بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

PHYSIOLOGY

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

MID | Lecture 8

Synapses

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Emad Aljammal

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Introduction to Neurophysiology 2

Synapses

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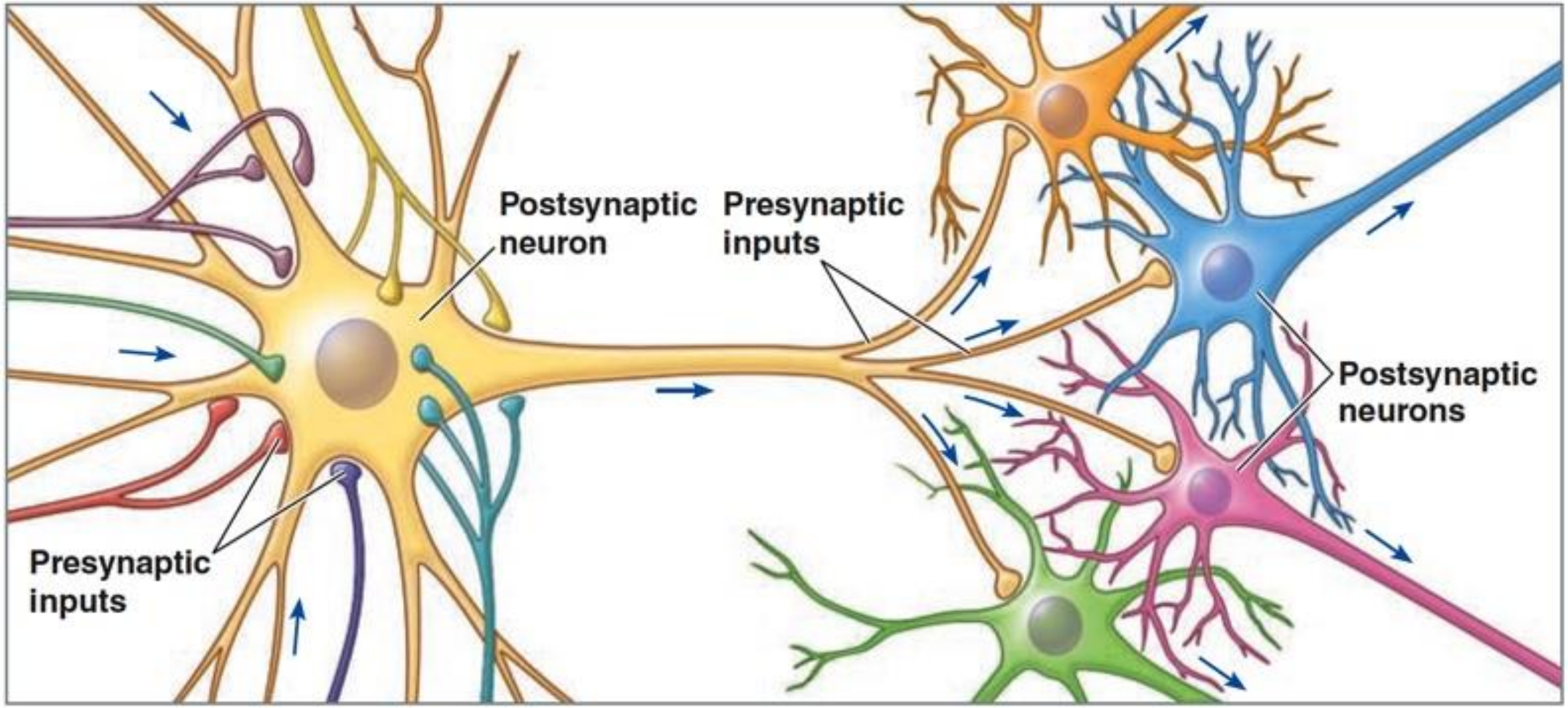

Postsynaptic neuron
Presynaptic inputs
Postsynaptic neurons
Presynaptic inputs

Synapses

"The area of communication"

- The synapse is a region where communication occurs between two neurons or between a neuron and an effector cell (muscle cell or glandular cell).

The generation of the action potential occurs in the axon hillock (will be discussed later)

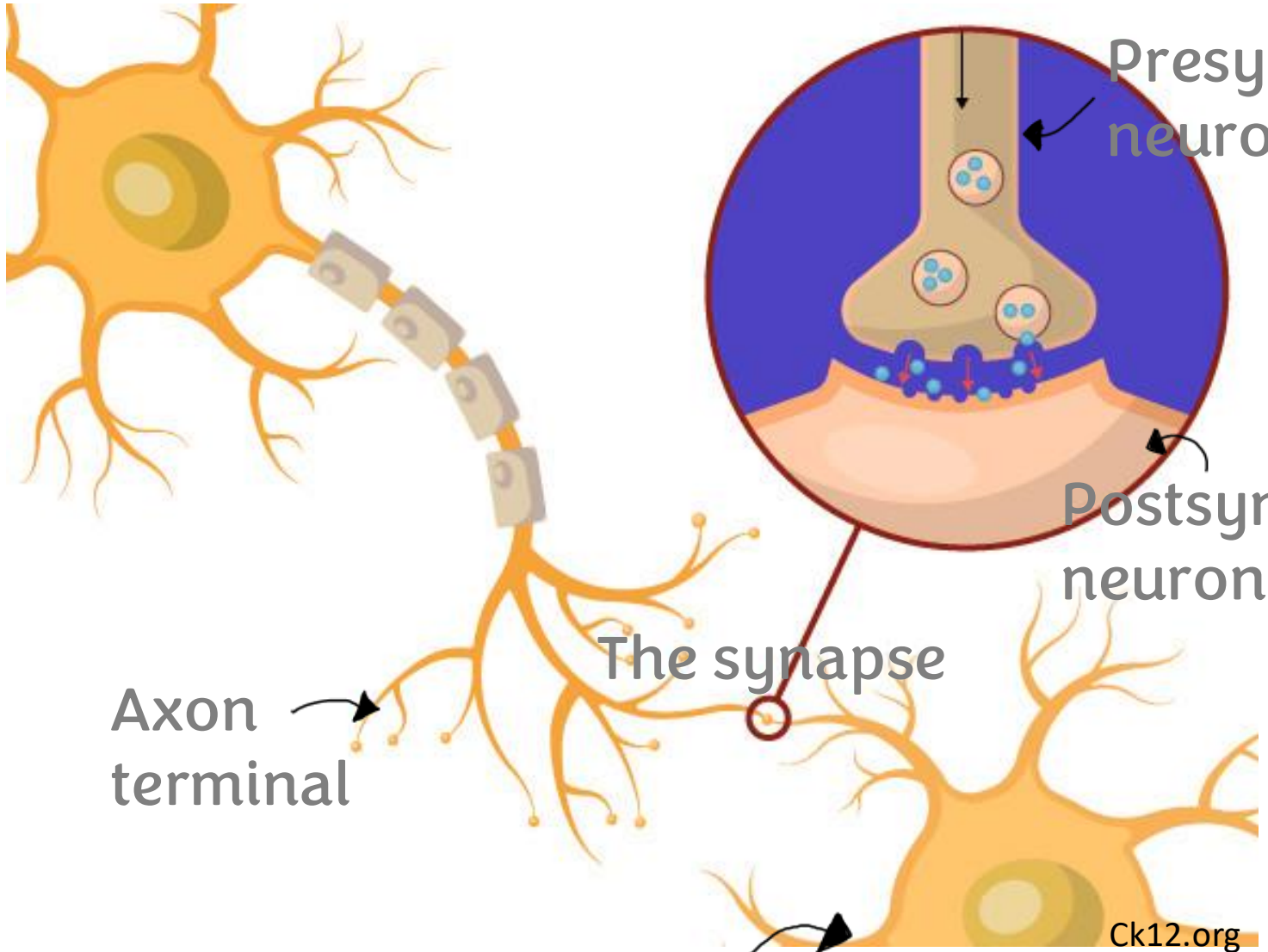
Synaptic functions of neurons

Information is transmitted in the central nervous system mainly in the form of nerve action potentials, called nerve impulses, through a succession of neurons, one after another.

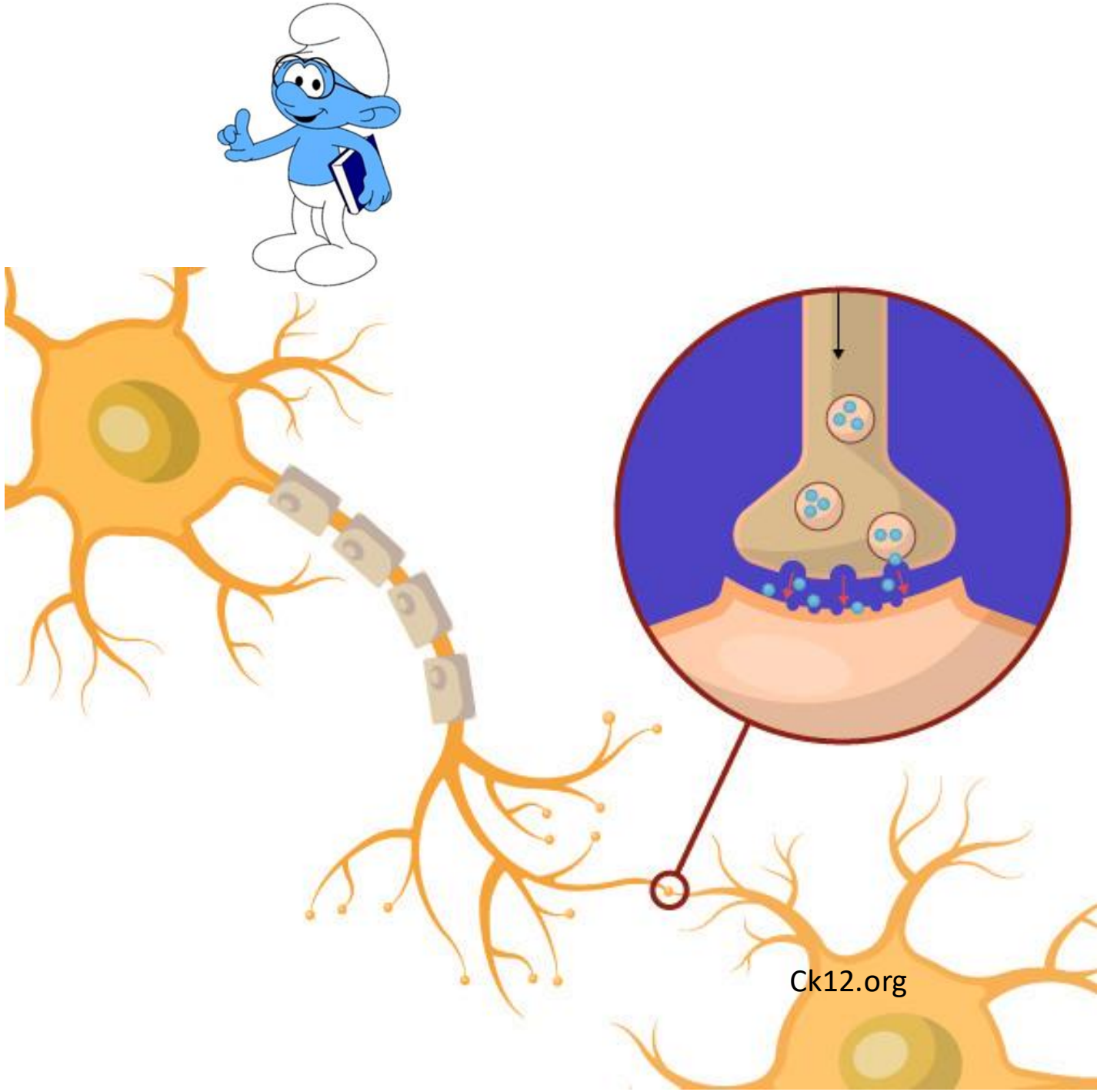
However, this impulse may be blocked, changed into repetitive impulses, or integrated with other impulses.

