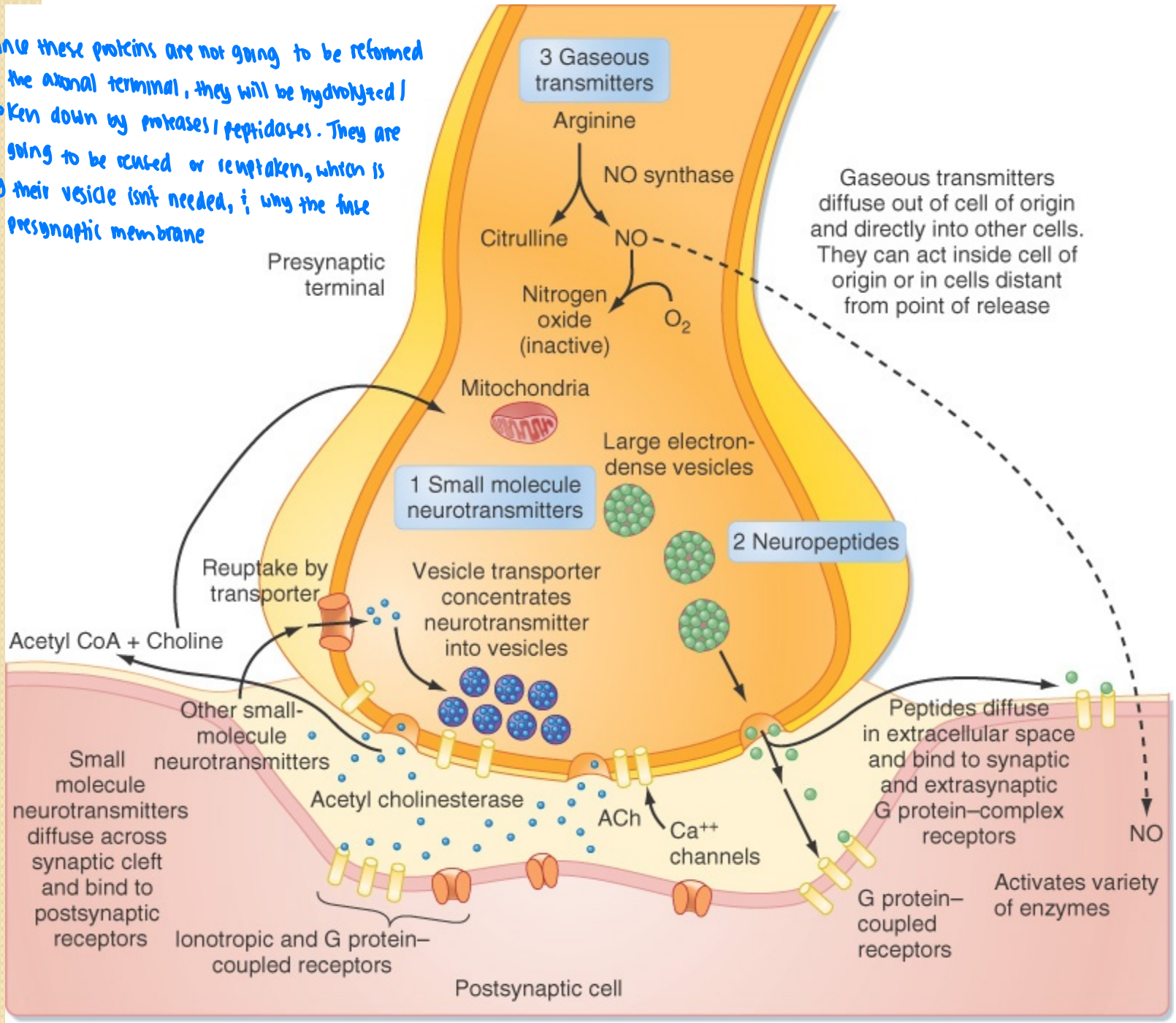
- peptides also diffuse in the extracellular space & bind to the synaptic & extrasynaptic G-protein complex
- these proteins are broken down by proteases / peptidases

- vesicle of Ach is usually pushed inside the presynaptic terminal, so it will not fuse w/ the membrane

2) Neuropeptides

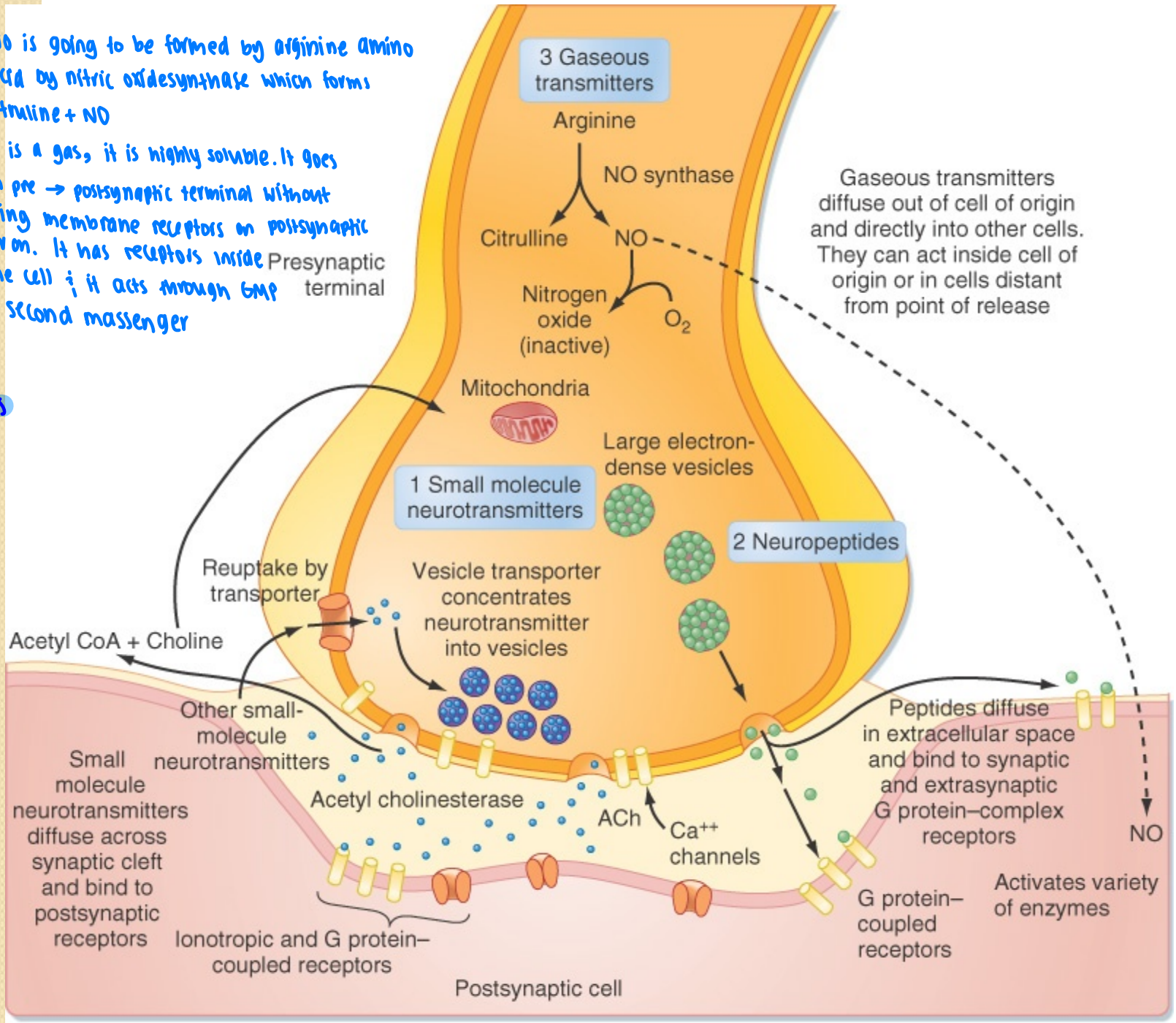
- only proteins can be formed in the soma, they reach the axon terminal through axonal transport, which is extremely slow (1-2 mm per day)
- proteins form in the soma → Nissl granules
- golgi apparatus - for post-translational modification & packaging
- vesicles of neuropeptides fuse w/ the membrane because these proteins are formed in the soma, where no Nissl's granules or ribosome-like structures are present in the presynaptic terminal

- Since these proteins are not going to be reformed at the axonal terminal, they will be hydrolyzed / broken down by proteases / peptidases. They are not going to be reused or reuptaken, which is why their vesicle isn't needed, i, why the fuse w/ presynaptic membrane



- NO is going to be formed by arginine amino acid by nitric oxidesynthase which forms citruline + NO
- NO is a gas, it is highly soluble. It goes from pre → postsynaptic terminal without having membrane receptors on postsynaptic neuron. It has receptors inside the cell ; it acts through GMP second massenger

3) gases



Comparison between Small Molecules and Neuropeptides Neurotramsmitters (NT)

- Small molecules NT are rapidly acting as compared to slowly acting neuropepides → long-lived ← short-lived
- 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 → formed in the soma, long journey to arrive at the terminal
- Small molecules NT vesicles are recycled but neuropeptide ones are not → no reuptake ↓ reuptake
- 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

norlepinephrine are broken down by monoamineoxidases or catechol-O-methyltransferase