These functions are called **synaptic functions of neurons**.

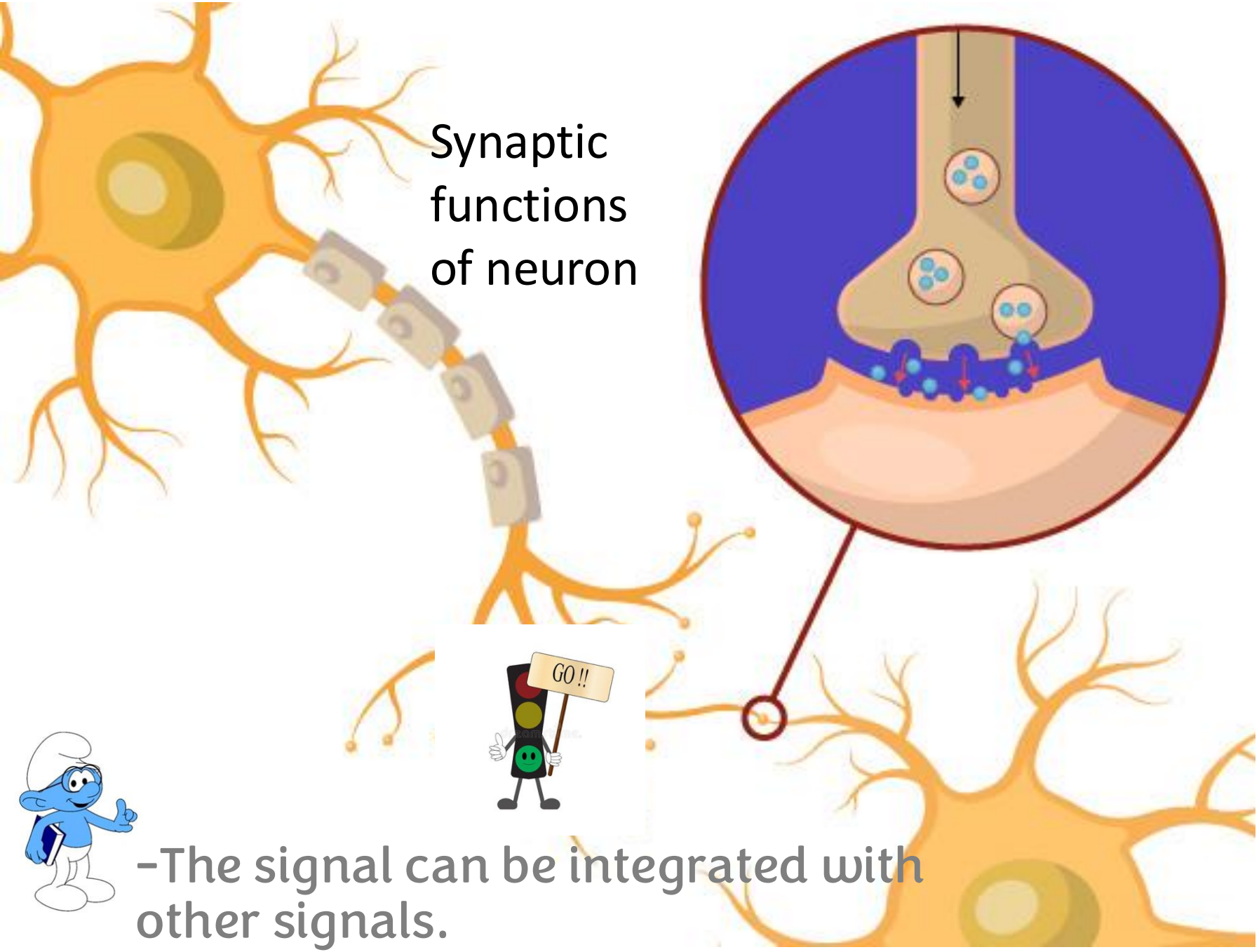
-When the signal reaches the first neuron if it's strong enough to produce an action potential, the signal will be transmitted all the way until it reaches the axon terminal and then to the next neuron (the Postsynaptic neuron).



-The transmission is not straight forward, and many processes can occur at the level of synapse.



Synaptic functions of neuron



-The signal can be integrated with other signals.

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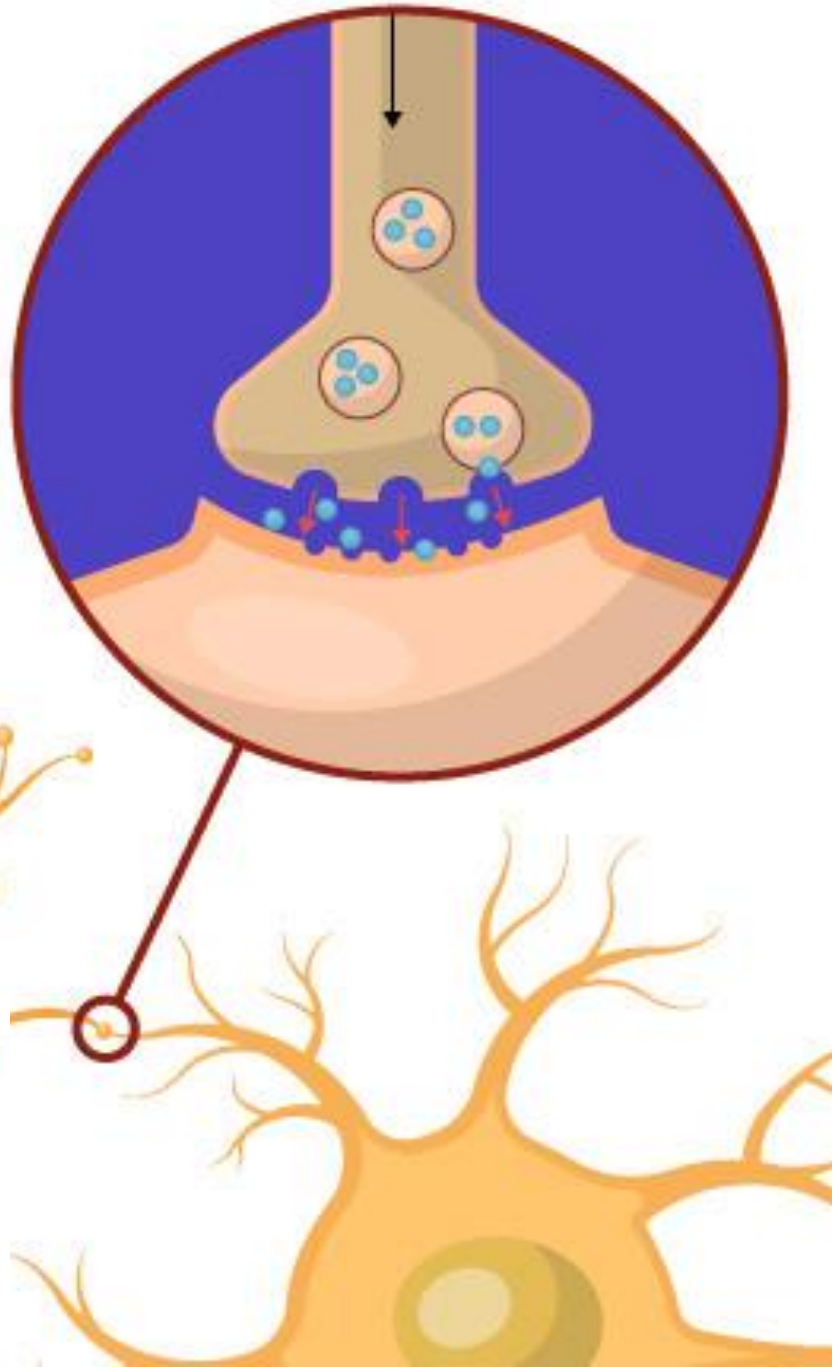
Synaptic functions of neuron

-In other situations, the transmission of signals between the synaptic neuron and the post synaptic neuron may be blocked/ inhibited.



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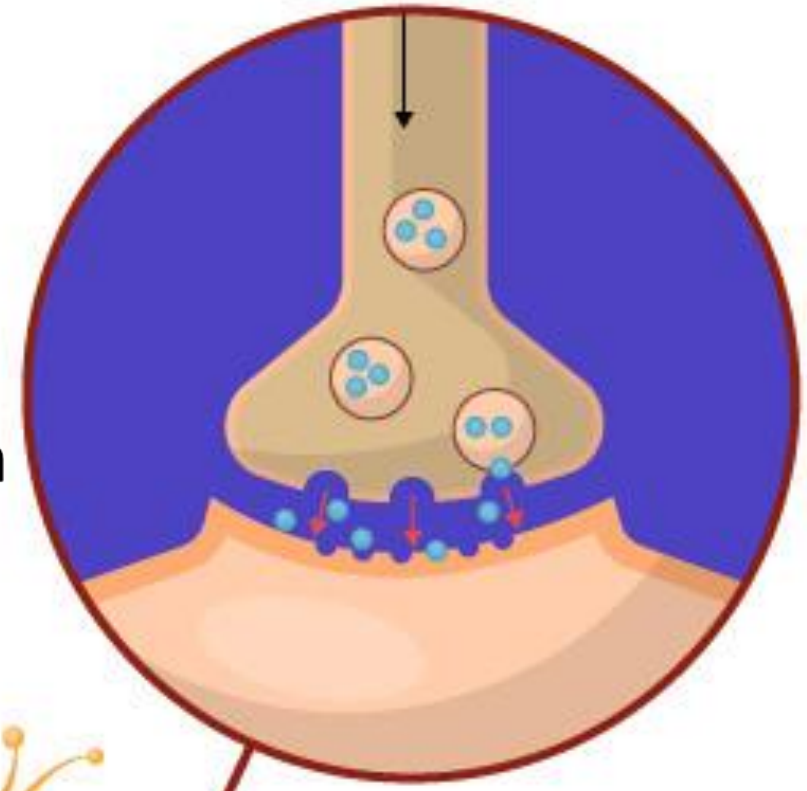
Synaptic functions of neuron



-In other cases
At the level of synapse there will be repetition of the signal over and over again for this signal (circuit) to be transmitted for a longer time across this pathway.
(to be discussed later)

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Types of Synapses

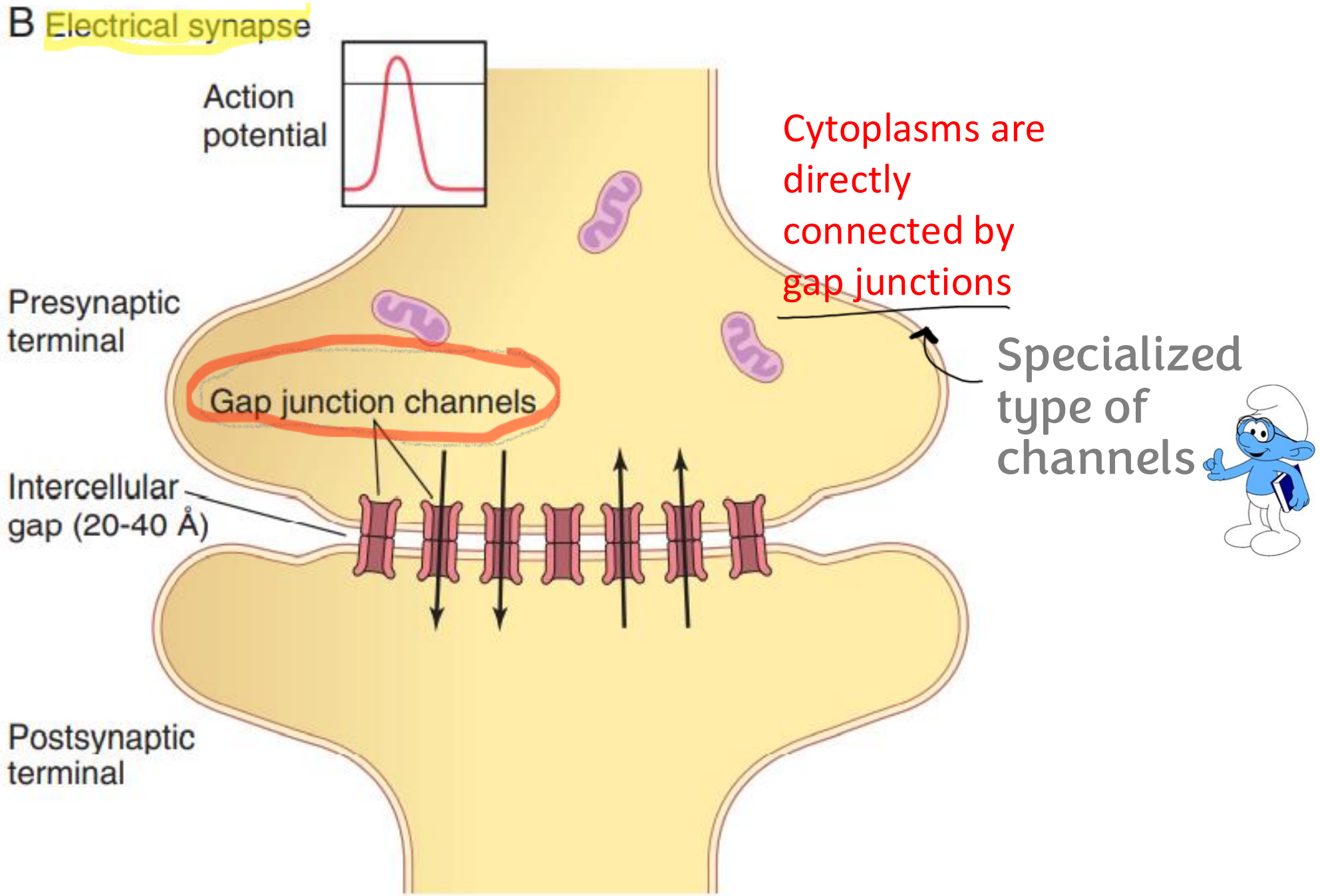
- Chemical synapses. (more common)
- Electrical synapses.

Electrical Synapses

-In neurophysiology when we say electrical synapses then we mean that there's a flow of ions across the membrane, this movement of charged ions will create electrical changes.

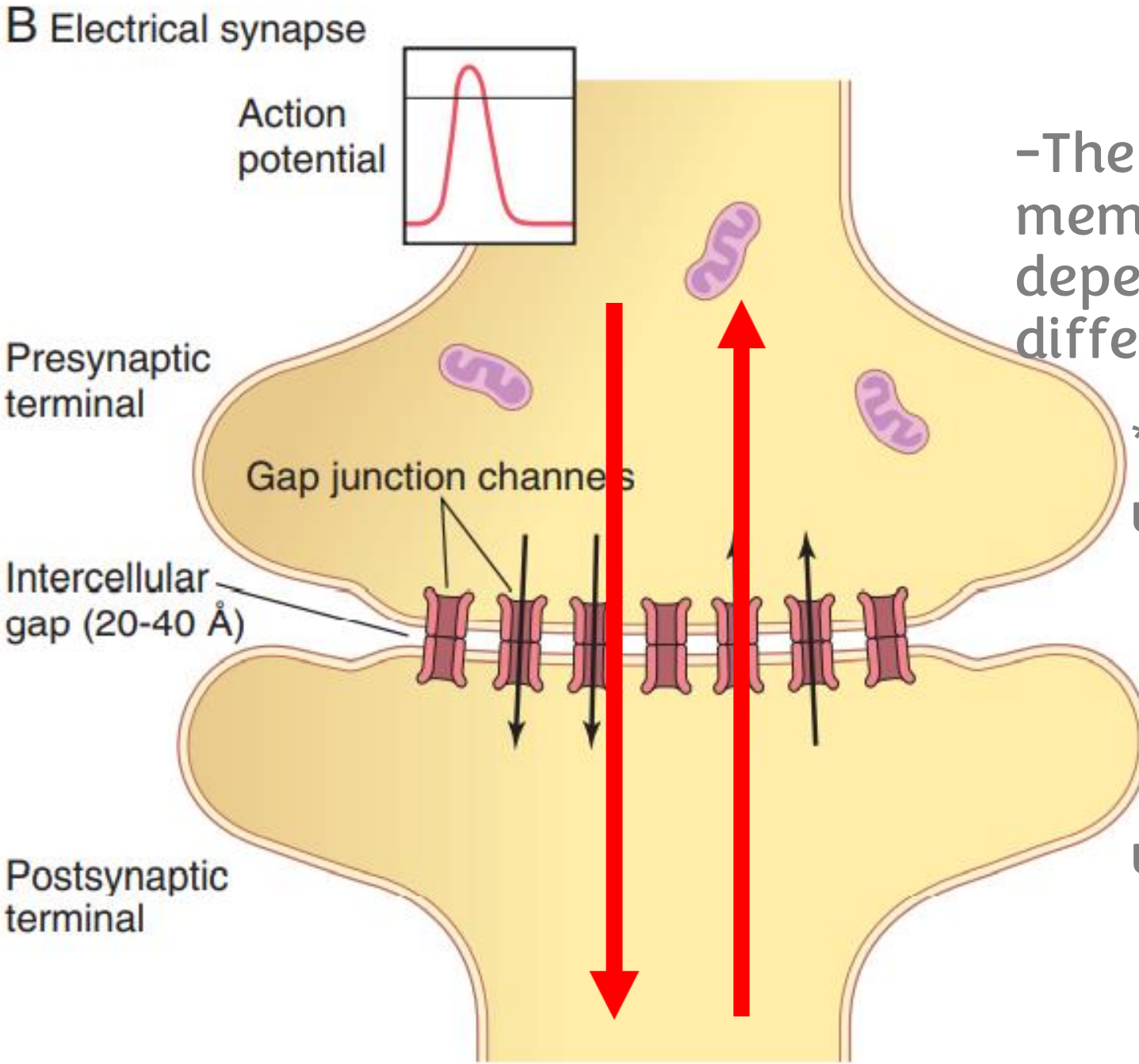
- The **cytoplasms of adjacent cells are directly connected by gap junctions** that allow free movement of ions between cells.
- Similar to the ones in <u>smooth muscles and cardiac muscles.</u>

Electrical synapses are not common in the nervous system
The body needs it when there is a necessity to transmit a certain nerve impulse simultaneously to several neurons or effector cells (such as cardiac muscle cells and smooth muscle cells).



Cytoplasms are directly connected by gap junctions

Specialized type of channels



-The movement of ions across the membrane can be **bidirectional** depending on the concentration difference.

*It can start either way from this neuron

.

.

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to this or the other way around.