- Uptake by neurons or glia cells
- neurotransmitter transporters

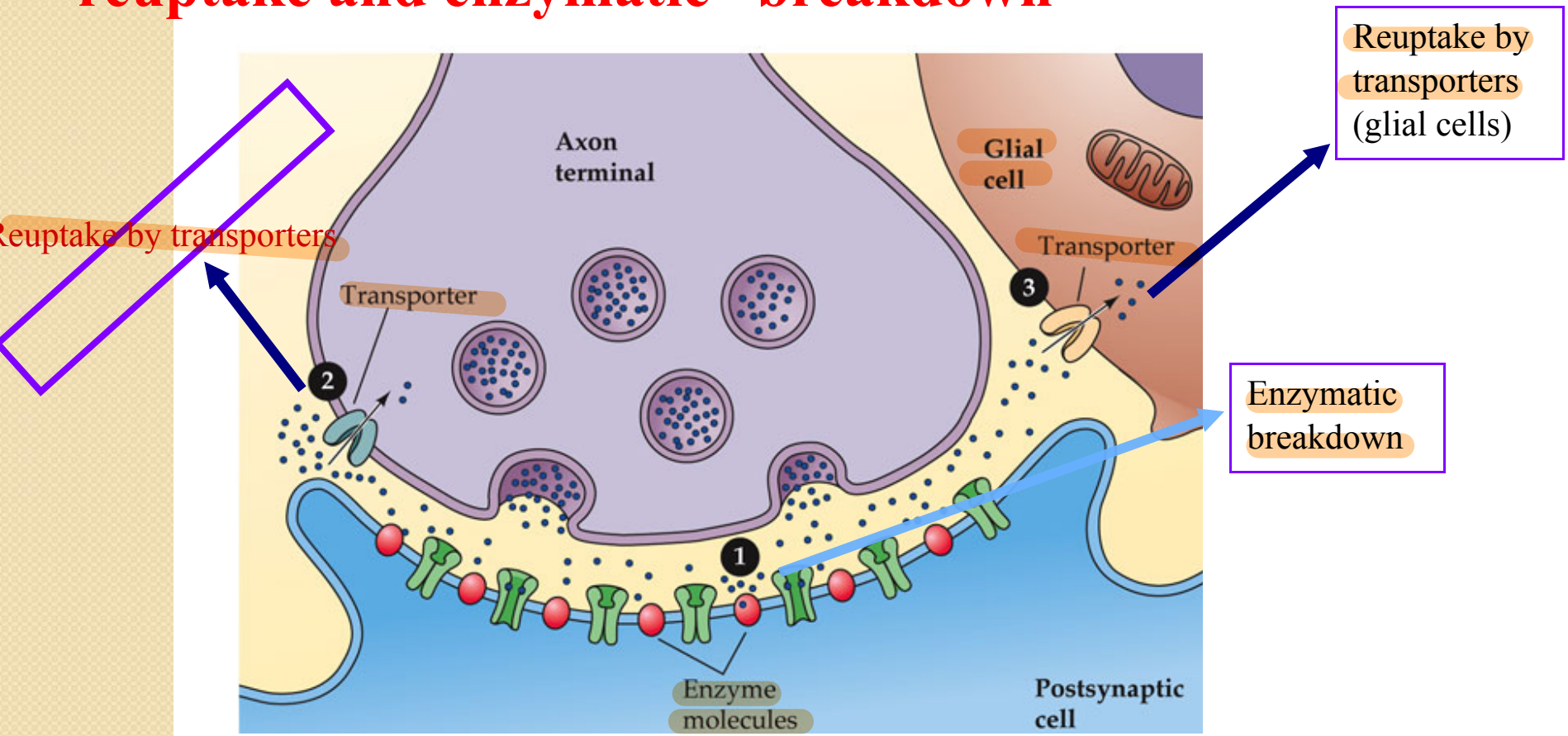
ex. Ach, NE/Ep

→ sodium, Ach co-transport

- Prozac = serotonin reuptake inhibitor

blocks action of serotonin

- **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

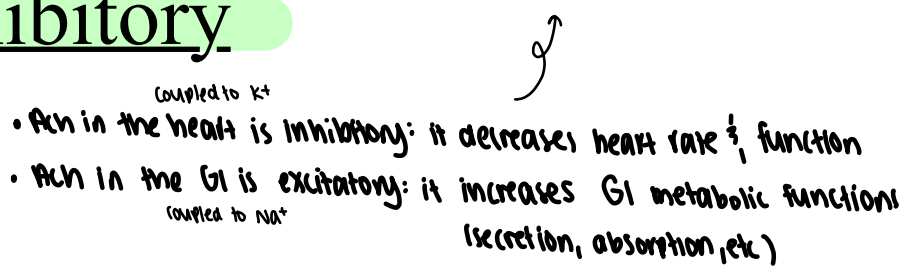
Basic Concepts of NT and receptor

found inside our bodies

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

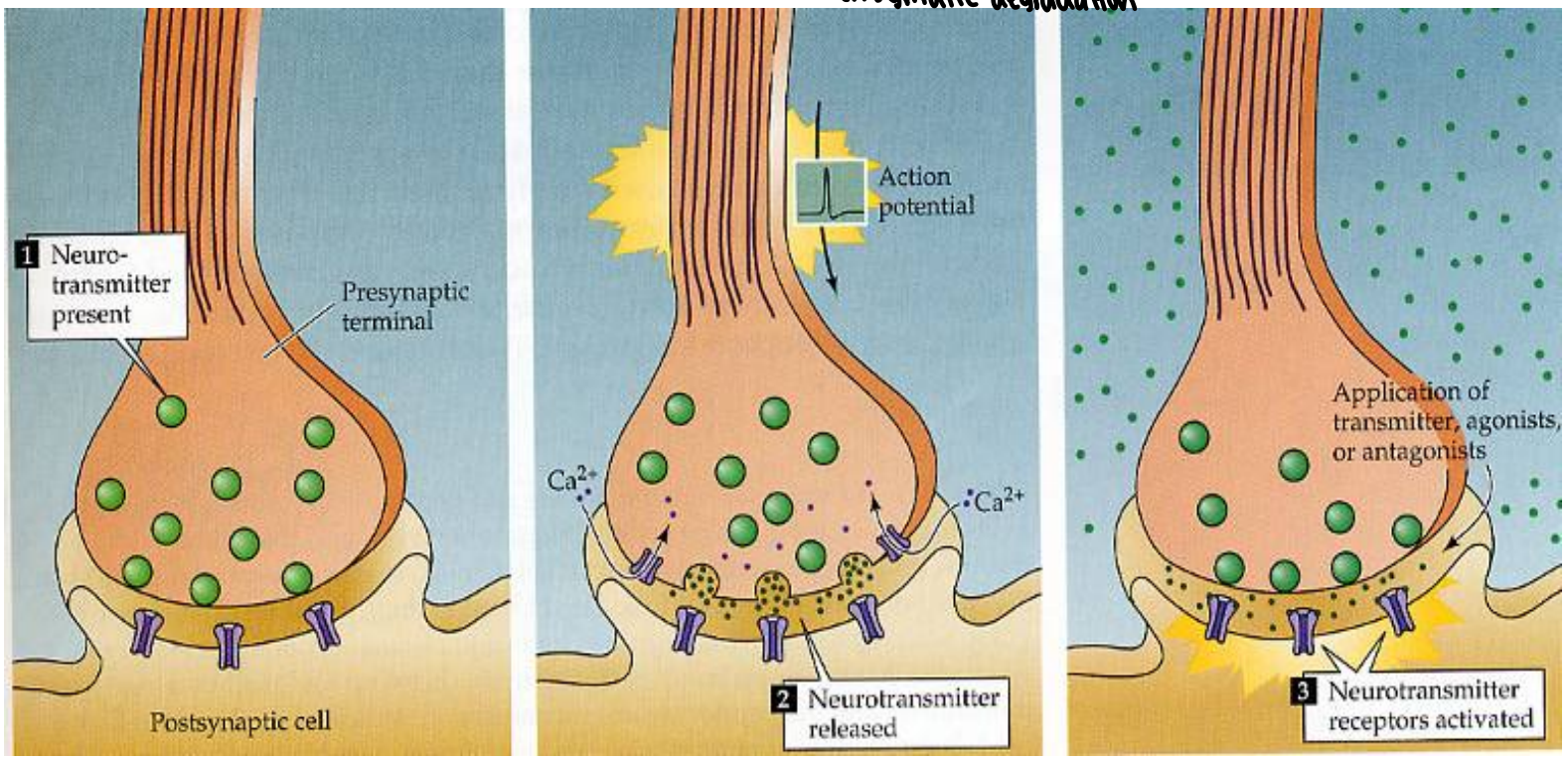
Neuroreceptor: Proteins on the cell membrane or in the cytoplasm that could bind with specific neurotransmitters and alter the behavior of neurons of effector cells

- 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 → diffusion → reuptake → enzymatic degradation



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.

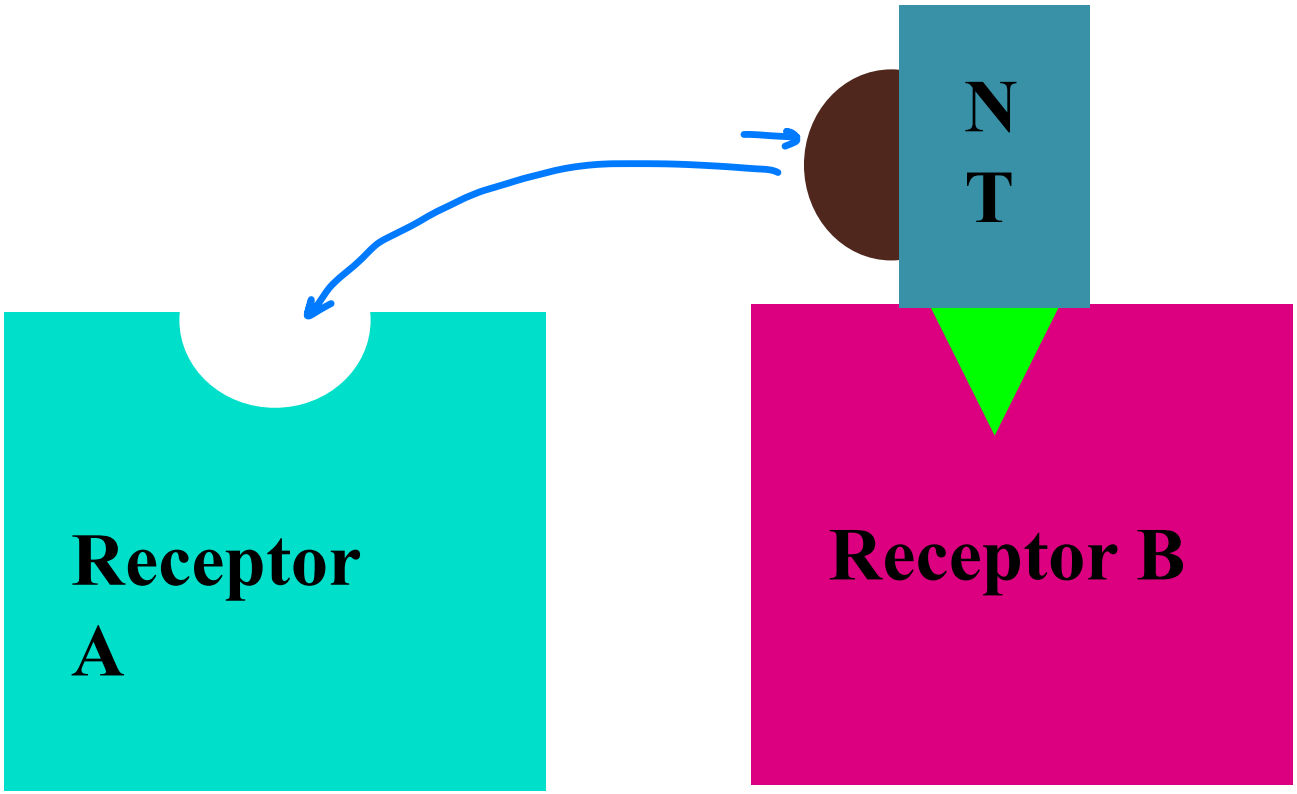
Drugs are often designed as receptor agonists to treat a variety of diseases and disorders when the original chemical substance is missing or depleted.

Antagonist

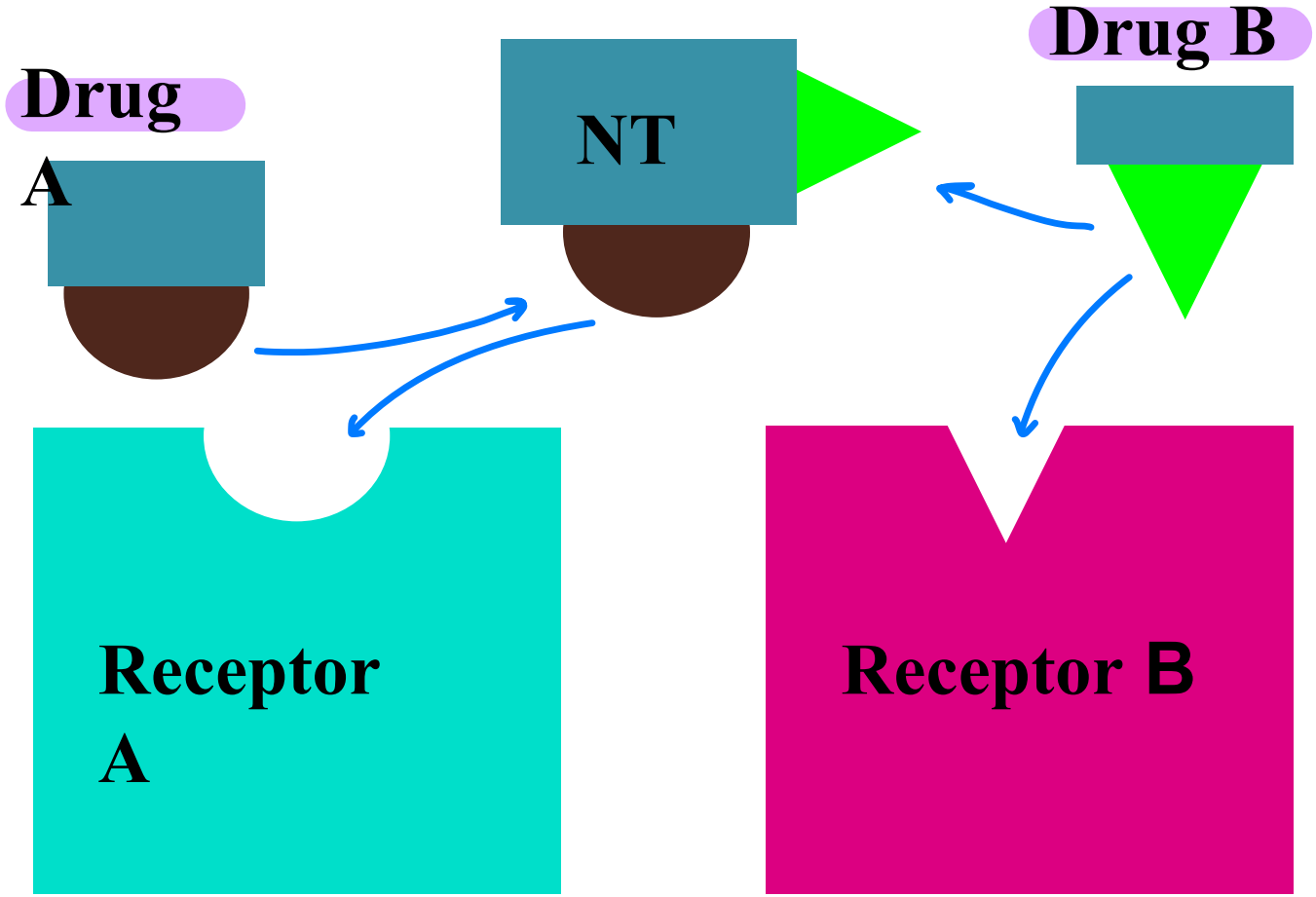
Drugs that bind to but do not activate neuroreceptors,

thereby blocking the actions of neurotransmitters or the neuroreceptor agonists.

- Same NT can bind to different -R (receptors)
- different part of NT ~ (binds to different receptors)