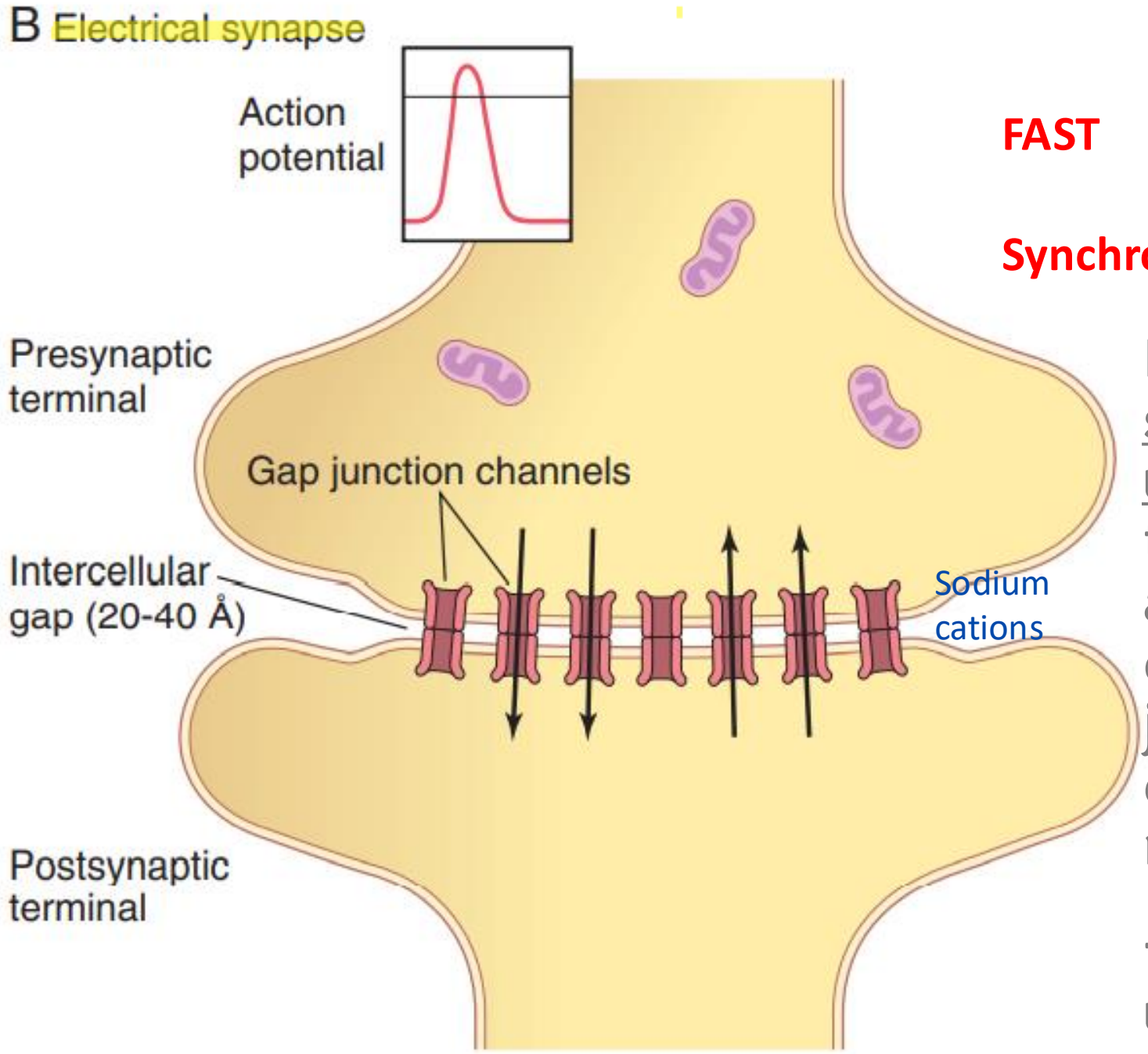
Bidirectional transmission of electrical synapses

Two main advantages:

- 1. **Faster communication**. Because action potentials conduct directly through gap junctions, electrical synapses are faster than chemical synapses.
- 2. **Synchronization**. (important characteristic)

Electrical synapses can synchronize (coordinate) the activity of a group of neurons or muscle fibers. As well as increasing neuronal sensitivity of connected neurons.

*Example: cardiac and smooth muscles



FAST

Synchronization

Electrical synapses act as **specialized communication units** where cells work together almost as one unit, as their cytoplasm is directly connected through gap junctions, allowing them to generate action potentials at nearly the same time.

-The signals are transferred very fast in a short time

Chemical synapses

-Action potential CAN NOT be transmitted directly from cell to the next (ions cannot flow directly).

*It's called chemical synaptic because the electrical energy will be converted into a chemical type of energy to transmit these signals, then it will be converted again in the postsynaptic neuron as electrical energy again.

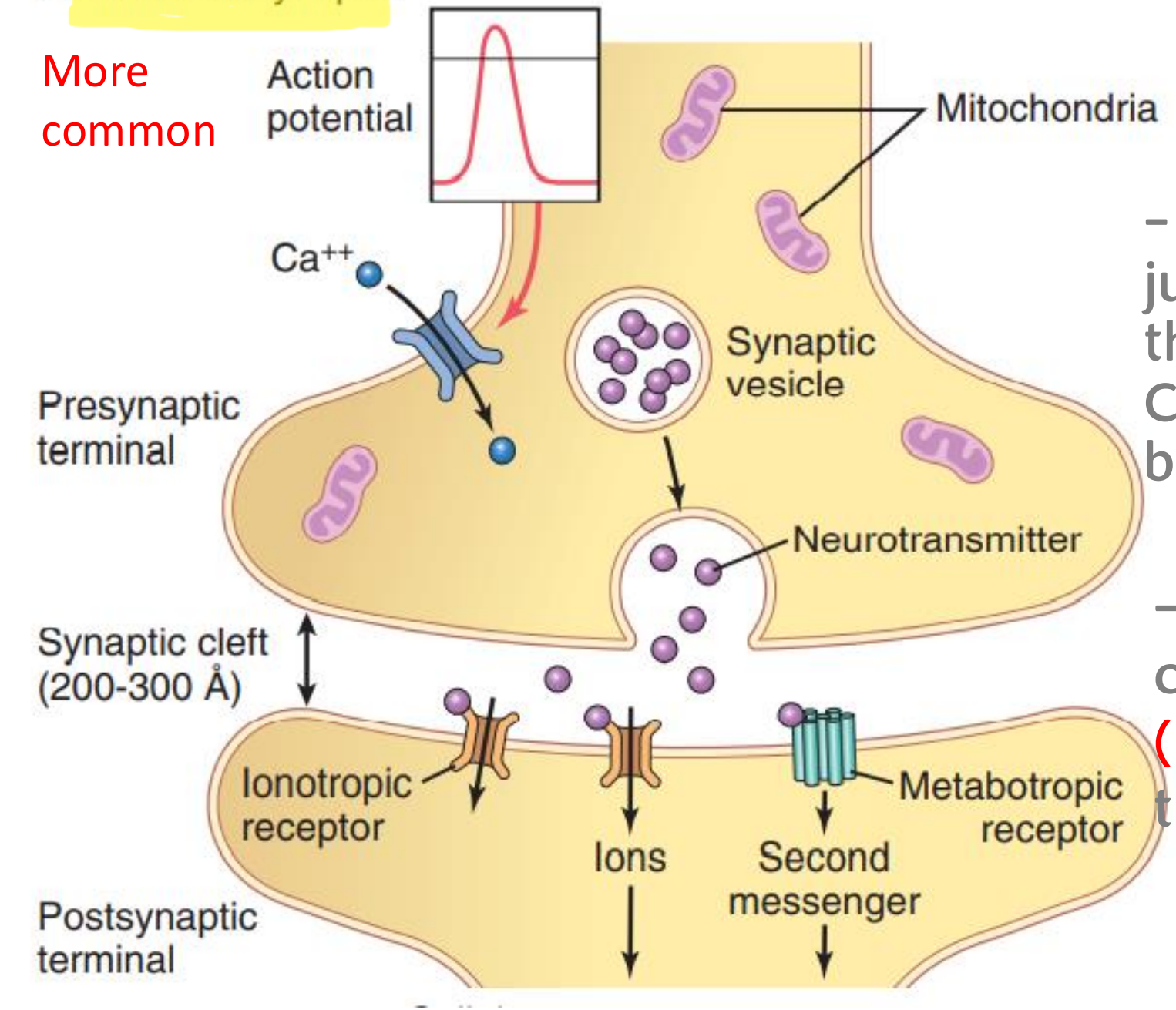
- **Most of the synapses** in the CNS are chemical synapses.
- The first neuron secretes at its nerve ending synapse a chemical substance called a **neurotransmitter.**

- Neurotransmitters are chemicals that are synthesized within the neurons and be transmitted FROM the presynaptic neurons

- Neurotransmitter acts on receptor proteins in the membrane of the next neuron **to excite the neuron, inhibit it, or modify its sensitivity in some other way**.