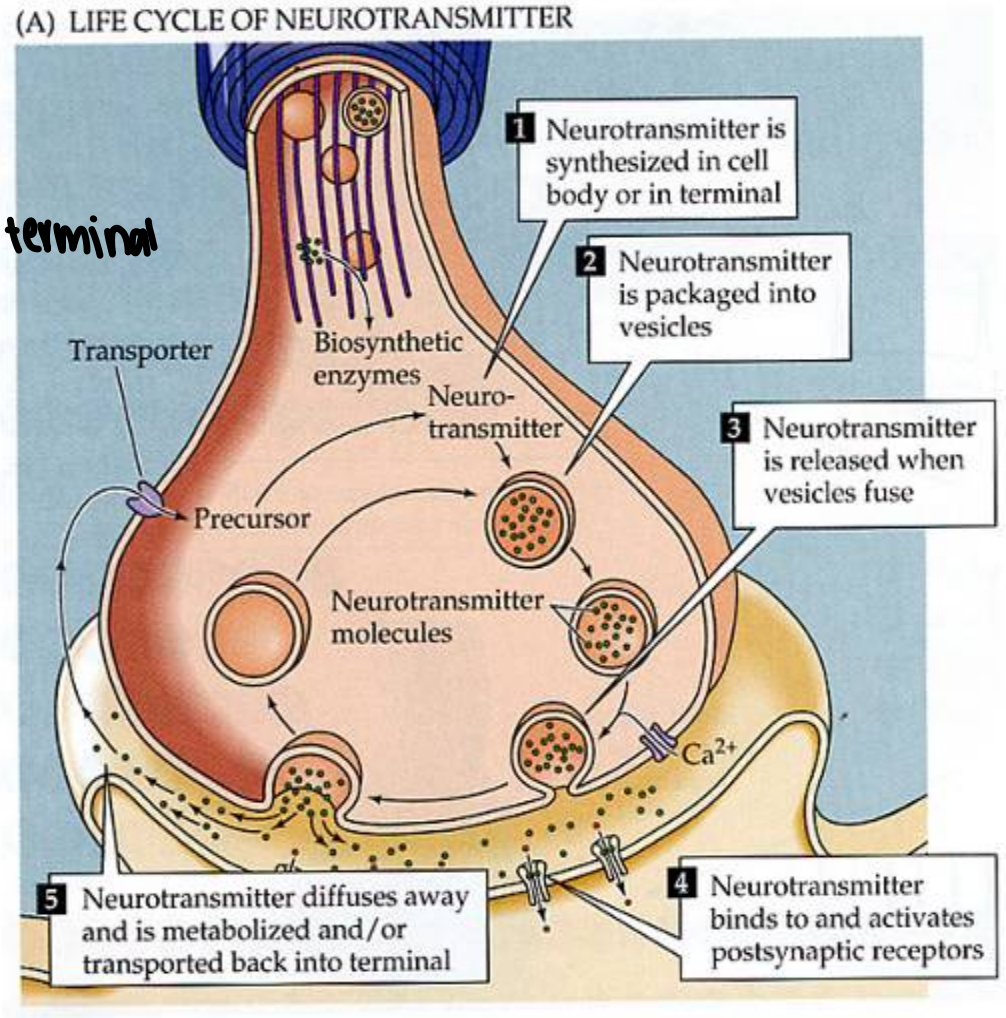


Specificity of drugs



Five key steps in neurotransmission

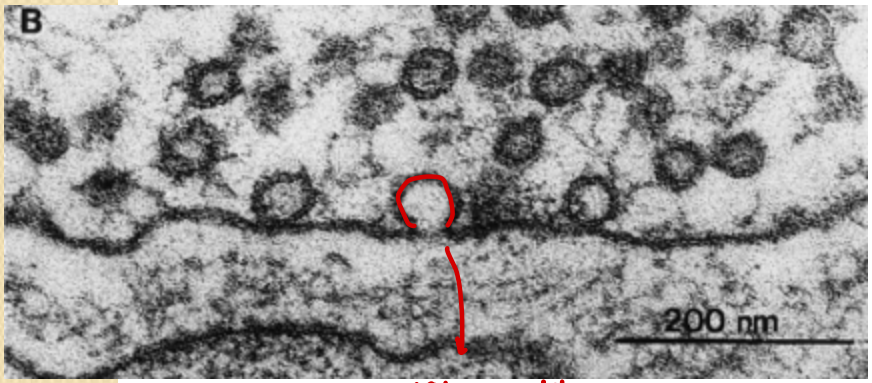
- Synthesis in presynaptic terminal
- Storage vesicles
- Release vesicles fuse & NT are released
- Receptor Binding to specific
- Inactivation
  - diffusion
  - reuptake
  - enzymatic breakdown



Synaptic vesicles

electron microscopy

small, dense-like vesicles for small molecules rapidly acting NT



large vesicles, dense-core for peptides

- 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.

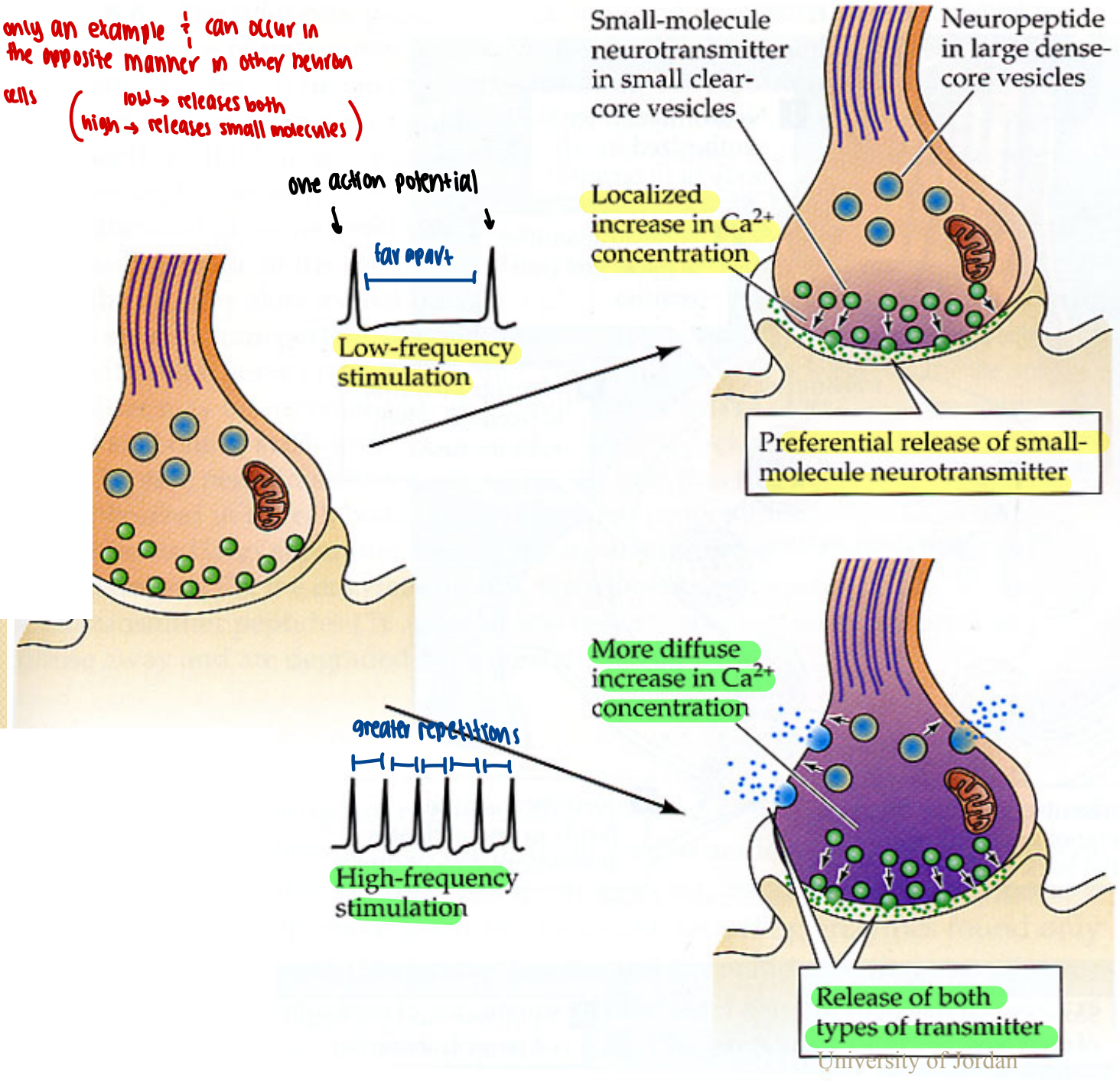
can only have one

can have more than one polypeptide

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.

- only an example ↑↓ can occur in the opposite manner in other neuron cells (low → releases both; high → releases small molecules)



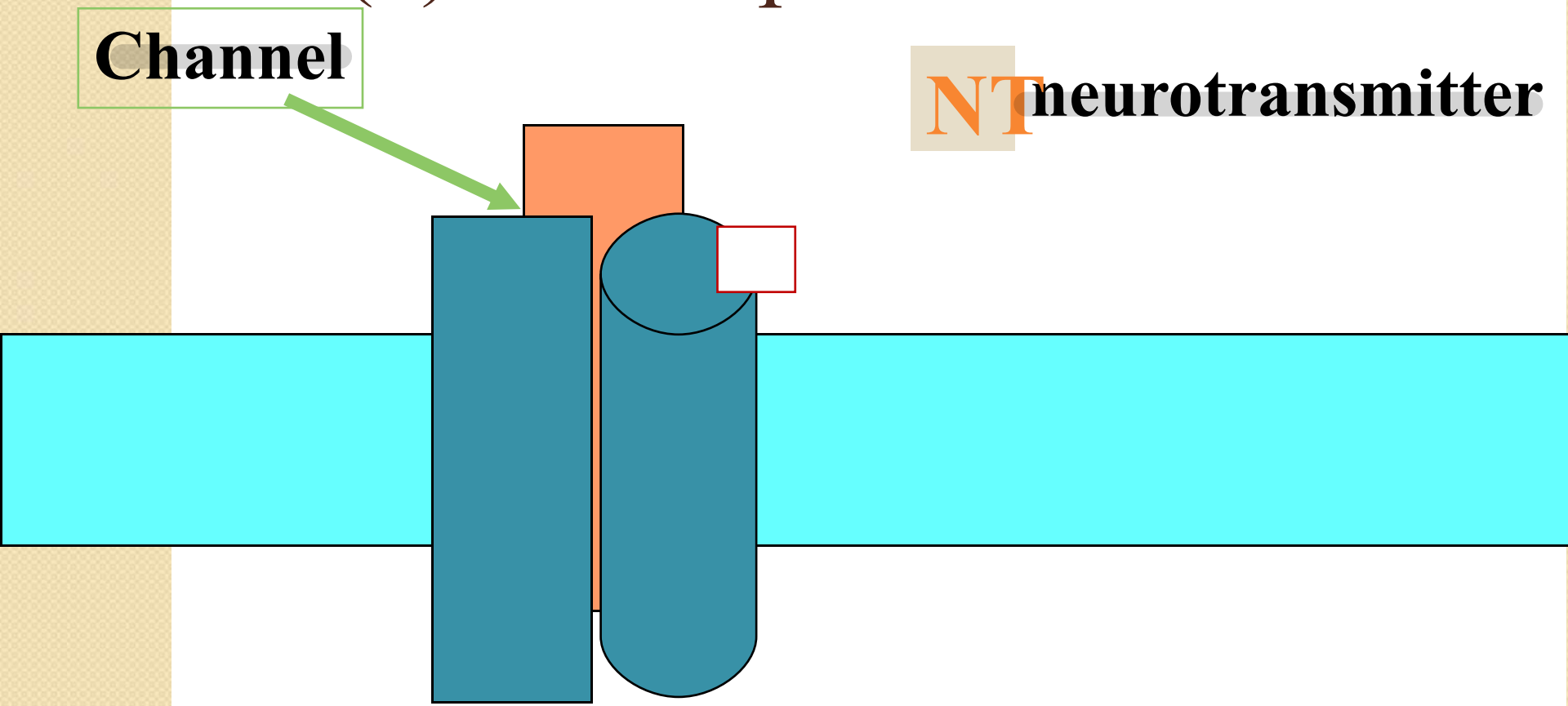
Receptors determine whether:

- 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 (ion channels)
    - fast
  - Indirectly
    - metabotropic receptors, ex
    - G-protein coupled → α subunit dissociates ↓ carries out its role
    - slow → secondary messenger mechanism

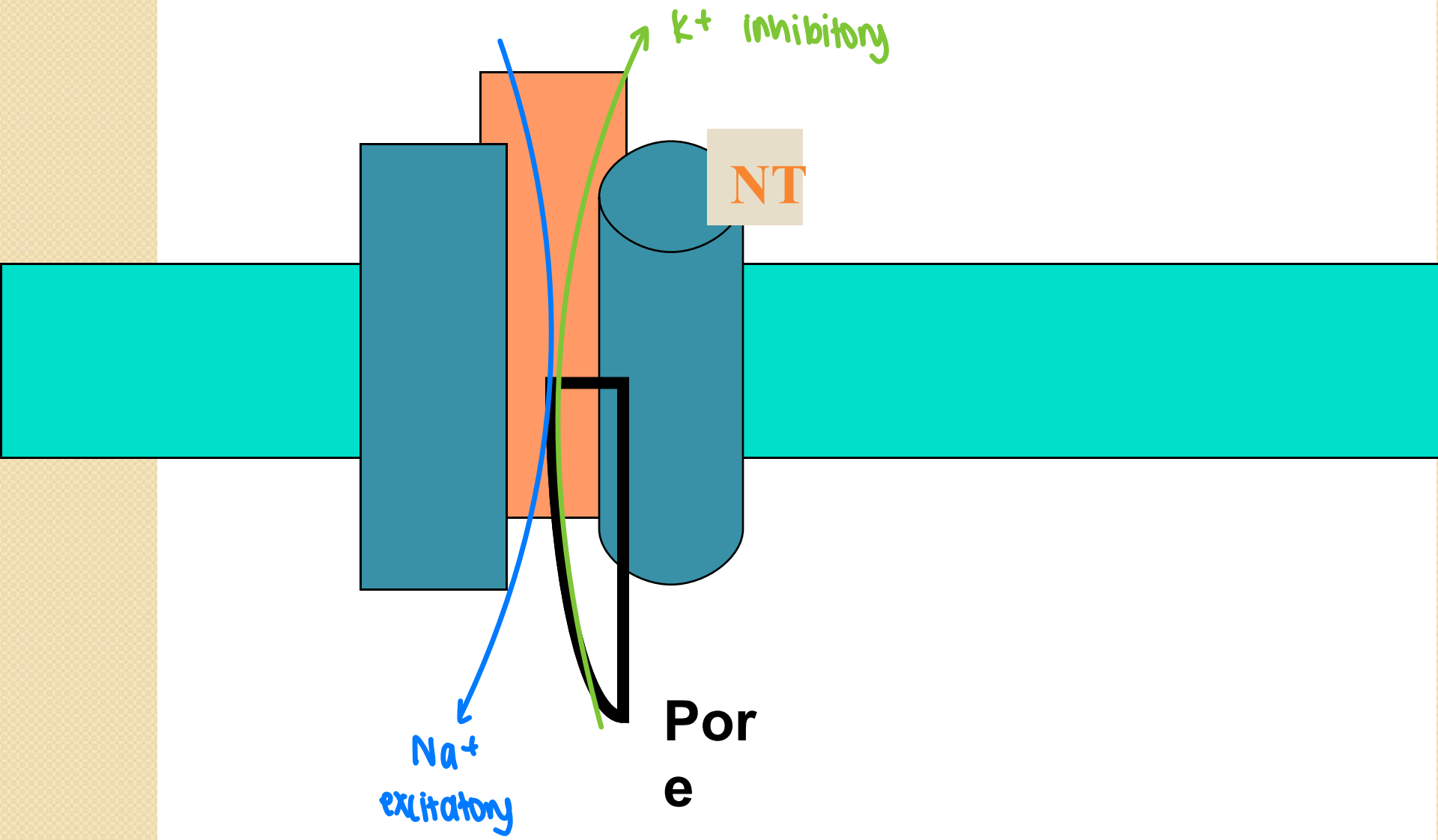
Receptor Activation

- Ionotropic channel
  - directly controls channel
  - fast
- Metabotropic channel
  - second messenger systems Ca^{2+}, cAMP
  - receptor indirectly controls channel ~