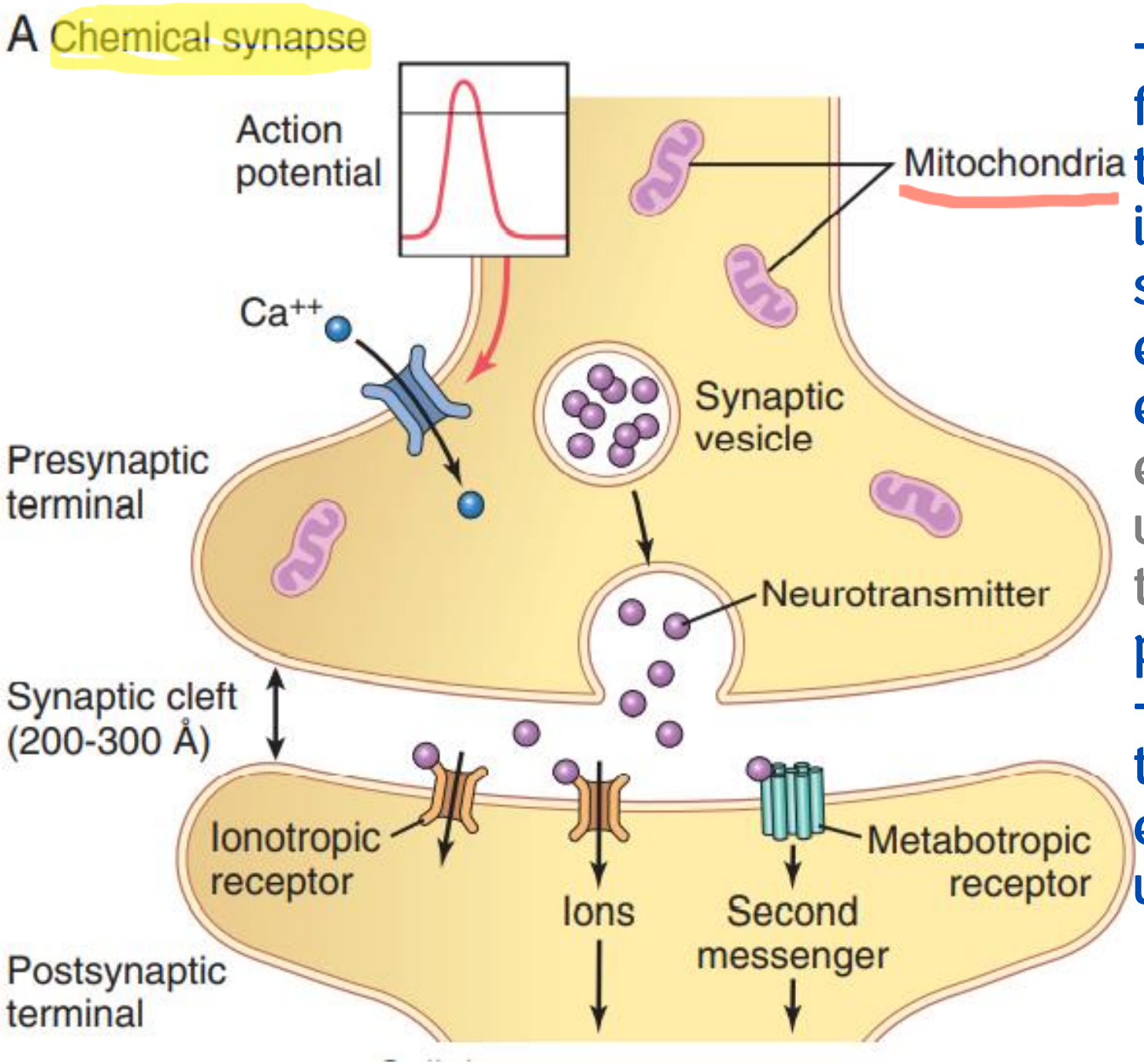
A Chemical synapse

More common



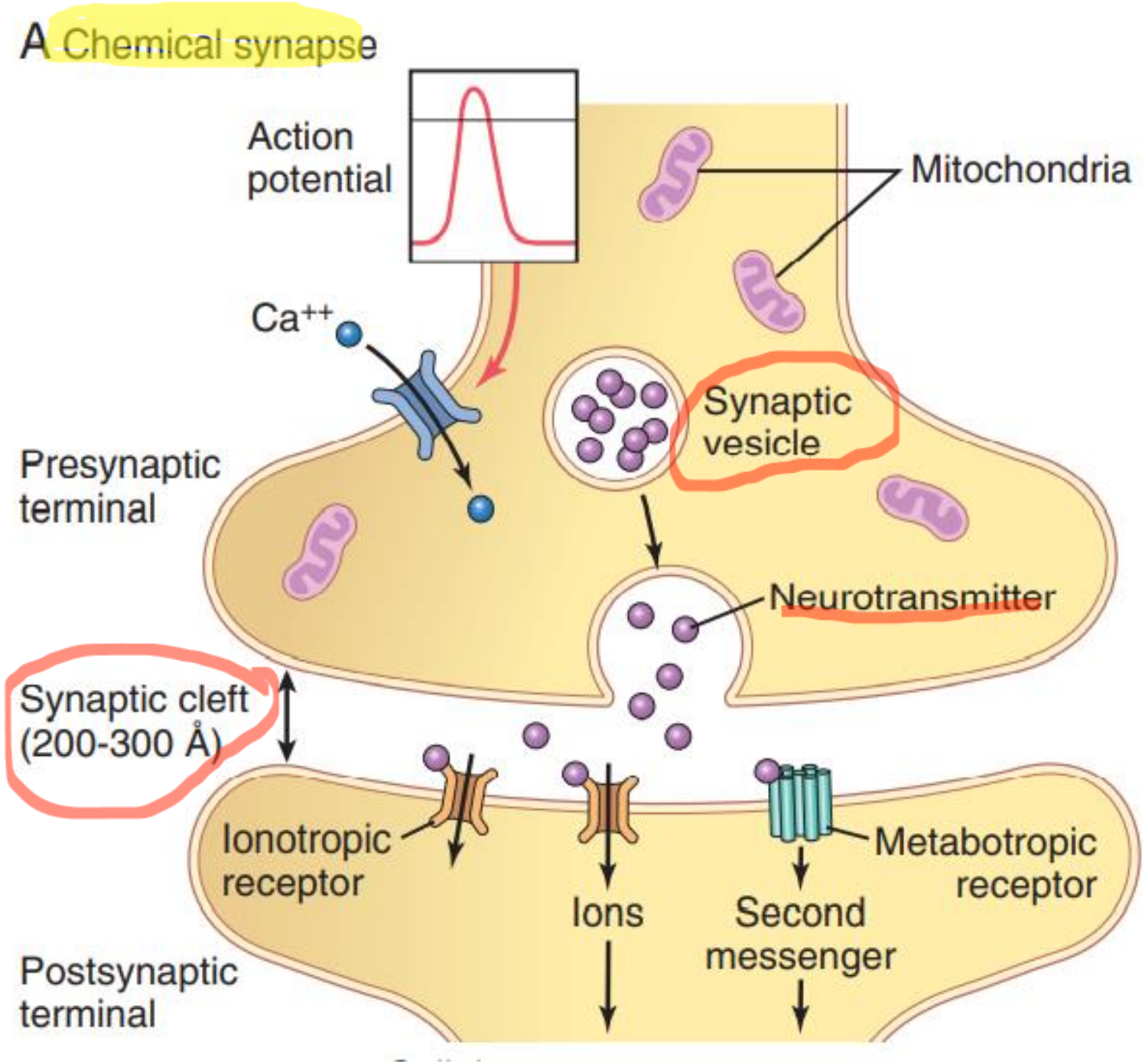
- There's no gap junctions here therefore no direct Communication between cells.

-The space between the cells is filled with fluid (ECF) which the signal pass through.



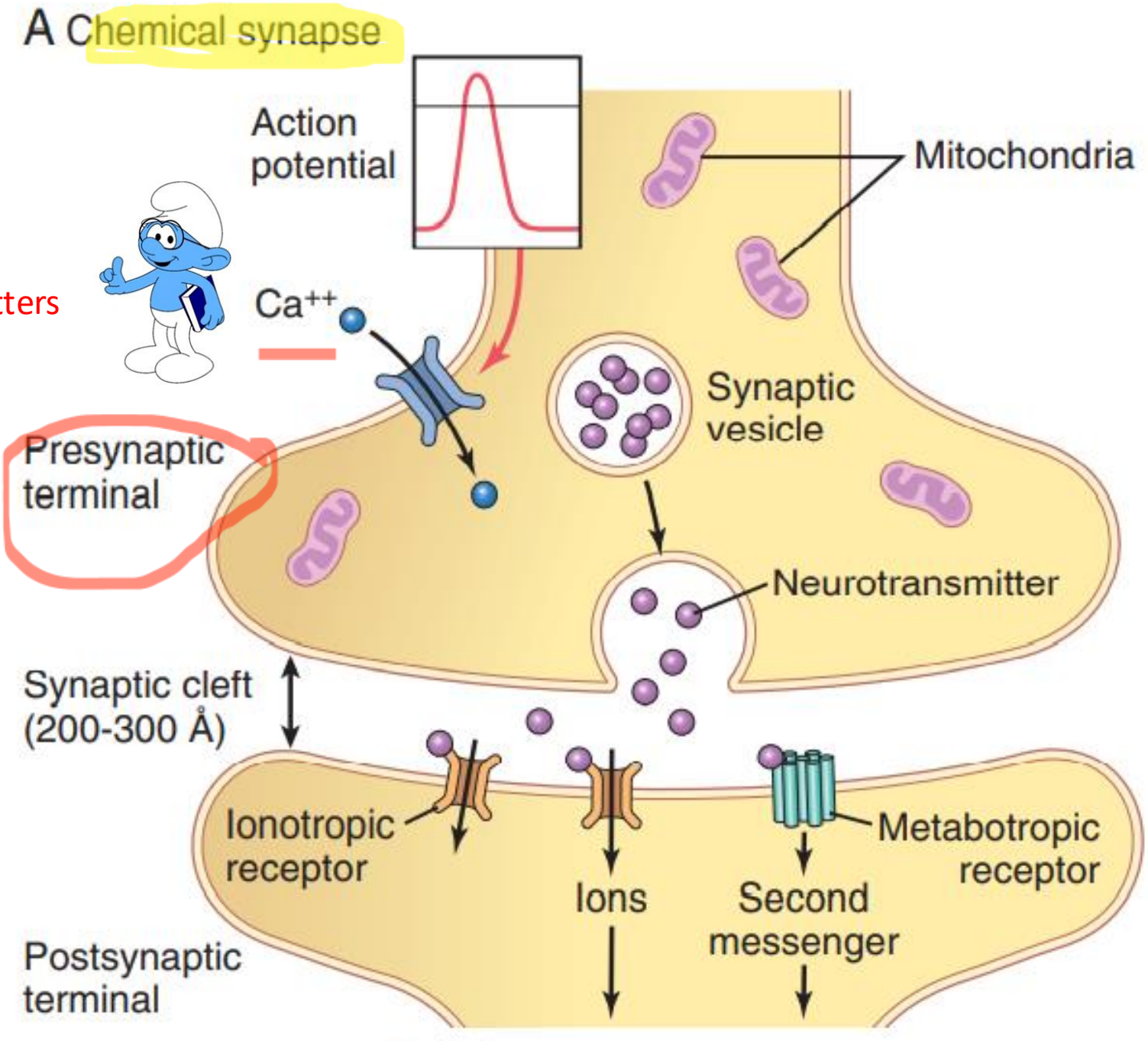
-Also, we need mitochondria for the process of exocytosis, the transmitters will be stored in a synaptic vesicles until a stimulus comes and allows exocytosis– which requires energy (specifically most of the energy is needed to move the vesicles along the cytoskeletal track) (it is **an Active** not a passive process).

-Furthermore, the synthesis of these neurotransmitters needs energy (endergonic process) so we need ATP.



Neurotransmitters can be stored anywhere else but **most** of them (**not all**) are stored within synaptic vesicles, so when action potential comes these chemicals will be released by the process of exocytosis into the synaptic cleft and then they will bind to specific receptors on the membrane of the postsynaptic neurons

More Ca++ → More Neurotransmitters exocytosis



Presynaptic terminals

- The terminal has two important internal structures:

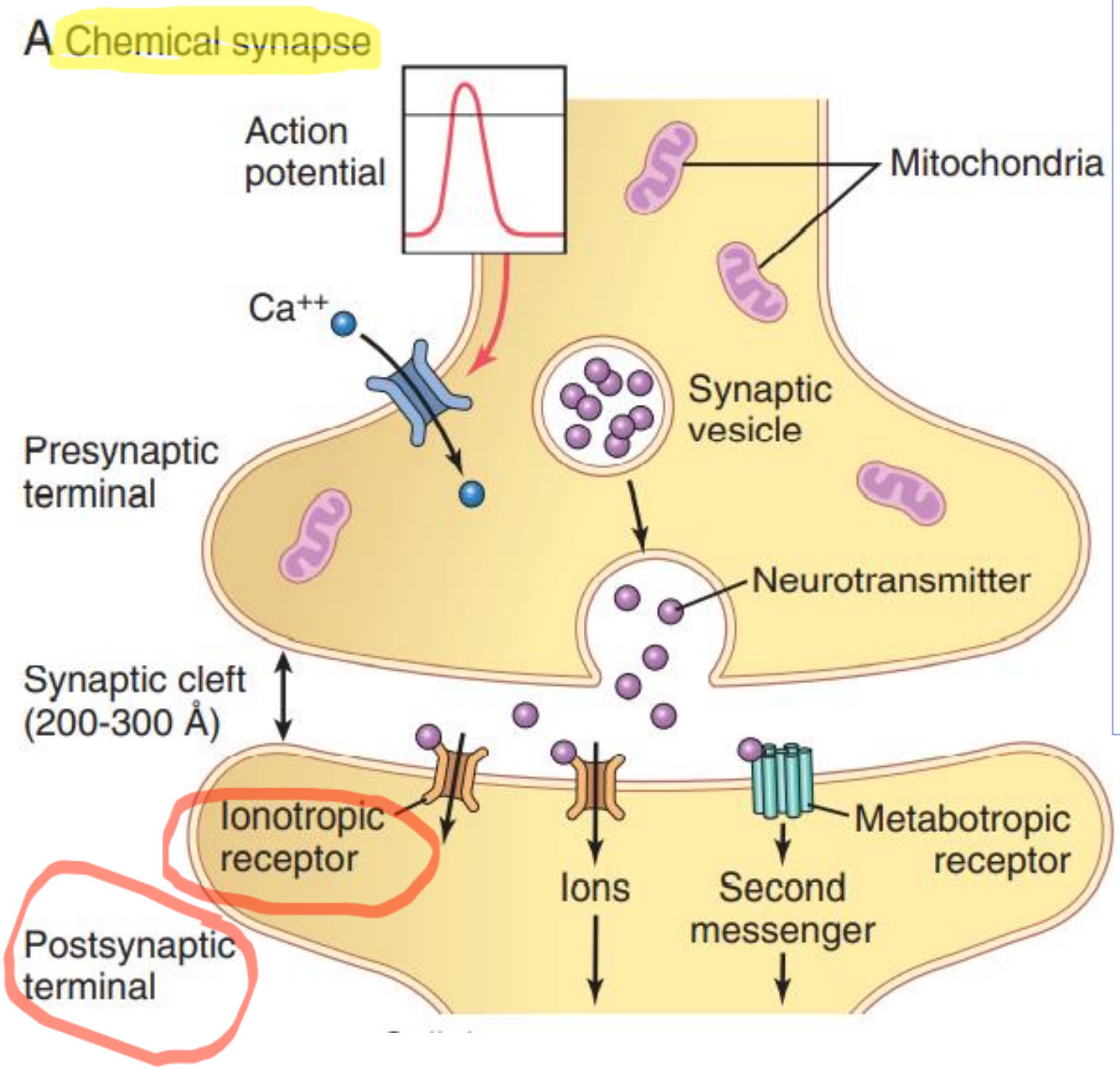
- The transmitter vesicles contain the neurotransmitter that, when released into the synaptic cleft, either excites or inhibits the postsynaptic neuron.

- The mitochondria provide adenosine triphosphate (ATP), which in turn supplies the energy for synthesizing new transmitter substance.

Presynaptic terminals

- The presynaptic membrane contains large numbers of **voltage-gated calcium channels**.

- When an action potential depolarizes the presynaptic membrane, these calcium channels open.
- The more influx of calcium → the more calcium concentrations inside these axon terminals → the more process of exocytosis → the more neurotransmitter to be released → the stronger the transmitted signal.
- The quantity of neurotransmitter that is released is directly related to the number of calcium ions that enter.



We have two types of specific receptors:

1) **Ionotropic receptor** are ligand-gated ion channels. When a neurotransmitter binds to a specific site on the receptor, the channel opens and allows ions to flow across the membrane.

This ion movement **(influx or efflux)** depends on the ion type and changes the postsynaptic membrane potential.

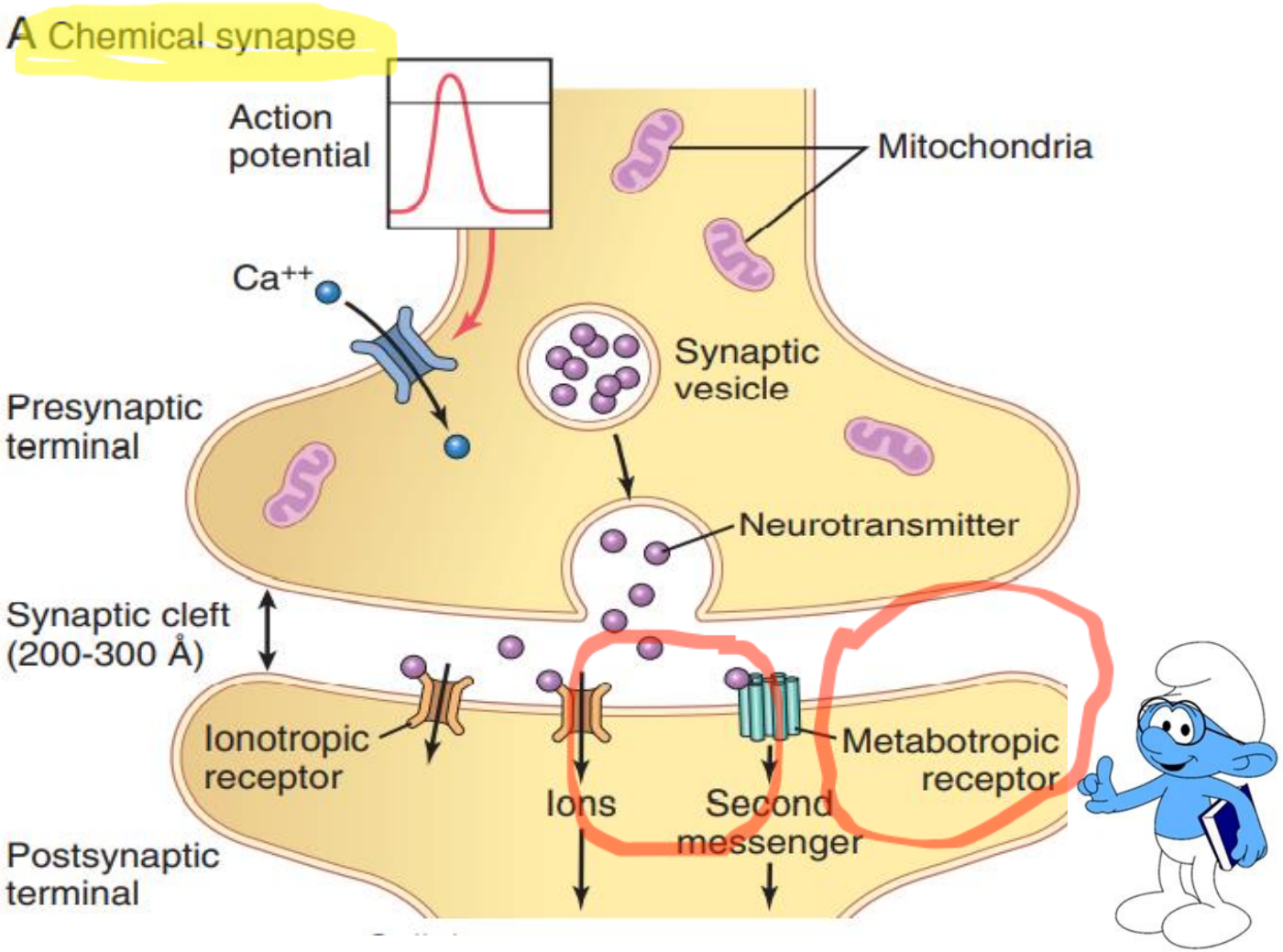
Ionic receptors act fast and for a short duration.

Ionotropic receptors can be cationic or anionic channels.

The effect may be:

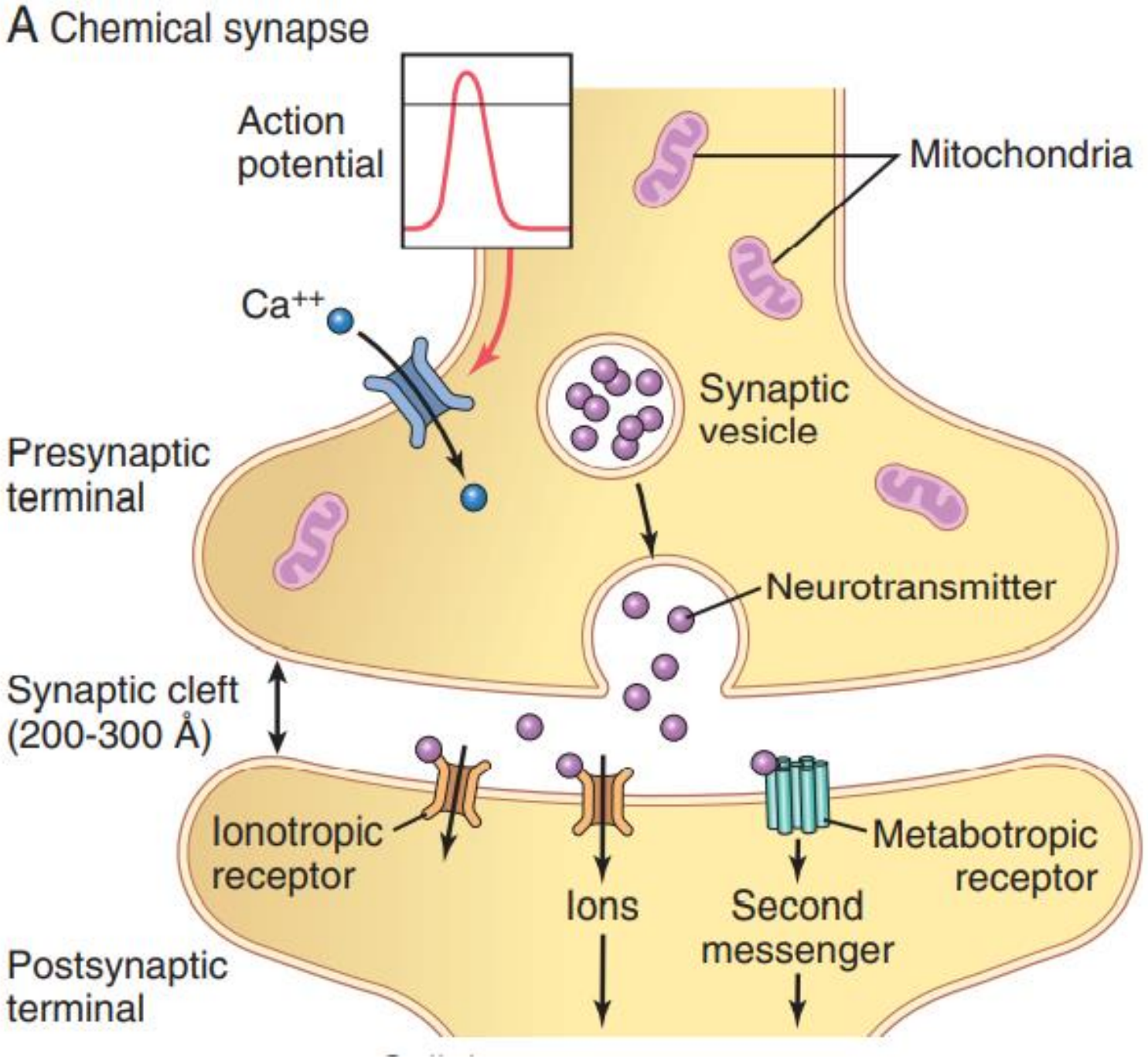
1) **Excitation** (depolarization) due to Na^+ influx

2) **Inhibition** (hyperpolarization) due to Cl^- influx or K^+ efflux.



2) **Metabotropic receptors** are the second type of receptors in the postsynaptic membrane. They work through a second messenger system such as G-protein-coupled receptors **(GPCRs).** Their action is slower, and longer time is required before ion channels are affected to change the membrane potential or before structural changes occur in the cell. However, their effect lasts longer and can produce prolonged actions, which are important for processes such as memory and thinking, and can contribute to long-term memory that may last for days, weeks, or even years.

The neurotransmitter should not remain in the synaptic cleft for a long time, so it is removed from the receptors by different mechanisms. Some neurotransmitters are broken down by specific enzymes (distract and bark it down) so they can no longer bind to receptors. Some diffuse out of the synaptic cleft, while others are taken back up (reuptake) into the presynaptic terminal to be reused or resynthesized.

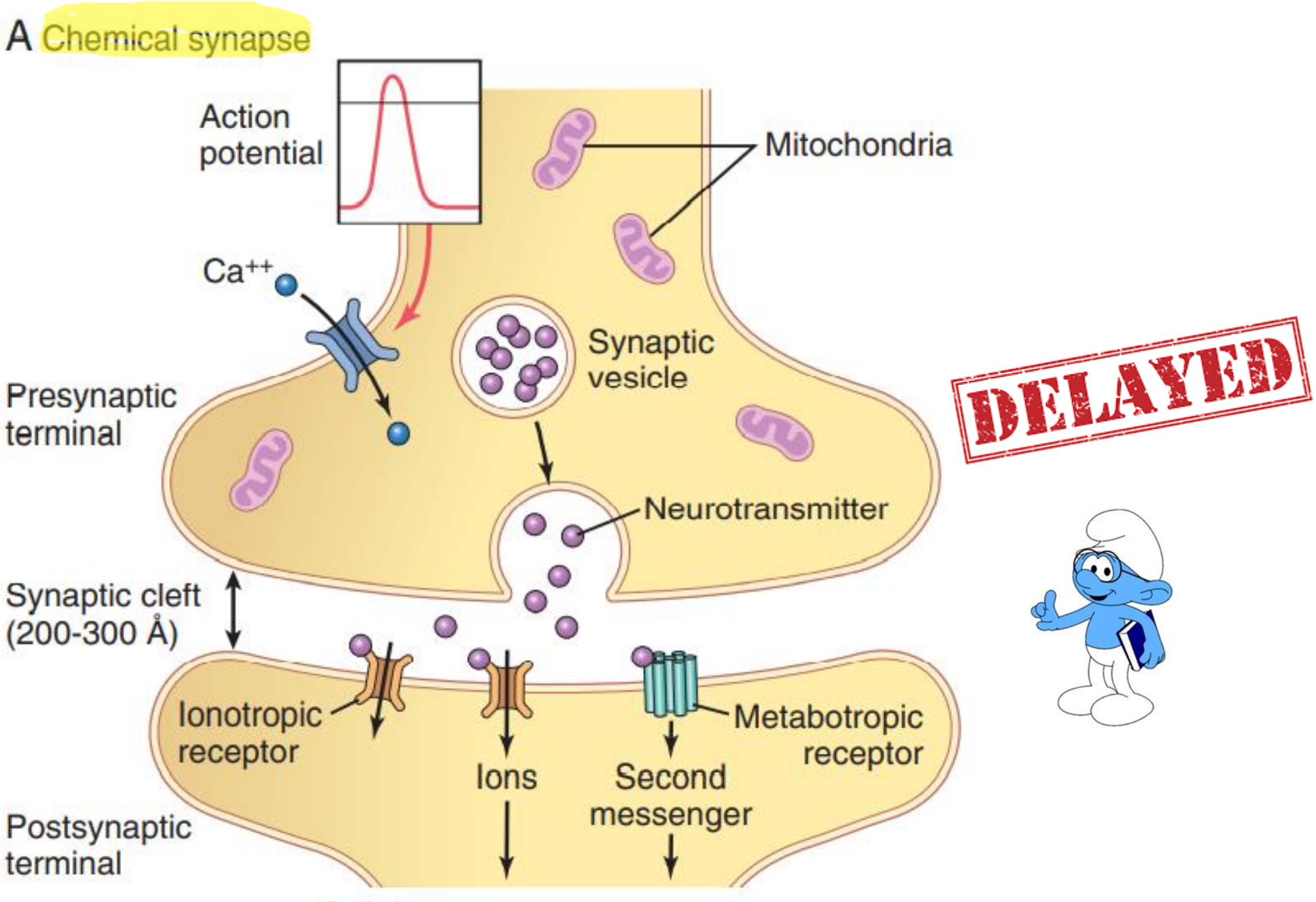


Principle of one-way conduction at chemical synapse

Principle of one-way conduction at chemical synapses

- **Always transmit the signals in one direction:** from the presynaptic neuron to the postsynaptic neuron.

- Allows signals to be directed toward specific goals and perform specific nervous functions.


A Chemical synapse
Action potential
Mitochondria
Ca++
Synaptic vesicle
Presynaptic terminal
Neurotransmitter
Synaptic cleft (200-300 Å)
Ionotropic receptor
Ions
Metabotropic receptor
Second messenger
Postsynaptic terminal
DELAYED

- Delayed of conduction of signal in(chemical synapse) or transmission of signal compared to electrical synapse ,
- Remember that electrical synapses there's almost instantaneous changes in the membrane potential between these cells because of presence of gap junctions and the very fast transmission of ions .
- However, in the chemical synapse when the action potential comes all the way from the axon to the axon termina. , there a steps need before development of an action potential in the post synaptic
- 1) Activate the voltage gated calcium channel
- 2) Calcium influx will induce exocytosis so the vesicles will transmit to membrane to fuse with it and release these neurotransmitter
- 3) Neurotransmitter will go away through synaptic cleft until they bind to specific site on specific receptor – then a response will be initiated such as opening of Ligand Gated Sodium Channels causing depolarization which transmit the action potential to the postsynaptic neuron. However, it might be the opposite response which is the activation of Voltage Gated Potassium Channels causing the efflux of Potassium ions outside the postsynaptic neurons making the interior of the postsynaptic neuron more negative due to the positive charge leaving the postsynaptic neuron, leading to hyperpolarization (more negative inside) moving away from the threshold, inhibiting the postsynaptic neuron from firing an action potential.

- **At the synapse, ligand gated sodium ion channels open in the postsynaptic membrance, not voltage gated ones.**
- Voltage gated sodium channels open when threshold is reached.

Synaptic delay

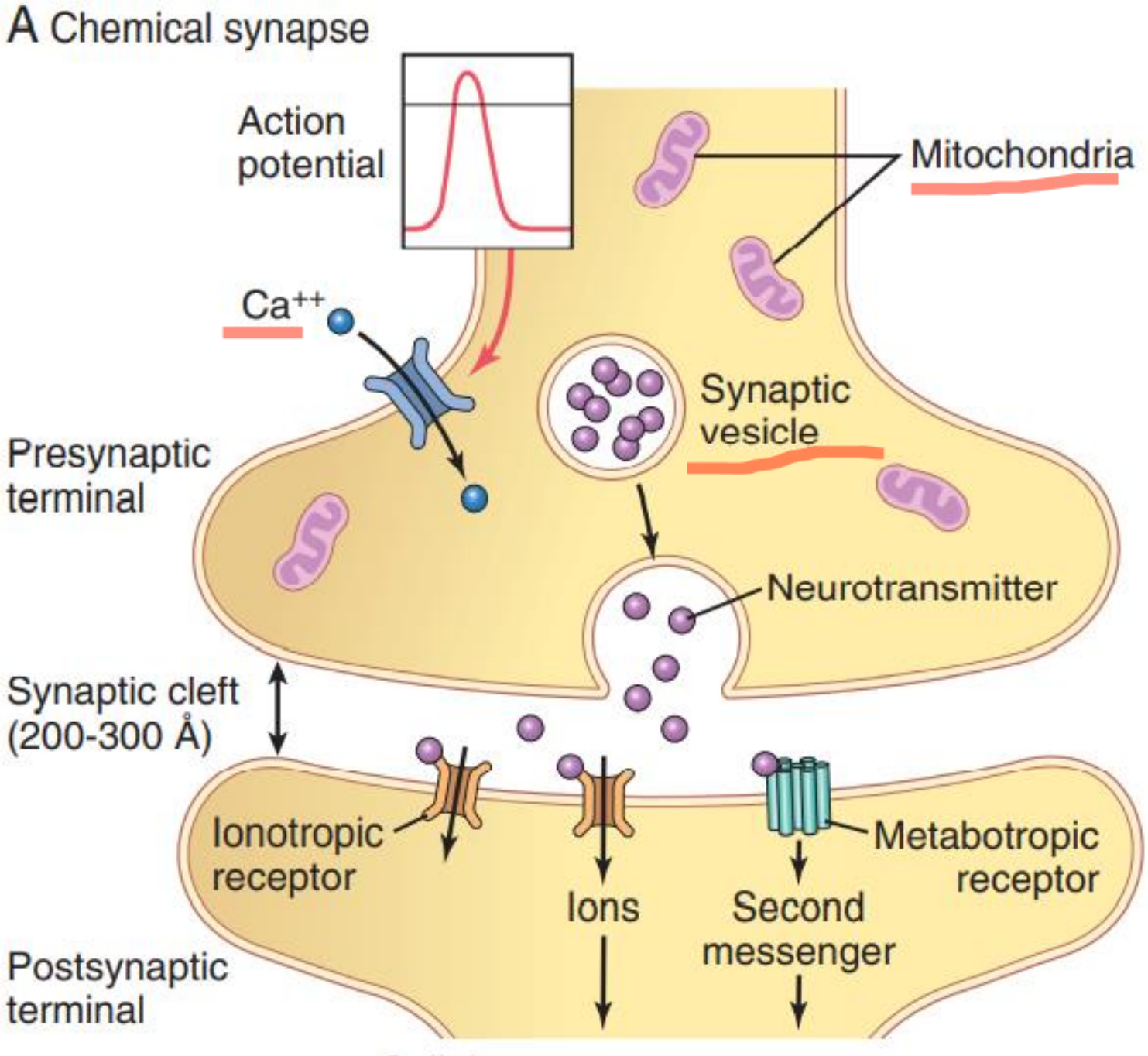
- During transmission of a neuronal signal from a presynaptic neuron to a postsynaptic neuron, a certain amount of time **(0.5 msec)** is consumed in the process of

- (1) discharge of the transmitter substance by the presynaptic terminal,

- (2) diffusion of the transmitter to the postsynaptic neuronal membrane,

Synaptic delay

- (3) action of the transmitter on the membrane receptor,
- (4) action of the receptor to increase the membrane permeability,
- (5) inward diffusion of sodium to raise the EPSP (Excitatory PostSynaptic Potential) (will be discussed later in details)to a high enough level to elicit an action potential.