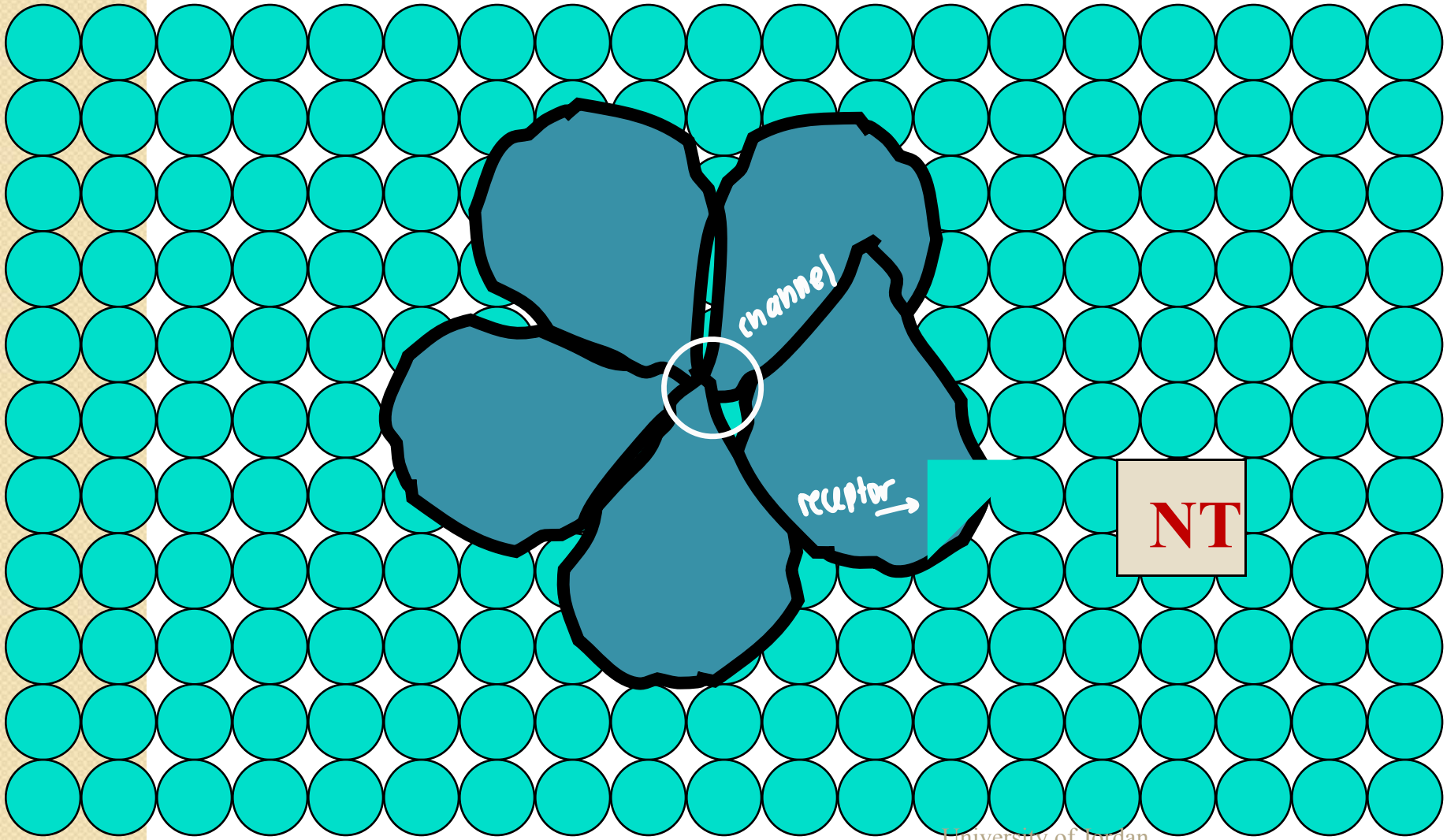
(1) Ionotropic Channels



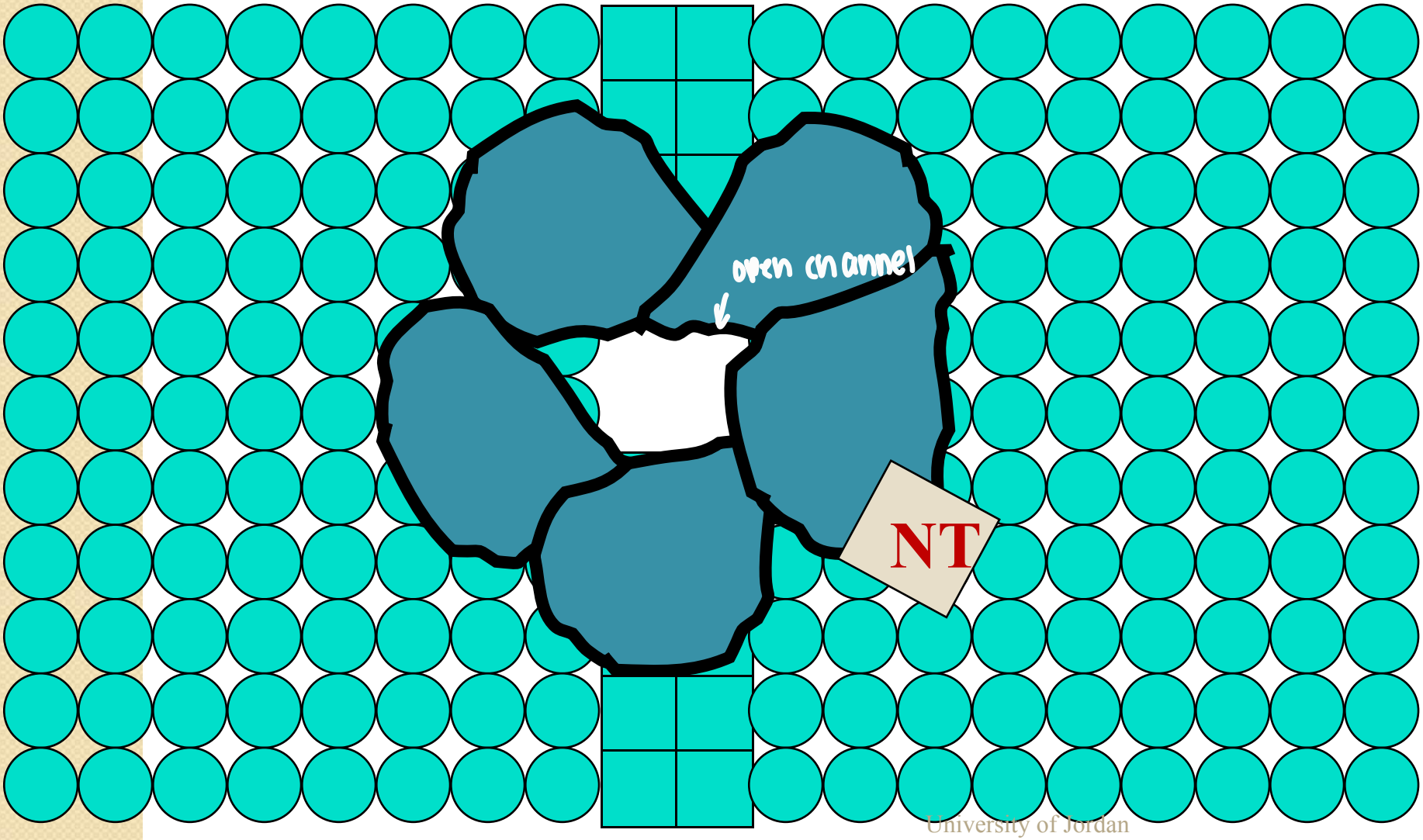
Ionotropic Channels



Ionotropic Channels

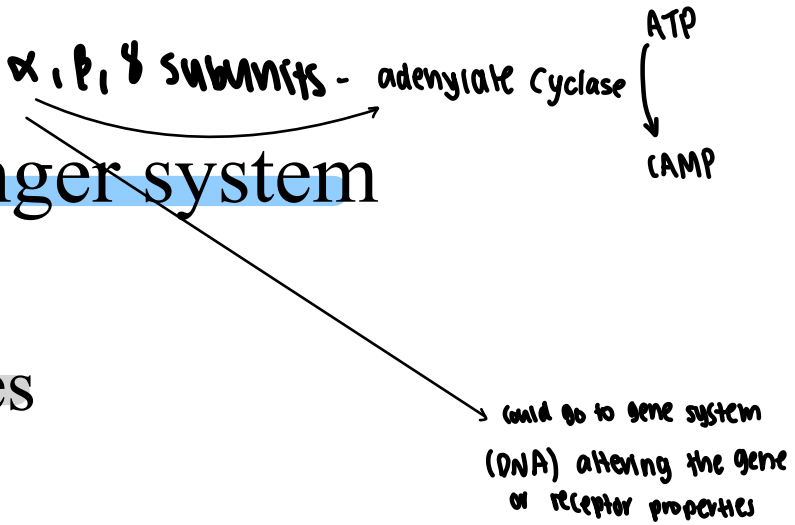


Ionotropic Channels



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 ~

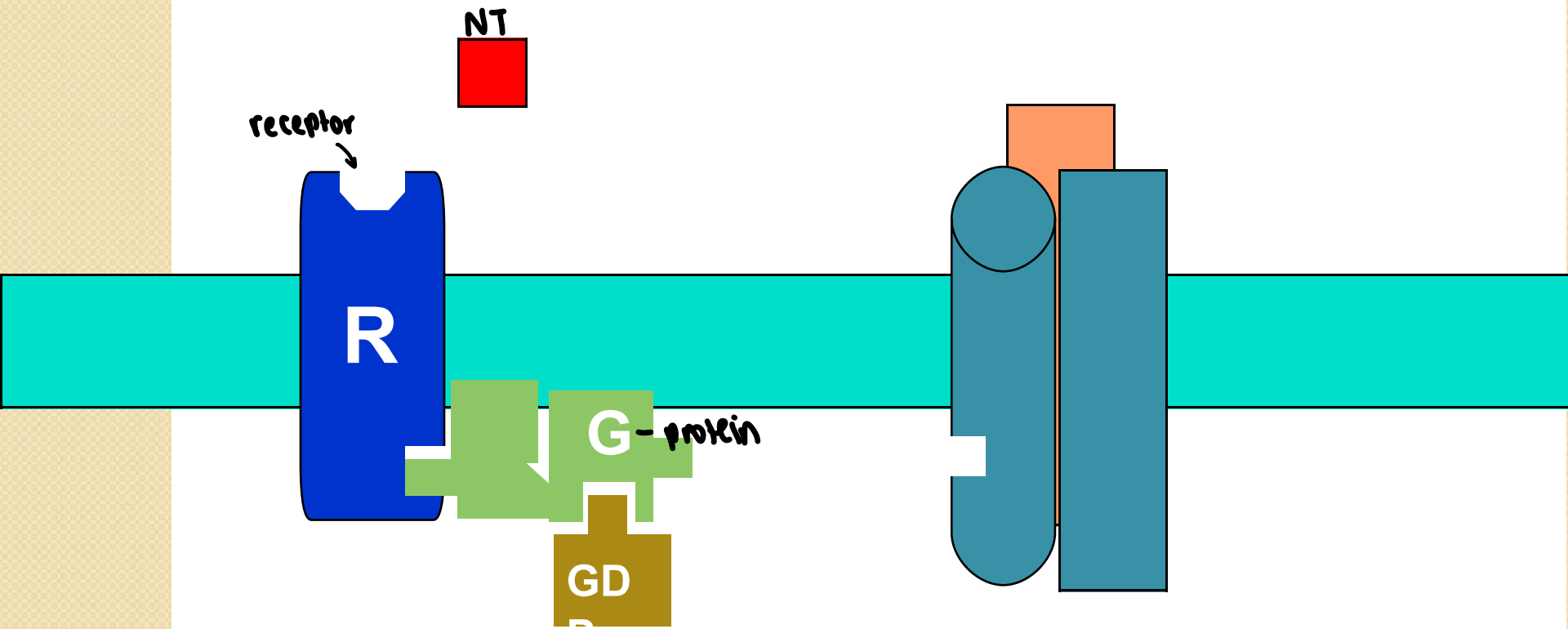


G protein: direct control

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