A Chemical synapse
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Neurotransmitter
Synaptic cleft (200-300 Å)
Ionotropic receptor
Ions
Metabotropic receptor
Second messenger
Postsynaptic terminal

Postsynaptic neurons

- Receptor activation controls the opening of ion channels in the postsynaptic cell in one of two ways:

Both are slower than electric synapses

(1) by gating ion channels directly (Ionotropic receptors). Ionotropic receptors are ligand-gated ion channels. (relatively fast)

(2) by activating a second messenger (metabotropic receptors). -- mainly for prolonged effects such as prolonged excitation or prolonged inhibition. E.g. (Memory) (slower)

Excitation of postsynaptic neuron

- Opening of sodium channels. (Ionotropic)

- Changes in the internal metabolism of the postsynaptic neuron to excite cell activity or to increase the number of excitatory membrane receptors or decrease the number of inhibitory membrane receptors. (Metabotropic)

Inhibition of postsynaptic neuron

- Opening of chloride ion channels through the postsynaptic neuronal membrane. (Ionotropic)
- Increase in conductance of potassium ions out of the neuron. (Ionotropic)
- Activation of receptor enzymes that inhibit cellular metabolic functions or that increase the number of inhibitory synaptic receptors or decrease the number of excitatory receptors. (Metabotropic)

Second-messenger system

- Many functions of the nervous system—for instance, the process of memory—require prolonged changes in neurons for seconds to months after the initial transmitter substance is gone.

- The ion channels are not suitable for causing prolonged postsynaptic neuronal changes because these channels close within milliseconds after the transmitter substance is no longer present.

Second-messenger system

- However, in many instances, **prolonged** postsynaptic neuronal excitation or inhibition is achieved by activating a “second messenger” chemical system inside the postsynaptic neuronal cell itself, and then it is the **second messenger that causes the prolonged effect.**

Questions:

Q1: Which of the following is not true about chemical synapses?

A) Unidirectional

B) It requires active transport during the transmission of nerve impulse to the post synaptic neuron

C) relatively fast

D) It requires passive transport during the transmission of nerve impulse to the post synaptic neuron

E) More common than electrical synapses

Ans: C

D is true because it requires diffusion of the neurotransmitters in the synaptic cleft to reach its receptors on the post synaptic neuron's membrane

Q2: Voltage gated Ca++ channels are present on the membrane of post-synaptic neuron

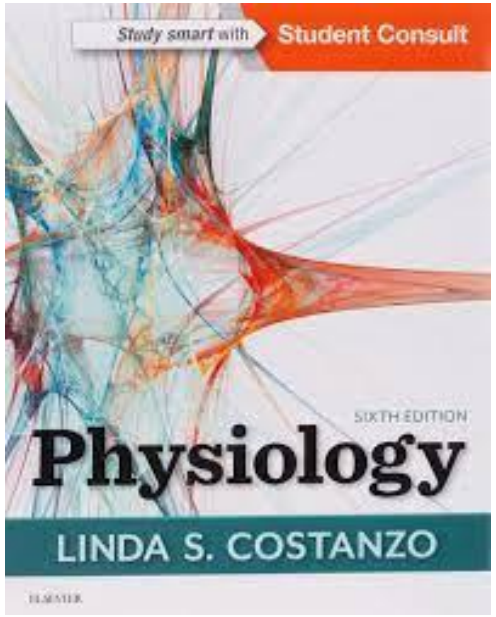
A)True

B)False

Ans: B

Presynaptic neuron not postsynaptic

References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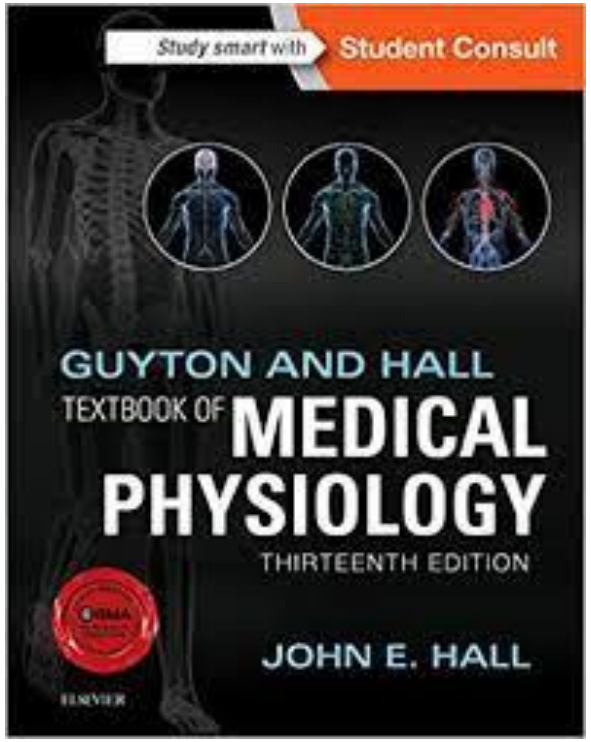
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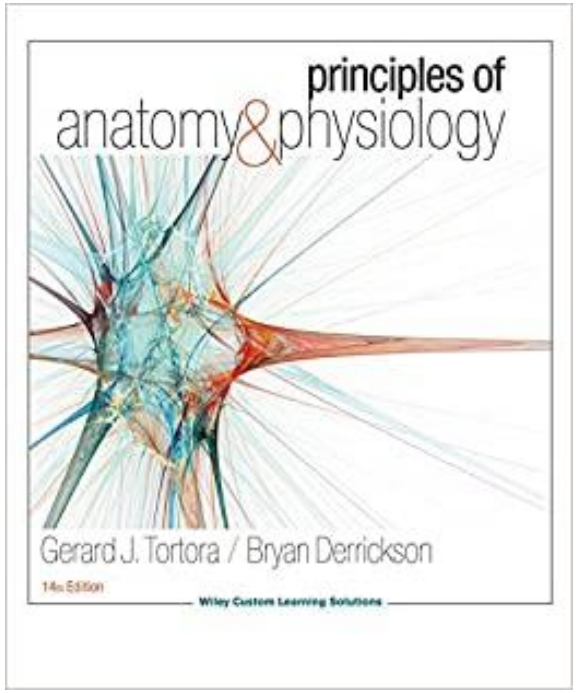
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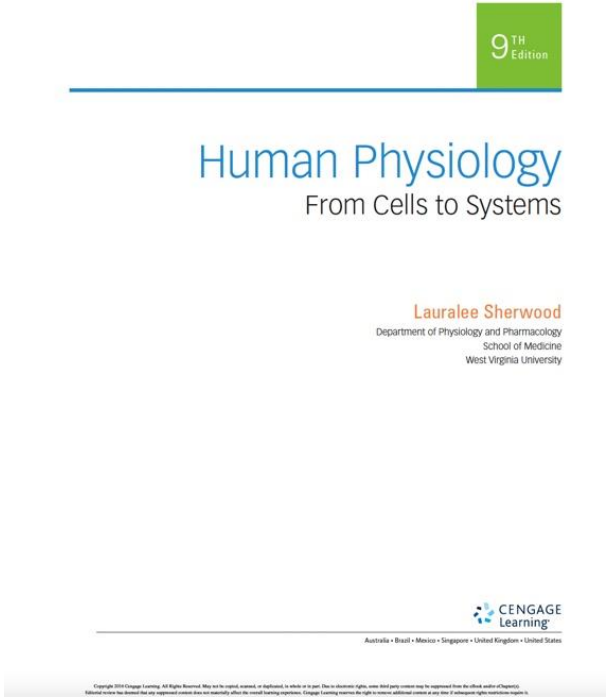
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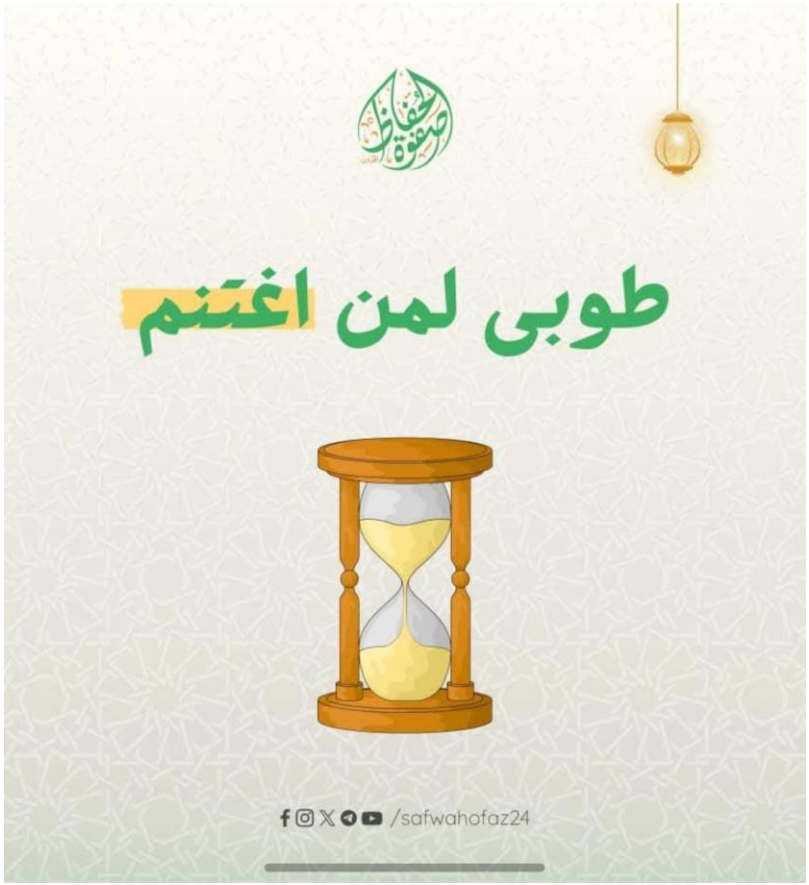

تنقضي أيام الشهر وتنقضي أيام العمر معها

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