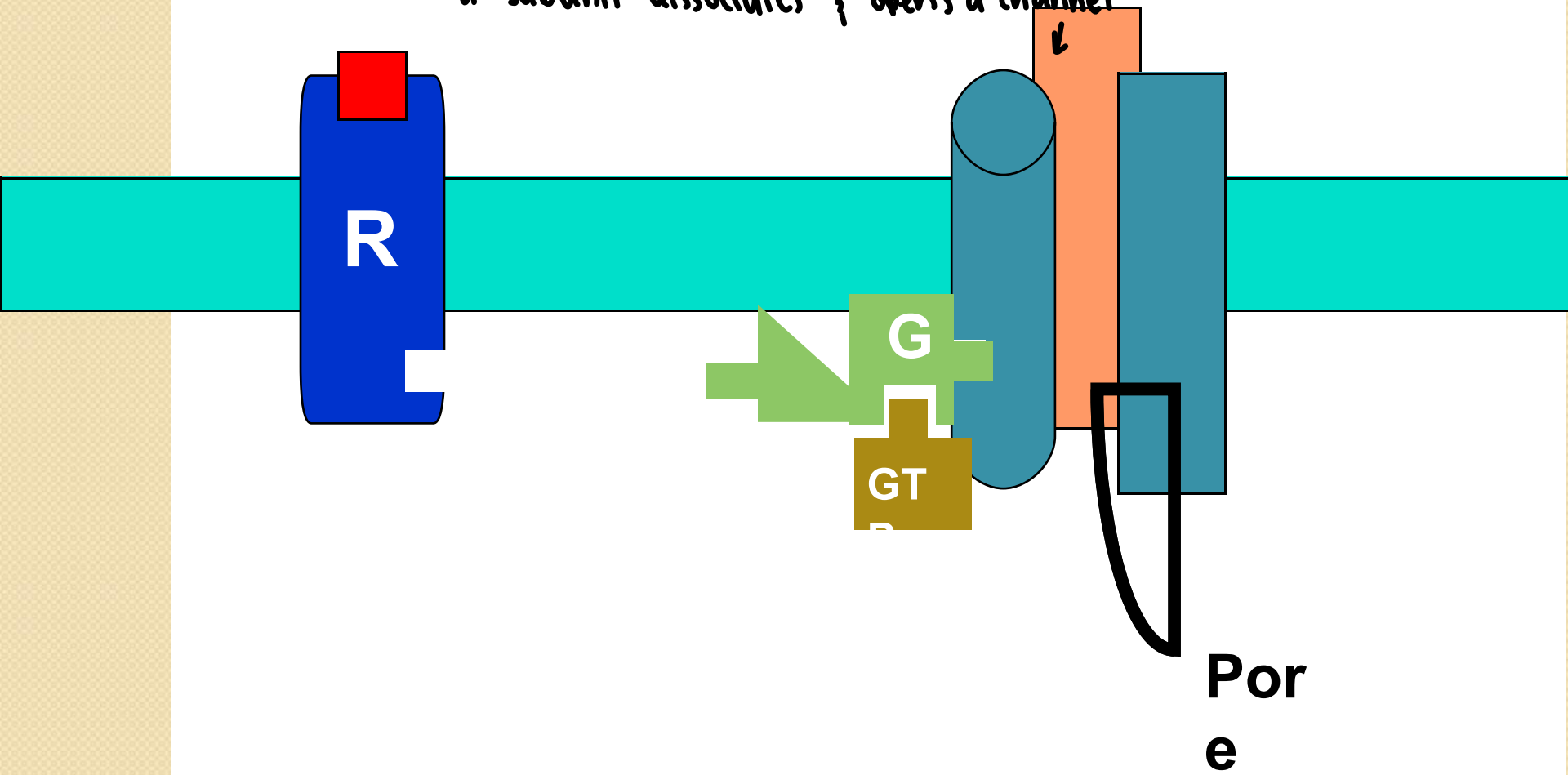
↓
not faster than ionotropic

G protein: direct control

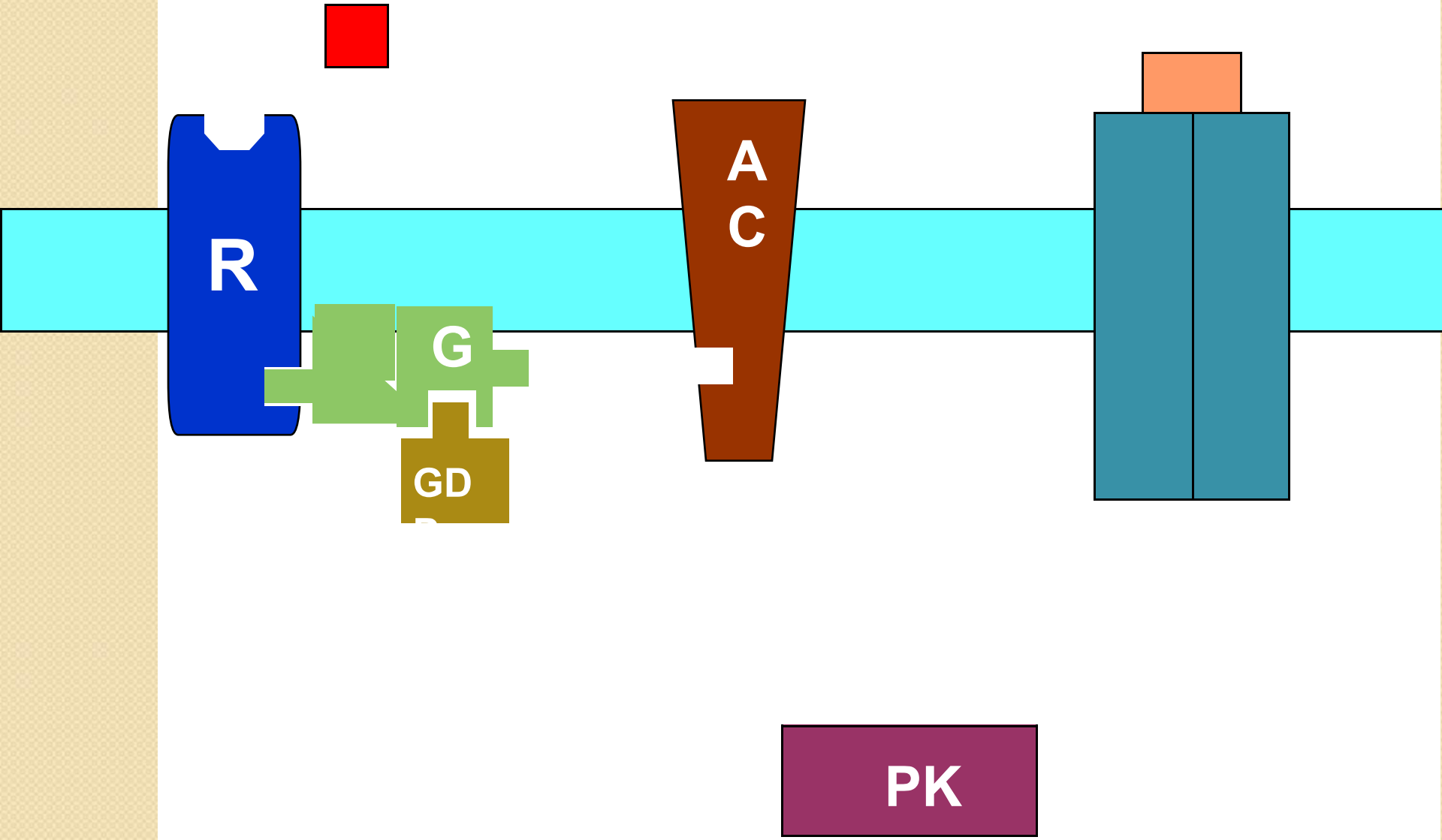


G protein: direct control

- neurotransmitter binds to receptor
- α subunit dissociates & opens a channel



G protein: Protein Phosphorylation



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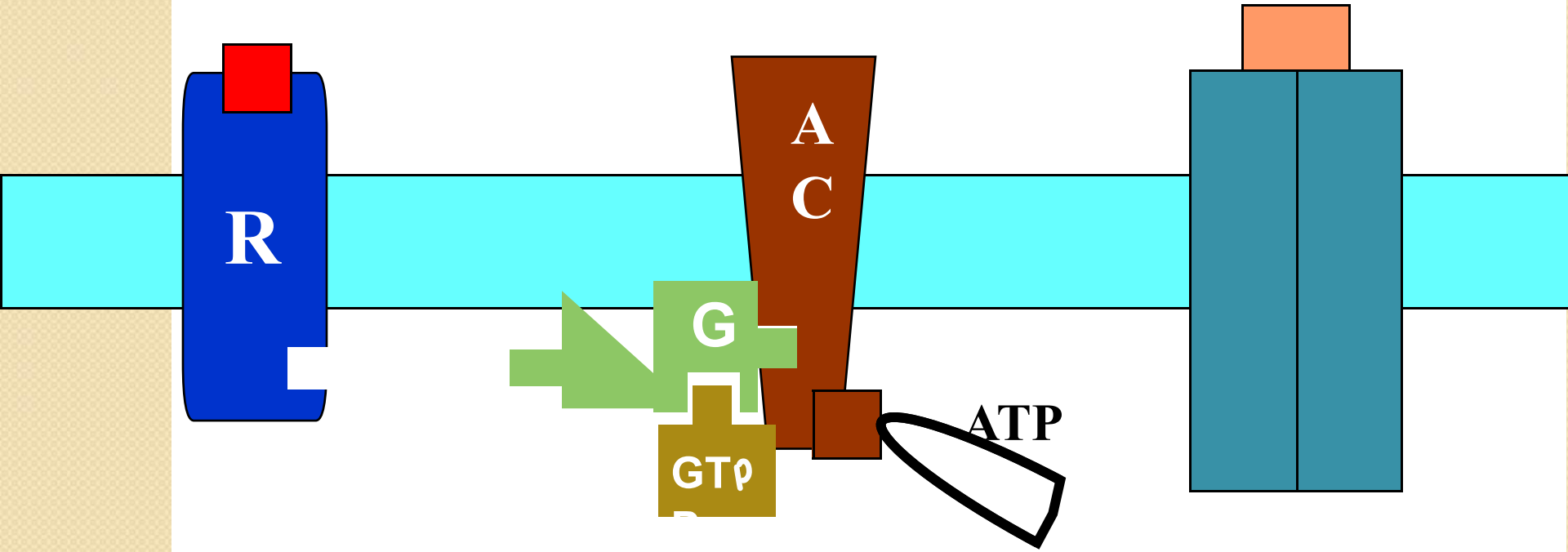


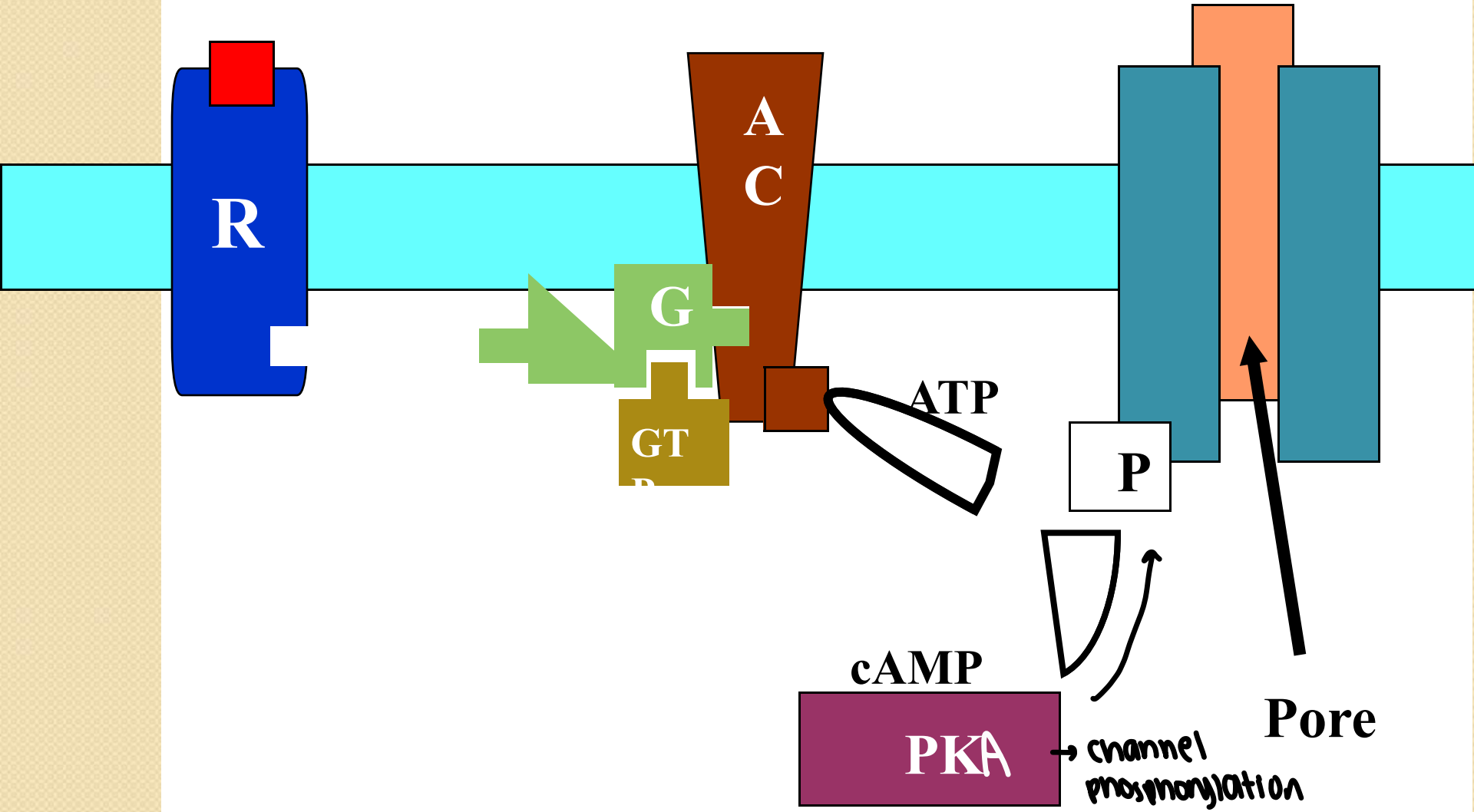
- G-protein binds to adenylate cyclase which activates it & converts AMP → cAMP
- cAMP activates protein kinase A, cAMP dependent protein kinase

cAMP

PKB · calcium dependent protein kinase

PKA

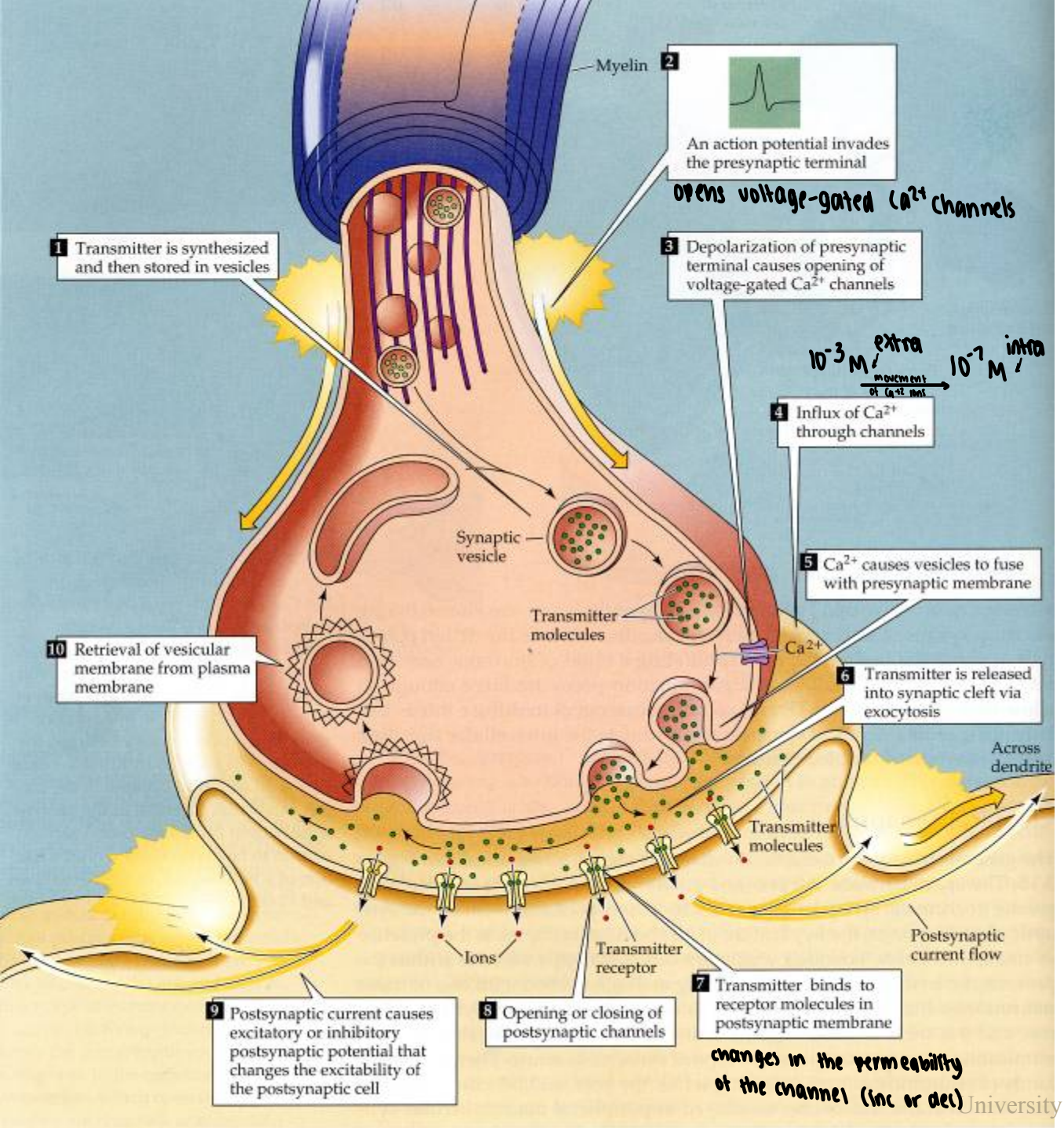
G protein: Protein Phosphorylation



Transmitter Inactivation

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

Summary of Synaptic Transmission



Purves,2001


THANK YOU